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Formulation and Evaluation of Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate *In-situ* Ocular Gel

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ABSTRACT: The objective of our research was to create an ocular gel comprising Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate in order to enhance its bioavailability when applied to the surface of the eye. An in-situ ocular gel was created using a temperature-sensitive gelling agent called Kolliphor 407, along with a viscosity building polymer known as HPMC K100. The selection of polymer quantities was based on the optimal amount needed for the prolonged release of the medication from the preparation. This was determined by consulting relevant literature and conducting a comprehensive investigation with varying amounts. The temperature-triggered in-situ ocular gel was prepared using Kolliphor 407 and HPMC K100 polymer. The evaluation of all formulations included assessments of their appearance, pH levels, viscosity at various pH levels, gelling capacity, percentage of drug content, and release research. 3^2 factorial designs were used to successfully prepare and optimize nine formulations. The optimization process was performed using DoE software, namely Version 13.0.10.064. Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate were effectively synthesized in a temperature-triggered in-situ gelling system employing Kolliphor 407 in combination with HPMC K100. The significance of HPMC K100 and Kolliphor 407 in the in-situ gel behavior is witnessed based on primary influence of the concentration of HPMC K100 and Kolliphor 407. The *in-vitro* findings suggest that the in-situ gel system can effectively replace traditional ocular drops due to its capacity to provide a continuous delivery of medication.

Keywords: Kolliphor 407, HPMC, temperature trigged *in-situ* ocular gel and bioavailability.

INTRODUCTION

Moxifloxacin hydrochloride is an antibiotic that inhibits bacterial DNA replication, resulting in the eradication and cessation of bacterial infection proliferation. Dexamethasone Sodium Phosphate is a corticosteroid that mitigates inflammation and related symptoms of infection, such as redness and irritation, by reducing the production of prostaglandins, which are natural substances that induce inflammation. By combining Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate, the spread of redness, allergies, inflammation, and bacterial infection in the eyes is effectively prevented (Li *et al*., 2018a,b; Morsi *et al*., 2017; Saxena and Patil, 2014; Sharma *et al*., 2012).

Ophthalmic solutions are hindered by the drawback of inadequate achievement and preservation of the ideal drug concentration at the targeted area within the eye. This is caused by the fast dilution during application and subsequent removal. The challenges can be resolved through the application of eye ointments and gels. However, the limited ease of administration and the occurrence of blurred vision restrict their usage and lead to inadequate patient adherence (Makwana *et al*., 2016; Morsi *et al*., 2016; Patil *et al*., 2015; Reena *et al*., 2022; Suresh *et al*., 2022).

The issue of rapid loss of dosage form at the site of application can be resolved by developing the medicine as a formulation that quickly forms a gel following ocular administration. Gelation occurs after instillation because of physico-chemical changes resulting from the eye's physiological features. This would enhance the duration of the drug's presence on surface of cornea, potentially leading to an enhancement in drug's capacity to be absorbed by the body (Danilo *et al*., 2014; Geethalakshmia *et al*., 2013).

MATERIALS AND METHODS

Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate were obtained as a complimentary sample from Celogen pharma Pvt Ltd., located in Mumbai, Maharastra. The chemicals used in the experiment, including Kolliphor 407 (BASF), HPMC K100 (DuPont), deionized water (In-house), and other solvents, were of high purity and met the analytical grade/IP/BP/USP equivalent standards available in the laboratory.

Formulation development of Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate temperature trigged *in-situ* Ocular gel

Preparation of Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate *in-situ* ocular gel. The process involved dissolving Hypromellose K100 in filtered water, followed by gradual addition of Kolliphor 407 to solution while continuously stirring at a temperature ranging from 10 to 20°C.

Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate were separately dissolved in purified water, each accounting for 10% of the total volume. The resulting solutions were then combined with a polymeric solution while continuously stirring. Benzalkonium chloride was dissolved in a small quantity of pure water and added prior to reaching desired volume, which was achieved by adding more pure water.

The current research will utilize a complete 3^2 factorial design to investigate the impact of two crucial variables: Kolliphor 407 (X1) and HPMC K100 (X2), at three different levels of concentration. All variables and their levels are displayed in Table 1. Nine formulations will be prepared in total, resulting from the multiplication of three by three (3x3=9). The table 2 presents the composition of the formulations for Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate temperature-triggered in-situ ocular gels, using a full factorial design.

Table 1: Variables and their levels for preparing Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate temperature trigged *in-situ* ocular gels.

Levels / Factors	Low(-1)	Medium(0)	High(+1)
Kolliphor 407 (X1)	12.0	14.0	16.0
HPMC K100 (X2)	0.40	0.50	0.60

Table 2: Full 3^2 factorial design for the preparation of Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate temperature trigged *in-situ* ocular gels.

Batch Code / Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Moxifloxacin Hydrochloride (g)	0.545	0.545	0.545	0.545	0.545	0.545	0.545	0.545	0.545
Dexamethasone Sodium Phosphate	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13
Kolliphor 407	**12.0**	**14.0**	**16.0**	**12.0**	**14.0**	**16.0**	**12.0**	**14.0**	**16.0**
Hypromellose K100 (g)	**0.40**	**0.40**	**0.40**	**0.50**	**0.50**	**0.50**	**0.60**	**0.60**	**0.60**
Benzalkonium chloride (g)	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Purified water q.s.	100	100	100	100	100	100	100	100	100

Evaluation of the Prepared Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate *In-Situ* Ocular Gels

Physical examination. The prepared Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate *in-situ* ocular gels were evaluated visually for their color as well as homogeneity (Buchan *et al*., 2010; Gupta *et al*., 2007; Kumar *et al*., 2016; Yadav *et al*., 2011; Nanjawade, 2007).

Measurement of pH. pH of in-situ ocular gel was measured by a digital pH meter (Ludwig, 2005).

Rheological studies using Brookfield viscometer. Viscosity of Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate in-situ ocular gel was assessed utilizing a Brookfield viscometer with spindle 62. The formulations were let to stand at a temperature of 20°C for an hour for evaluation. The spindle was put vertically into the beaker, ensuring that it did not make contact with the bottom.

The viscosity was determined at rotational speeds of 5, 10, 20, and 50 revolutions per minute (rpm). Three readings, obtained at distinct places, were averaged. Viscosity of formulations was assessed at two different temperatures: 20°C and 36°C. Temperature of compositions was adjusted from 20°C to 36°C using a computerized water bath equipped with temperature control (Khan *et al*., 2015; Nagarwal *et al*., 2009; Yu *et al*., 2017).

Gelation temperature determination of the prepared in-situ gels. Gelation temperature of prepared *in-situ* gels was determined by temperature increases by digital water bath. 10 ml of formulation was taken in a test tube and warmed up to 36˚C (Gupta *et al*., 2007; Kumar *et al*., 2016; Yadav *et al*., 2011; Nanjawade 2007; Ludwig 2005; Khan *et al*., 2015; Nagarwal *et al*., 2009; Yu *et al*., 2017; Preis *et al*., 2015; Sharma *et al*., 2014).

Drug content determination. A volume of 1 ml (measured by weight) of the formulation was extracted and subsequently mixed with Methanol to obtain a final volume of 100 ml. A 5 ml portion was extracted and subsequently diluted to a volume of 100 ml using methanol. The concentrations of Moxifloxacin hydrochloride and Dexamethasone Sodium Phosphate were measured using HPLC (Douroumis *et al*., 2011; Patro *et al*., 2011).

***In-vitro* drug release studies.** *In-vitro* release tests were conducted on six units utilizing a Dissolution Apparatus (12 Units, DS14000 Smart with Auto Sampler). The temperature was set to 36±0.2˚C in order to replicate the ocular surface temperature. A plastic tube with open ends was chosen and one end was sealed using a dialysis membrane (which had been soaked in phosphate buffer saline at pH 7.4 for 24 hours prior to usage). 2 grams of each formulation were inserted into the plastic tube from the opposite end. Tubes were affixed to the paddle of dissolution apparatus in a

manner that ensured that tube was fully submerged in the reservoir. Paddle was rotated at a speed of 50 revolutions per minute in a 250 milliliter (ml) solution of phosphate buffer saline with a pH of 7.4. Samples of 5 ml were taken at specific time intervals of 15, 30, 45, 60, 120, 180, 240, and 300 minutes. A new medium was used to maintain a consistent volume. Samples underwent analysis using HPLC in order to ascertain the percentage of release (Ludwig, 2005; Daphal *et al*., (2012); Patil & Rokade, 2013).

Kinetic treatment of release data

Dissolution data of drug passage in solution was analyzed using various release models as given below:

- zero-order (plotting cumulative % of drug released against time)
- first-order (plotting logarithm of cumulative % of drug release against time)
- Higuchi's (plotting cumulative % of drug released against square root of time)
- Hixson Crowell's (plotting cube root of % of drug unreleased against time)
- Korsmeyer's Peppas (plotting fraction of drug release against time)

The kinetic constant (k) and diffusional release exponent (n) were calculated using the formula provided by Korsmeyer and Peppas (Khan *et al*., 2015).

RESULTS AND DISCUSSION

Figure 1 displays an image of prepared formulation.

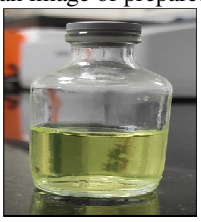

Fig. 1. Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate *in-situ* ocular gel.

Physical appearance of manufactured Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate in-situ gels was assessed, revealing that the formulations were yellow, transparent, clear, and homogeneous. Table 3 displays the results.

Table 3: Physical examination of the Prepared Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate *in-situ* ocular gels.

Formulation	Color	Homogeneity
F1	Yellow and Transparent	Homogenous
F2		
F3		
F4		
F5		
F6		
F7		
F8		
F9		

The pH of the prepared Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate *in-situ* gels was found to be between 6 to 7, which is suitable for application in eye. Outcomes are given in Table 4.

Table 4: pH of prepared Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate *in-situ* ocular gels.

Formulation	pH
F1	6.51±0.07
F2	6.32±0.03
F3	6.71±0.06
F4	6.53±0.04
F5	6.23±0.06
F6	6.50±0.05
F7	6.41±0.04
F8	6.46±0.05
F9	6.43±0.08

(Results: mean±SD, n=3)

The viscosity of Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate in-situ ocular gels was assessed at various revolutions per minute (rpm). The findings are displayed in Table 5 and 6, as well as Figs. 2 and 3. The study revealed a direct linear relationship between the concentration of the viscosity enhancer, Hypromellose K100, and viscosity of formulations. The viscosity of the formulations exhibited a non-linear increase with higher concentrations of the gelling ingredient, Kolliphor 407. Additionally, it was discovered that the viscosity of the formulations significantly rose as the temperature of the formulations increased.

An observed phenomenon known as shear thinning occurred, where the viscosity decreased as the shear rate increased from 5 to 50 rpm. In-situ gel formulations that were created demonstrated shear thinning behavior, as viscosity dropped as shear rate increased. As shear stress is heightened, disorganized molecules align themselves in a specific pattern, resulting in a decrease in resistance to flow, also known as viscosity. This is advantageous because the surface of the eye experiences significant shear rates during the act of blinking and lower shear rates in the intervals between blinks.

Table 5: Viscosity of prepared *in-situ* gels at temperature 20°C.

RPM	5	10	20	50
F1	332.62 ±1.21	245.85±1.43	147.96±1.49	105.95±1.29
F2	410.52±1.93	291.63±1.42	184.62±1.42	133.85±1.93
F3	655.82±1.81	536.86±1.29	344.36±1.98	185.96±1.05
F4	405.62±1.25	326.35±1.93	251.76±1.76	144.13±1.77
F5	533.94 ±1.96	456.63±1.59	311.25±1.63	181.79±2.28
F6	750.69±1.15	588.36±2.61	431.96±1.54	233.79±1.86
F7	455.94±1.93	383.24±1.21	284.68±1.71	199.45±1.33
F8	597.25±1.54	424.96±1.92	318.22±1.29	289.25±1.06
F9	890.51±2.63	632.96±2.32	473.76±1.25	305.85±1.96

*Viscosity unit- cps (Results: mean±SD, n=6)

Table 6: Viscosity of prepared *in-situ* gels at temperature 36°C.

RPM	5	10	20	50
F1	1451.11±1.31	1382.52±2.11	901.75± 1.88	492.22± 1.75
F2	1720.52± 1.62	1444.25± 2.62	1170.38± 1.37	685.91± 1.32
F3	5121.15± 1.45	3840.29± 1.95	2751.94± 1.29	2015.35±1.34
F4	2032.32± 1.63	1333.63± 1.95	1111.38± 1.39	712.76± 1.12
F5	3024.74± 1.39	2143.18± 1.63	1525.33±1.32	833.62± 1.32
F6	6514.33± 1.69	5422.72± 1.87	3815.95±1.44	2428.23± 1.22
F7	3840.27± 1.73	3011.51± 1.85	1833.75± 1.25	1085.84± 1.13
F8	4732.15± 1.01	3366.63± 1.75	2426.85± 1.95	1254.95± 1.32
F9	7495.34± 1.98	5752.61±1.45	4133.52± 1.75	2801.76± 1.28

*Viscosity unit- cps (Results: mean±SD, n=6)

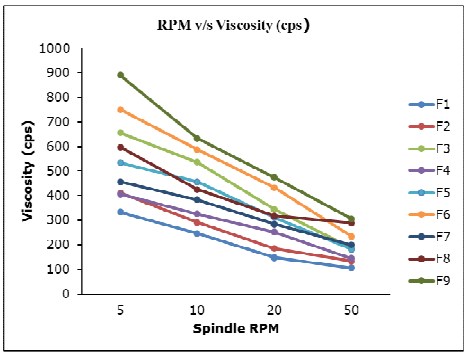

Fig. 2. Effect of rpm on viscosity of prepared Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate *in-situ* ocular gel at 20°C temperature.

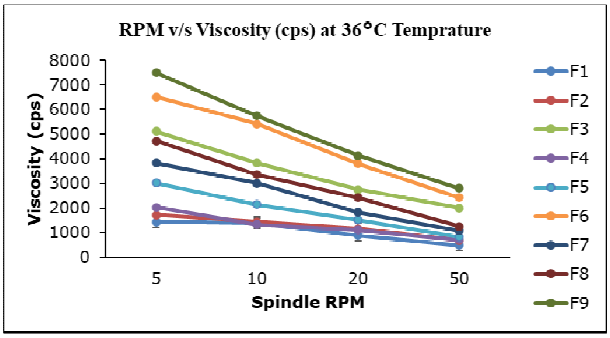

Fig. 3. Effect of rpm on viscosity of prepared Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate *in-situ* ocular gel at 36°C temperature.

The average effect of varied concentrations of Hypromellose K100 and Kolliphor 407 on the viscosity of the prepared Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate and *in-situ* ocular gels at 20°C temperature is displayed in Table 7 and Figs. 4 and 5.

Table 7: Average effect of varied concentrations of Hypromellose K100 and Kolliphor 407 at 20°C temperature.

Name of Polymer	Concentration of Polymer	Formula for Calculation of Average effect	Calculation of Average effect	Average effect (cps)
Kolliphor 407	12.0	(F1+F4+F7)/3	(147.96+251.76+ 284.68)/3	228.13
	14.0	(F2+F5+F8)/3	(184.62+311.25 + 318.22)/3	271.36
	16.0	(F3+F6+F9)/3	(344.36+431.96+ 473.76)/3	416.69
Hypromellose K100	0.40	(F1+F2+F3)/3	(147.96+184.62 + 344.36)/3	225.64
	0.50	(F4+F5+F6)/3	(251.76+311.25 +431.96)/3	331.65
	0.60	(F7+F8+F9)/3	(284.68+318.22+ 473.76)/3	358.88

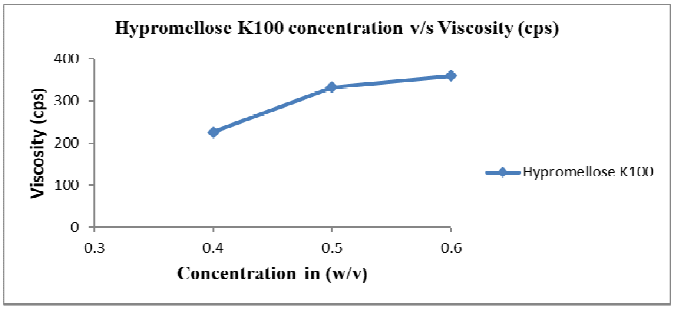

Fig. 4. Average effect of varied concentrations of Hypromellose K100 at 20°C temperature.

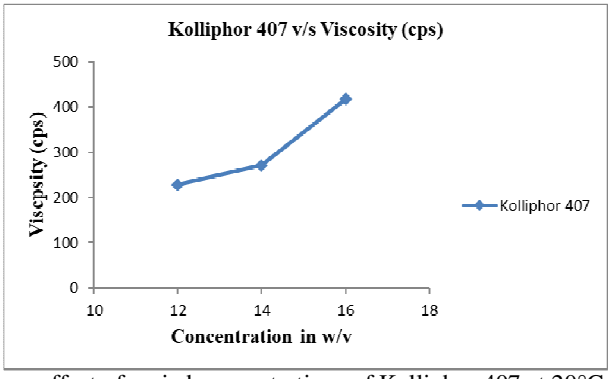

Fig. 5. Average effect of varied concentrations of Kolliphor 407 at 20°C temperature.

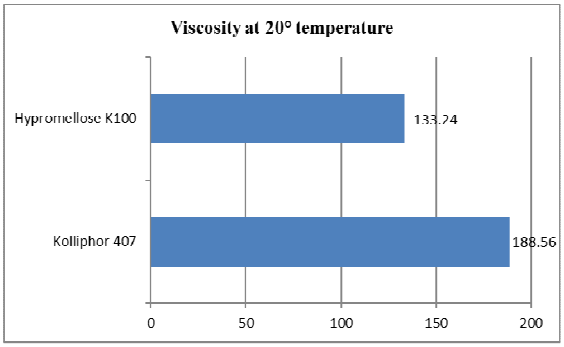

Fig. 6. Main effect of concentration of Hypromellose K100 and Kolliphor 407 on Viscosity at 20°C temperature.

The average effect of varied concentrations of Hypromellose K100 and Kolliphor 407 on the viscosity of the prepared Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate *in-situ* ocular gels at 36°C temperature at 20 rpm is shown in Table 8 and Figs. 7 and 8

Table 8: Average effect of varied concentrations of and Kolliphor 407 and on the viscosity of the prepared Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate *in-situ* ocular gels at 36°C temperature at 20 rpm.

Name of Polymer	Concentration of Polymer	Formula for Calculation of Average effect	Calculation of Average effect	Average effect (cps)
Kolliphor 407	12.0	(F1+F4+F7)/3	(901.75+1111.38+ 1833.75)/3	1282.29
	14.0	(F2+F5+F8)/3	(1170.38+1525.33 + 2426.85)/3	1707.52
	16.0	(F3+F6+F9)/3	(2751.94+3815.95+ 4133.52)/3	3567.13
Hypromellose K100	0.40	(F1+F2+F3)/3	(901.75+1170.38+ 2751.94)/3	1608.02
	0.50	(F4+F5+F6)/3	(1111.38+1525.33 + 3815.95)/3	2150.88
	0.60	(F7+F8+F9)/3	(1833.75+2426.85+ 4133.52)/3	2798.04

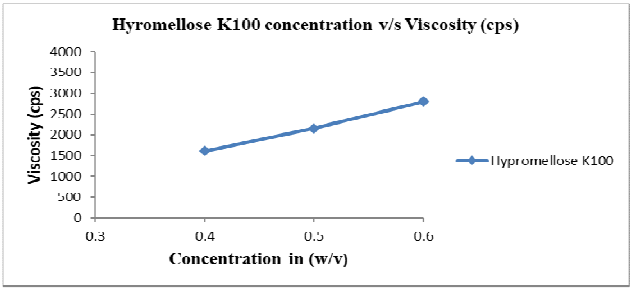

Fig. 7. Average effect of varied concentrations of Hypromellose K100 at 36°C temperature.

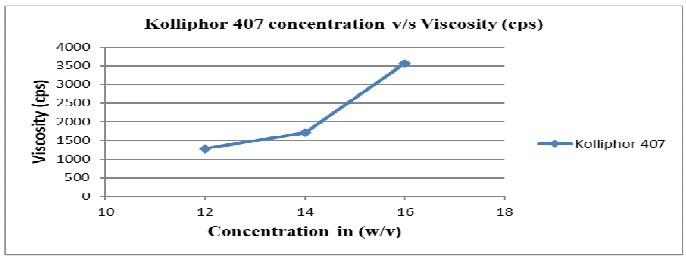

Fig. 8. Average effect of varied concentrations of Kolliphor 407 at 36°C temperature.

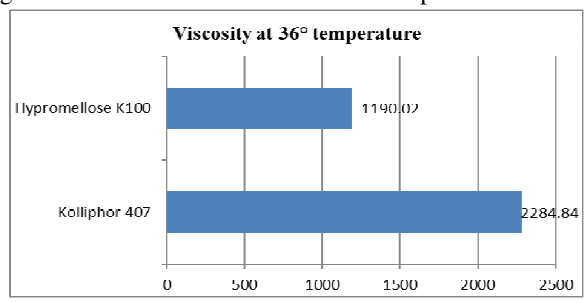

Fig. 9. Main effect of concentration of Hypromellose K100 and Kolliphor 407 on Viscosity at 36°C temperature.

Fig. 10 shows interaction effect between Kolliphor 407 and Hypromellose K100 on viscosity at 20 rpm at 20°C temperature.

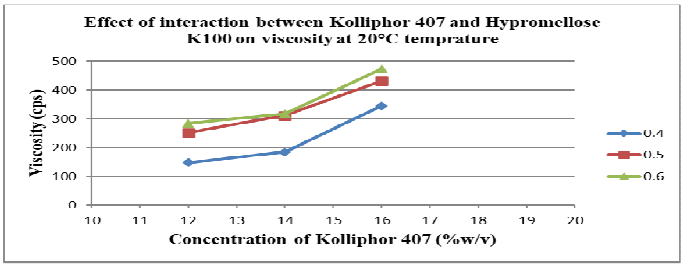

Fig. 10. Effect of interaction between Kolliphor 407 and Hypromellose K100 on viscosity of prepared Moxifloxacin Hydrochloride and dexamethasone sodium phosphate *in-situ* ocular gel at 20 rpm at 20°C **temperature.**

Fig. 11 shows interaction effect between Kolliphor 407 and Hypromellose K100 on viscosity at 20 rpm at 36°C temperature.

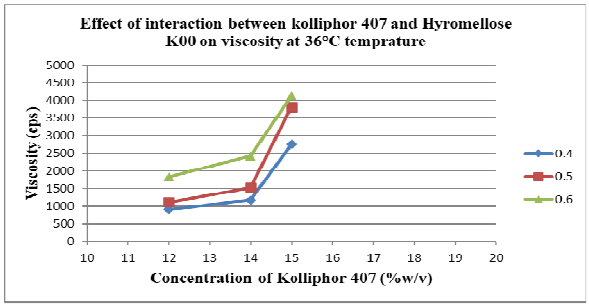

Fig. 11. Effect of interaction between Kolliphor 407 and Hypromellose K100 on viscosity of prepared Moxifloxacin Hydrochloride and dexamethasone sodium phosphate *in-situ* ocular gel at 20 rpm at 36°C temperature.

All formulation was converted into gel at temperature between 31-36°C. This gelation temperature is good for gelation at eye surface.

The drug content of the produced Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate in-situ ocular gels was analyzed. It was found to be within range of 98.00% to 102.00%. It might be stated that a % medication content is suitable for all formulations. No deterioration was found during the manufacturing process.

Table 9: Gelation temperature of the prepared *in-situ* gels.

Formulations	Gelation temperature (°C)
F1	33-36
F2	33-36
F3	31-33
F4	33-36
F5	33-36
F6	31-33
F7	33-36
F8	33-36
F9	31-33

Table 10: Drug content (Assay) of the prepared *in-situ* gel.

Formulation	% Drug Content for Moxifloxacin Hydrochloride	% Drug Content for Dexamethasone Sodium Phosphate
F1	99.56 ± 2.11	99.56 ± 1.09
F2	100.26 ± 0.97	100.26 ± 1.02
F3	100.96 ± 2.15	100.96 ± 1.69
F4	99.42 ± 1.86	99.42 ± 2.11
F5	99.11 ± 0.39	99.11 ± 1.63
F6	100.28 ± 1.02	100.28 ± 1.52
F7	100.96 ± 1.63	100.96 ± 2.03
F8	101.13 ± 1.86	101.13 ± 0.98
F9	98.99 ± 1.39	98.99 ± 2.09

(Results: mean±SD, n=3)

In-vitro release studies were performed and depicted in Fig. 12. After 300 mins, the release of Moxifloxacin Hydrochloride from formulations F1, F2, F3, F4, F5, F6, F7, F8 and F9 were found to be 95.112, 91.22, 86.85, 92.25, 84.85, 83.86, 75.23, 72.31, and 66.26 respectively. The release of Dexamethasone Sodium Phosphate from formulations F1, F2, F3, F4, F5, F6, F7, F8 and F9 were found to be 96.23, 89.85, 84.96, 91.23, 85.85, 82.96, 77.22 70.63, and 68.35 respectively.

Table 11: *In-vitro* drug release from prepared *in-situ* gels (Moxifloxacin Hydrochloride).

Time (min)	Cumulative % release								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
15	4.52 ± 1.62	5.32 ± 1.26	5.02 ± 0.98	5.65 ± 1.06	5.63 ± 1.24	4.32 ± 1.95	5.62 ± 1.32	6.21 ± 1.87	6.32 ± 1.63
30	20.25 ± 1.32	15.23 ± 1.65	12.65 ± 1.95	13.26 ± 1.85	12.63 ± 1.62	11.62 ± 1.75	13.65 ± 1.95	11.85 ± 1.93	10.32 ± 1.54
60	32.25 ± 1.52	25.23 ± 1.22	20.23 ± 1.32	27.75 ± 1.35	22.26 ± 1.32	19.85 ± 1.62	21.32 ± 1.76	21.25 ± 1.95	19.85 ± 1.76
90	45.25 ± 1.62	32.52 ± 1.54	26.23 ± 1.52	31.84 ± 1.36	28.39 ± 2.95	26.74 ± 1.54	23.26 ± 1.22	22.19 ± 1.85	24.16 ± 1.32
120	54.23 ± 1.63	51.85 ± 1.95	47.28 ± 1.44	50.23 ± 1.96	41.96 ± 1.75	39.26 ± 0.96	35.96 ± 0.87	32.25 ± 1.02	31.23 ± 0.63
180	71.23 ± 1.23	58.25 ± 1.52	53.11 ± 1.63	60.33 ± 1.85	52.36 ± 1.63	51.23 ± 1.63	46.89 ± 1.85	41.23 ± 1.63	38.29 ± 1.85
240	80.25 ± 1.25	76.12 ± 1.95	72.85 ± 1.95	71.26 ± 1.23	66.12 ± 1.89	58.36 ± 1.53	62.89 ± 1.36	61.29 ± 1.63	54.26 ± 1.24
300	95.112 ± 1.52	91.22 ± 1.75	86.85 ± 1.33	92.25 ± 1.24	84.85 ± 1.28	83.86 ± 1.95	75.23 ± 1.65	72.31 ± 1.56	66.26 ± 1.29

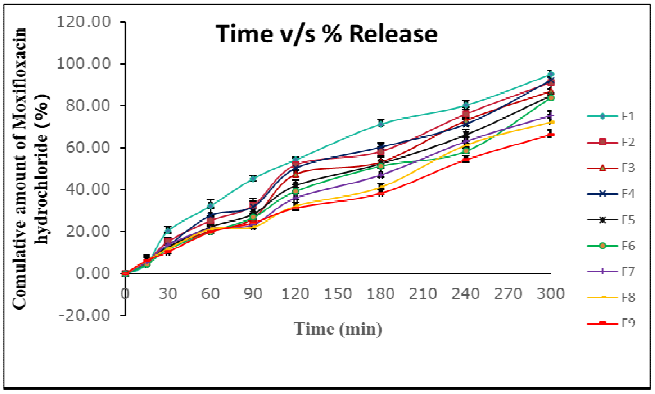

Fig. 12. *In-vitro* release of Moxifloxacin Hydrochloride from the prepared *in-situ* gels.

Table 12: *In-vitro* drug release from prepared *in-situ* gels (Dexamethasone Sodium Phosphate).

Time (min)	Cumulative % release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
15	5.33 ± 1.52	5.12 ± 1.36	4.25 ± 1.25	5.42 ± 1.32	5.63 ± 1.87	5.36 ± 1.62	6.25 ± 1.63	5.36 ± 1.87	6.23 ± 1.56
30	18.85 ± 1.74	14.96 ± 1.38	13.29 ± 1.75	12.85 ± 1.23	13.85 ± 1.96	12.23 ± 1.56	12.75 ± 1.42	12.38 ± 1.03	9.96 ± 2.50
60	34.23 ± 1.63	27.65 ± 1.48	22.85 ± 1.32	29.95 ± 1.85	24.26 ± 1.96	21.96 ± 1.92	22.93 ± 1.75	23.38 ± 1.32	21.36 ± 1.36
90	40.11 ± 1.00	35.85 ± 1.25	29.96 ± 1.85	33.83 ± 2.25	31.76 ± 3.62	29.11 ± 2.65	26.93 ± 2.02	23.93 ± 1.85	27.93 ± 2.63
120	57.84 ± 1.96	54.23 ± 1.53	50.13 ± 1.85	53.85 ± 1.36	43.23 ± 1.95	41.23 ± 0.96	38.13 ± 0.85	33.25 ± 2.36	31.33 ± 1.63
180	73.32 ± 1.52	62.32 ± 2.85	55.85 ± 0.98	63.96 ± 1.05	55.96 ± 1.32	54.36 ± 2.03	50.23 ± 1.75	43.78 ± 1.96	41.26 ± 2.32
240	82.63 ± 1.63	78.63 ± 1.32	74.37 ± 2.85	73.96 ± 2.38	68.36 ± 2.36	59.32 ± 1.96	65.85 ± 1.63	63.39 ± 2.87	56.86 ± 2.30
300	96.23 ± 1.86	89.85 ± 1.36	84.96 ± 1.85	91.23 ± 1.86	85.85 ± 1.39	82.96 ± 1.82	77.22 ± 1.56	70.63 ± 1.44	68.35 ± 1.97

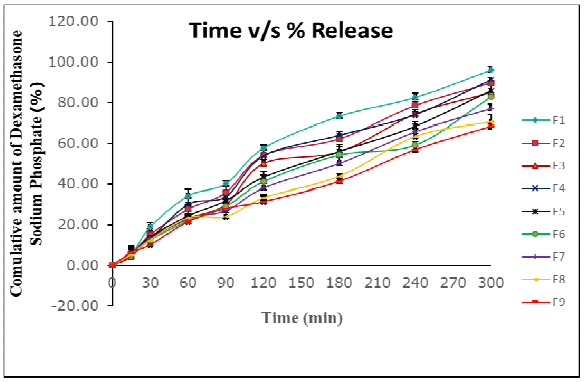

Fig.13. *In-vitro* release of Dexamethasone Sodium Phospahte from prepared *in-situ* gels.

Release data was analyzed utilizing ANOVA. Analysis revealed that increasing the concentration of Kolliphor 407 from 12.0% to 16.0% resulted in a decrease in release at 300 mins that was not statistically significant (P = 0.60, df = 2, F = 0.53, and Fcrit = 5.143). On the other hand, increasing concentration of Hypromellose K100 from 0.4% to 0.6% resulted in a statistically significant decrease in release at 300 mins (P = 0.005, df = 2, F = 13.75, and Fcrit = 5.143).

Average effect of Hypromellose K100 and Kolliphor 407 on Moxifloxacin Hydrochloride release at 300 mins is represented in Table 13 and Fig. 14 and 15. The main effect of Kolliphor 407 and Hypromellose K100 on release at 300 mins is represented in Fig. 16.

Table 13: Average effect of varied concentrations of Hypromellose K100 and Kolliphor 407 on Moxifloxacin Hydrochloride Drug Release

Name of Polymer	Concentration of Polymer	Formula for Calculation of Average effect	Calculation of Average effect	Average effect (%)
Kolliphor 407	12.0	(F1+F4+F7)/3	(95.11+92.25+ 75.23)/3	87.53
	14.0	(F2+F5+F8)/3	(91.22+84.85 + 72.31)/3	82.79
	16.0	(F3+F6+F9)/3	(86.85+83.86+ 66.26)/3	78.99
Hypromellose K100	0.40	(F1+F2+F3)/3	(95.11+91.22+ 86.85)/3	91.06
	0.50	(F4+F5+F6)/3	(92.55+84.55 + 83.85)/3	86.98
	0.60	(F7+F8+F9)/3	(75.23+72.31+ 66.26)/3	71.26

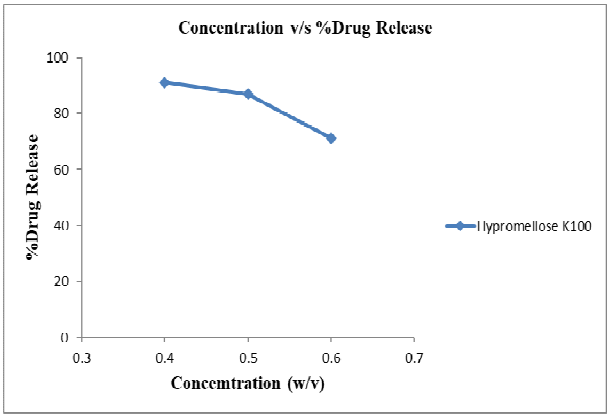

Fig. 14. Average effect of varied concentrations of Hypromellose K100 on Moxifloxacin Hydrochloride release at 300 mins.

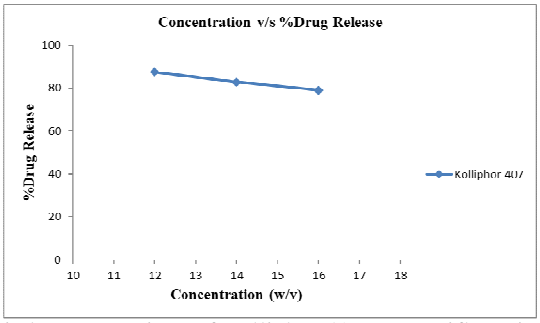

Fig. 15. Average effect of varied concentrations of Kolliphor 407 on Moxifloxacin Hydrochloride release at 300 mins.

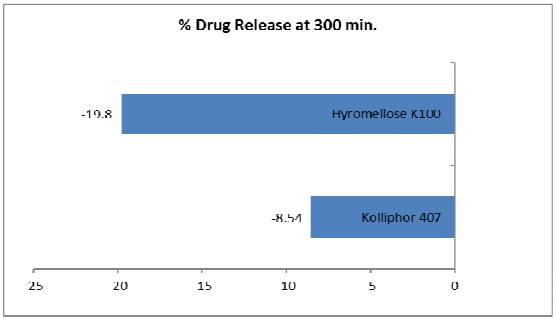

Fig. 16. Main effect of concentration of Hypromellose K100 and Kolliphor 407 on release of Moxifloxacin Hydrochloride at 300 mins.

Based on the provided data, it was observed that Hypromellose K100 had a more pronounced impact on the release of Moxifloxacin Hydrochloride. The elevation in the content of Hypromellose K100 leads to the creation of robust hydrophilic matrices, resulting in the delay of Moxifloxacin Hydrochloride release from formulations. Hypromellose K100 is a polymer that has a viscosity of 100 centipoise (cps), which is determined by its molecular weight and chain length. The hydrophilic matrix of Hydroxy Propyl Methyl Cellulose swells and slowly releases Moxifloxacin Hydrochloride, with the rate of release depending on its solubility in water. Polymer matrix undergoes gradual erosion concurrently. Upon the completion of the Moxifloxacin Hydrochloride release, the matrix undergoes complete dissolution, indicating that the duration of the release is regulated by the erosion of the polymer.

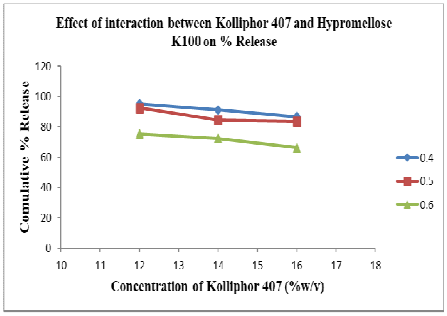

Fig. 17. Effect of interaction between Kolliphor 407 and Hypromellose K100 on percent release of prepared Moxifloxacin Hydrochloride *in-situ* ocular gel at 300 mins.

The average effect of Hypromellose K100 and Kolliphor 407 on Dexamethasone Sodium Phosphate release at 300 mins is represented in Table 14 and Fig. 18 and 19. The main effect of Kolliphor 407 and Hypromellose K100 on release at 300 mins is represented in Fig. 19.

Table 14: Average effect of varied concentrations of Hypromellose K100 and Poloxamer on Dexamethasone Sodium Phosphate Drug Release.

Name of Polymer	Concentration of Polymer	Formula for Calculation of Average effect	Calculation of Average effect	Average effect (%)
Kolliphor 407	12.0	(F1+F4+F7)/3	(96.23+91.23+ 77.22)/3	88.22
	14.0	(F2+F5+F8)/3	(89.85+85.85 + 70.63)/3	82.11
	16.0	(F3+F6+F9)/3	(84.96+82.96+ 68.35)/3	78.76
Hypromellose K100	0.40	(F1+F2+F3)/3	(96.23+89.85+ 84.96)/3	90.34
	0.50	(F4+F5+F6)/3	(91.23+85.85 + 82.96)/3	86.68
	0.60	(F7+F8+F9)/3	(77.22+70.63+ 68.35)/3	72.06

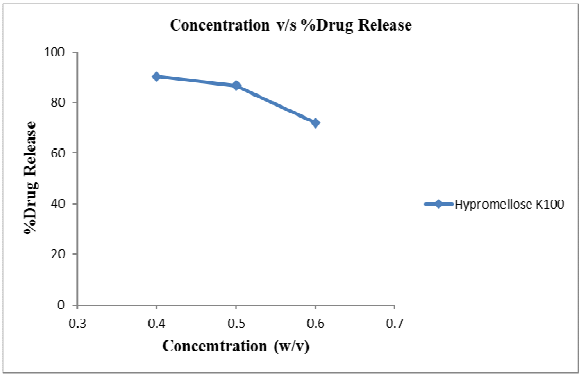

Fig. 18. Average effect of varied concentrations of Hypromellose K100 on Dexamethasone Sodium Phosphate release at 300 mins.

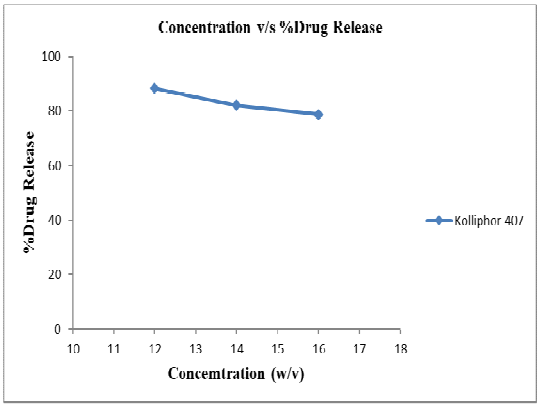

Fig. 19. Average effect of varied concentrations of Kolliphor 407 on Dexamethasone Sodium Phosphate release at 300 mins.

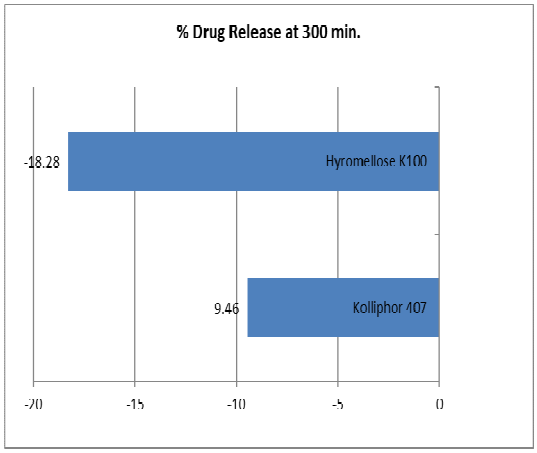

Fig. 20. Main effect of concentration of Hypromellose K100 and Kolliphor 407 on release of Dexamethasone Sodium Phosphate at 300 mins.

Based on the provided data, it was determined that Hypromellose K100 had a more pronounced impact on the release of Dexamethasone Sodium Phosphate. Higher concentrations of Hypromellose K100 lead to the production of robust hydrophilic matrices, which in turn slows down the release of Dexamethasone Sodium Phosphate from formulations. Hypromellose K100 is a polymer that has a viscosity of 50 centipoise (cps). The viscosity is determined by the molecular weight and chain length of the polymer.

A hydrophilic matrix of Hydroxy Propyl Methyl Cellulose is capable of swelling, allowing for the gradual diffusion of Dexamethasone Sodium Phosphate based on its solubility in water. Polymer matrix undergoes gradual erosion concurrently. Upon the conclusion of the Dexamethasone Sodium Phosphate release, the matrix undergoes complete dissolution, indicating that the duration of the release is regulated by the erosion of the polymer.

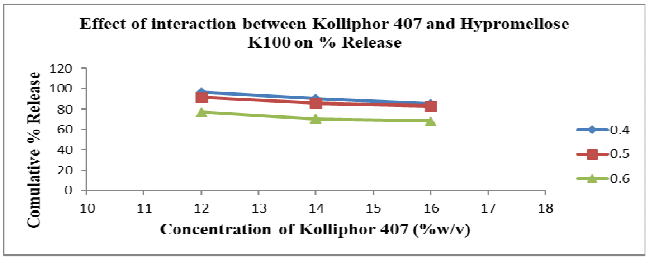

Fig. 21. Effect of interaction between Kolliphor 407 and Hypromellose K100 on % release of prepared Moxifloxacin Hydrochloride *in-situ* ocular gel at 300 mins.

For release of Moxifloxacin Hydrochloride. Formulations F1, F2, and F4 demonstrated the best fit to Higuchi's model, On the other hand, formulations F3, F5, F6, F7, F8, and F9 exhibited the best fit to the zero-order model as indicated by the correlation coefficients in Table 15.

The formulations that were most suitable for the zero-order model indicate that the release was not dependent on concentration. The formulation was most suitable for Higuchi's model, indicating that the release was controlled by diffusion. It also aligned with the Hixon-Crowell model, which shows that the release was limited by the dissolving rate. The 'n' value derived from the Korsmeyer-Peppas equation was below 0.43 (for no formulation), indicating that the release from the formulation was governed by the Fickian diffusion mechanism. For values between 0.43 and 0.85 (for F7-F9), the release followed an anomalous (non-Fickian) transport. For values between 0.85 and 1 (for F1-F6), the release belonged to Case II transport.

For release of Dexamethasone Sodium Phosphate. Formulations F1, F2, F3, and F4 exhibited the best fit to Higuchi's model, as indicated by the correlation coefficients in Table 16. On the other hand, formulations F5, F6, F7, F8, and F9 showed the best fit to zero-order model.

Formulations most suitable for zero-order model indicate that the release was not dependent on concentration. The formulation was most compatible with Higuchi's model, indicating that the release was governed by diffusion. It also aligned with the Hixon-Crowell model, which proposes that the release was limited by dissolving rate (Chidambaram *et al*., 1998; Narasimhan & Langer, 1997; Paarakh *et al*., 2018). The value of 'n' derived from the Korsmeyer-Peppas equation was found to be <0.43 for the formulation without any specific designation. This suggests that the release of the substance from the formulation is primarily governed by the Fickian diffusion mechanism. For formulations labeled as F7-F9, the 'n' value falls within the range of 0.43-0.85, indicating that the release follows an anomalous (non-Fickian) transport mechanism. On the other hand, for formulations labeled as F1-F6, the 'n' value falls within the range of 0.85-1, indicating that the release is attributed to Case II transport.

Table 15: Release kinetics of Moxifloxacin Hydrochloride in various formulations.

Release kinetics-Model Fitting							
Formulation Code	Co-relation Coefficient for the model				Korsemeyer-Peppas (M_t/M_∞ vs T)		
	0 - order R% vs T	1 - order log R% vs T	Highuchi R% vs $T^{1/2}$	Hixon-Crowell ($100^{1/3}$ - $R\%^{1/3}$) vs T	r	n	k
F1	0.976	0.813	**0.998**	0.976	0.976	0.919	0.006
F2	0.988	0.879	**0.992**	0.988	0.988	0.899	0.005
F3	**0.990**	0.909	0.985	0.990	0.986	0.911	0.005
F4	0.988	0.882	**0.991**	0.988	0.982	0.895	0.005
F5	**0.996**	0.908	0.990	0.996	0.993	0.870	0.005
F6	**0.991**	0.896	0.982	0.991	0.985	0.927	0.004
F7	**0.996**	0.916	0.985	0.996	0.982	0.818	0.006
F8	**0.994**	0.934	0.977	0.994	0.986	0.789	0.007
F9	**0.996**	0.929	0.985	0.996	0.994	0.770	0.007

Table 16: The release kinetics of Dexamethasone Sodium Phosphate in various formulations.

Release kinetics-Model Fitting							
Formulation Code	Co-relation Coefficient for the model				Korsemeyer-Peppas (M_t/M_∞ vs T)		
	0 - order R% vs T	1 - order log R% vs T	Highuchi R% vs $T^{1/2}$	Hixon-Crowell ($100^{1/3}$ - $R\%^{1/3}$) vs T	r	n	k
F1	0.976	0.834	**0.997**	0.976	0.947	0.899	0.006
F2	0.983	0.863	**0.996**	0.983	0.973	0.907	0.005
F3	0.985	0.870	**0.991**	0.985	0.972	0.957	0.004
F4	0.980	0.864	**0.994**	0.980	0.974	0.917	0.005
F5	**0.995**	0.893	0.994	0.995	0.988	0.866	0.006
F6	**0.989**	0.897	0.987	0.989	0.989	0.872	0.005
F7	**0.996**	0.915	0.992	0.996	0.994	0.819	0.007
F8	**0.992**	0.905	0.984	0.992	0.912	0.820	0.006
F9	**0.994**	0.915	0.989	0.994	0.992	0.793	0.007

CONCLUSIONS

The combination of Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate was effectively incorporated into a temperature-responsive in-situ gelling system. This system utilized Kolliphor 407 in conjunction with HPMC K100. The significance of HPMC K100 and Kolliphor 407 in influencing in-situ gel behavior was observed based on concentration of HPMC K100 and Kolliphor 407. The *in-vitro* findings suggest that the in-situ gel system can serve as a practical substitute for traditional ocular drops due to its capacity to maintain a continuous flow of medication.

FUTURE SCOPE

The future scope of the formulation and evaluation of in-situ ocular gels containing moxifloxacin hydrochloride and dexamethasone sodium phosphate is promising, with opportunities for enhanced therapeutic efficacy, extended drug release, combination therapies, and personalized treatment approaches. Continued research and innovation in this field has the potential to significantly impact the management of ocular diseases and improve patient outcomes.

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Conflict of Interest. None.

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