

Formulation and Characterization of pH Induced *in situ* Gels Containing Sulfacetamide Sodium for Ocular Drug Delivery: A Combination of Carbopol®/HPMC Polymer

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ABSTRACT

Introduction: Topical delivery of eye drops which currently accounts to 90% of available ocular dosage forms are ideal for the treatment of eye diseases but having limitations of poor therapeutic response and low bioavailability. **Objectives:** The objectives of present research was to develop and characterize sustained release *in situ* ocular gels containing sulfacetamide sodium using pH induced gelling polymers for improved therapeutic response and patient compliance. **Methods:** *In situ* gel formulations prepared by dispersion method using Carbopol® 940/Carbopol® 934 alone or in combination with hydroxypropyl methylcellulose (HPMC E4M). Formulations were evaluated for appearance, pH, viscosity, gelling capacity, drug content and *in vitro* drug release. The optimized formulation was assessed for sterility and antimicrobial efficacy using disk diffusion technique in comparison to commercial eye drops (Albucid®10%). **Results:** The appearance of *in situ* gels were clear and free flowing in nature however, a viscous clear solution with no flow was produced for formulations consisting of 0.8% w/v Carbopol® 940/Carbopol® 934 and 2% w/v HPMC E4M. pH of all the formulations was within the range of 5.9 to 6.7. *In situ* gels with Carbopol® 940 demonstrated higher viscosity compared to Carbopol® 934 and drug release was sustained over a period of 8 hr. The selected formulation containing 0.8% w/v Carbopol® 940 and 1.5% w/v HPMC E4M passed sterility test and demonstrated similar antimicrobial efficiency compared to commercial product. **Conclusion:** Carbopol®/HPMC-based *in situ* gels have potential to improve patient's compliance by reducing the dosing frequency and could be a viable alternative to commercial product.

Key words: *In situ* gel, Ocular, Sulfacetamide sodium, Carbopol®/HPMC, *In-vitro* release, Antimicrobial efficacy.

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INTRODUCTION

Ocular drug delivery is one of the most interesting and challenging areas of pharmaceutical research. Topical delivery of eye drops which currently accounts for 90% of accessible ocular formulations is an ideal treatment for ocular diseases especially when the drug needs to produce a localized action. However, topical delivery is not without problems such as the poor bioavailability and therapeutic response. These challenges are attributable to the rapid precorneal elimination due to tear secretion, non-productive absorption due to the biological barrier for drug penetration, absorp-



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tion into the gastrointestinal tract due to drainage through nasal lacrimal duct and poor patient's compliance due to increasing number of instillations and difficulty in self-administration.¹⁻⁴ Thus, the concept of polymeric *in situ* gel forming system was introduced to alleviate these problems. *In situ* gels are free flowing solutions at room temperature that undergo phase transition from solution-gel (sol-gel) as a result of exposure to physiological temperature, pH or ionic compositions of lacrimal fluid.⁵⁻⁷ The gel formed in the eye effectively prevents the rapid drainage of instilled drug from ocular site, improves the retention time of dosage form at the site of administration and sustains the drug release for a prolonged period of time. It aids to reduce the dosing frequency and to improve the therapeutic efficiency of drug. Furthermore, systemic side effects would also be reduced due to less systemic absorption. Therefore, it enhances patient's compliance and convenience.⁵

Carbopol® is a water soluble pH dependent *in situ* polymer. The formulations comprising of Carbopol® polymer remained as solution at acidic pH and forms a low viscosity gel when pH raised to alkaline. The pH difference between the formulations containing Carbopol® and human tear fluid makes the sol-gel transition occurs almost instantly. Besides, Carbopol® has an excellent mucoadhesive property. Therefore, the polymer is responsible to increase the contact time of a drug in the eye by adhering to the ocular surface and thereby release the drug in a controlled fashion. However, acidic nature of Carbopol® may cause damage to surface of eye before being neutralized by the lacrimal fluid. Thus, HPMC, a viscosity enhancing polymer is usually added to Carbopol® contained formulations to overcome this problem, which resulted in pH induced polymeric mixture (Carbopol®/HPMC). This polymeric mixture is in liquid state at its native formulated pH 4 to 6 at room temperature but rapid transition into gel phase occurs at the pH of tear fluid (pH 7.4).^{3,8-10} To date, many of the ocular *in situ* forming gels have been investigated with a combination of Carbopol® and cellulose derivatives.^{8,11-13} In addition, these two polymers are already listed in the FDA's Inactive Ingredient Guide (IIG) and widely used commercially for various drug applications including topical ophthalmic solutions.¹⁴⁻¹⁶ Therefore, these polymers are considered to be safe to use.

Sulfacetamide sodium is a sulfonamide with antibacterial activity. It is commercially available in the dosage forms of lotion and solution. The ocular dosage form is commonly used to treat conjunctivitis and other superficial ocular infections caused by susceptible micro-organisms such as *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus pneumoniae*, *Klebsiella* species and *Enterobacter* species. The major drawback of commercial

eye drops, however, is the dosing frequency, which has to be administered 1 to 2 drops every 2 to 3 hr (8 to 12 times in a day).¹⁷ This high frequency of sulfacetamide sodium eye drops administration is associated with poor patient compliance and convenience. To overcome all the aforementioned constraints offered by eye drops, an alternative approach of *in situ* gelling system with a combination of Carbopol® and HPMC was investigated as a vehicle for the formulation of sustained release smart eye drops containing sulfacetamide sodium. Furthermore, to the best of our knowledge, till date there is no published literature on the formulation of *in situ* gels containing sulfacetamide sodium.

MATERIALS AND METHODS

Materials

Sulfacetamide sodium, methyl paraben and propyl paraben were purchased from Sigma-Aldrich Chemical Co. (St. Louis, MO, USA). Carbopol® polymers (Carbopol® 940 and Carbopol® 934) were purchased from DCM personal care Sdn Bhd (Selangor, Malaysia). HPMC E4M was obtained as a gift sample from Dow Chemical Co. (Illinois, USA). Muller Hinton agar medium and fluid thioglycolate medium were purchased from Becton Dickinson Sdn Bhd (Selangor, Malaysia). All other solvents and chemicals used were of analytical grade.

Preparation of *in situ* gel formulations

The composition of *in situ* gel formulations containing sulfacetamide sodium is shown in Table 1. *In situ* gel formulations containing different concentrations of Carbopol® 940/Carbopol® 934 in combination with HPMC E4M were prepared by dispersion method.¹⁸⁻²⁰ Briefly, about 75 mL distilled water was preheated to 70°C to dissolve methyl and propylparaben and then sodium chloride (NaCl), HPMC and Carbopol® were incorporated into the solution. The mixture was left at room temperature overnight to allow the polymer to hydrate. Sulfacetamide sodium was dissolved in 25mL distilled water separately. It was added into above polymeric solution and stirred until a uniform solution was obtained. The final product was filled into sterile amber colour bottles and sterilized in autoclave at 121°C for 15 min. The prepared formulations were stored in refrigerator at 4°C until further use.

Evaluation of *in situ* gel formulations

Appearance and clarity, pH and drug content

The appearance and clarity of formulations were observed visually against a black and white background for presence of any particulate matter in the formulation.⁴

Table 1: Composition of *in situ* gels containing sulfacetamide sodium.

Ingredients (% w/v)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Sulfacetamide sodium	10	10	10	10	10	10	10	10	10	10
Carbopol® 940	0.3	0.5	0.8	0.8	0.8	0.8	-	-	-	-
Carbopol® 934	-	-	-	-	-	-	0.6	0.8	0.8	0.8
HPMC E4M	0.6	0.6	0.6	1.0	1.5	2.0	1.0	1.0	1.5	2.0
Sodium chloride	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9
Methyl paraben	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Propyl paraben	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Water qs ad	100	100	100	100	100	100	100	100	100	100

The pH of formulations was determined using a digital pH meter (METTLER Toledo, S220 SevenCompact™ pH/Ion) to ensure that the formulations do not cause any ocular irritation to the patient upon administration. To determine the drug content in the formulations, 1 mL of the formulation was dissolved in 100 mL simulated tear fluid (STF, pH 7.4) and further diluted with same medium to measure the absorbance using UV-Visible spectrophotometer at a wavelength of 257 nm. The composition of STF pH 7.4 is as follows: 0.670 g of NaCl, 0.200 g of NaHCO₃, 0.008 g of CaCl₂ · 2H₂O and distilled water up to 100 mL. The samples were measured in triplicate.

Viscosity

The viscosity of the formulations was determined using DV-III ULTRA Programmable Rheometer (Model LV) using a spindle-SC4-18 which is immersed in a formulation to be tested. The spindle speed was set at 20 rpm and the temperature was maintained at 25°C. The viscosity values were calculated using Bingham's calculation. The samples were measured in triplicate to ensure that the developed formulations having suitable viscosity to avoid the rapid pre-corneal elimination of drug.

Gelling capacity

The prepared formulations were evaluated for gelling capacity in order to ascertain the composition suitable for use as *in situ* gelling system. The gelling capacity was determined by placing 1 mL of prepared formulation into a test tube containing 5 mL of STF pH 7.4 at 37°C. The time taken to transition of solution to gel and the time taken for the formed gel to dissolve were visually observed. The congo red dye was added into the formulation to give visualised appearance of formed gel. The gelling capacity of the formulations was graded in four groups such as no gelation (-), poor (+), good (++) and excellent (+++) based on the gelation time

and time period for which the formed gel remains as such.^{21,22}

In-vitro drug release studies

In-vitro drug release studies were conducted using dialysis membrane method in triplicate.²³ Firstly, the dialysis membrane (molecular weight cut-off 12000-14000 Da) which was soaked overnight in the dissolution medium was opened as a bag and tied at one-end. About 1 mL of the selected formulation comprising a combination of Carbopol®/HPMC was placed into one-end tied dialysis bag and then added 0.5 mL of STF pH 7.4 to simulate the gel formation in the eye after instillation of *in situ* gel preparation. Thereafter, second-end of dialysis bag was also tied properly and immersed in a beaker containing 100 mL of STF pH 7.4 which simulates the tear fluid and its pH. The beaker was placed in a shaker water bath which was set at 50 rpm and 37°C. About 2 mL of the sample was withdrawn at 0.5, 1, 2, 3, 4, 6 and 8 h and replaced the same amount of freshly prepared STF to maintain the sink conditions. The samples were analyzed using UV-Visible spectrophotometer at 257 nm using STF as a blank.

The resultant release data was fitted into different release kinetic models i.e. zero order, first order, Higuchi, Hixon-crowell and Korsmeyer-peppas in order to determine the drug release pattern and release mechanism. The time taken to release 50% of the drug ($T_{50\%}$) was calculated and treated statistically using one-way analysis of variance (ANOVA). When there was a statistically significant difference, a post hoc Tukey's HSD (honestly significant difference) test was performed. A value of $p < 0.05$ was considered as statistically significant.

Sterility testing

Ocular products has to be sterile, thus it is necessary to carry out sterility testing. The selected formulation was aseptically transferred into sterile fluid thioglycolate medium and incubated for not less than 14 days at 35°C

to evaluate the growth of bacteria. The sterility of the formulation was visually determined by the clarity of the medium until 14 days.²⁴⁻²⁷

Antimicrobial efficacy studies

The antimicrobial efficacy studies were carried out by disk diffusion technique to ascertain the biological activity of the selected formulation. The conventional eye drops (Albucid®10%) served as a reference and selected formulation was placed into cups bored into sterile Muller Hinton Agar medium previously seeded with *Staphylococcus aureus*, *Escherichia coli* and *Klebsiella pneumoniae* microorganisms. The plates were incubated for 24 h at 37°C and the zone of inhibition was measured in mm. Each formulation was tested in triplicate. The results were treated statistically using Independent samples *t*-test. A value of $p < 0.05$ was considered as statistically significant.

RESULTS AND DISCUSSION

The obtained results of appearance and clarity, pH, drug content, viscosity and gelling capacity for prepared *in situ* gel formulations are shown in Table 2.

Appearance and clarity, pH and drug content

All the prepared formulations were found to be transparent and clear excluding the formulations consisting of 0.8% w/v of Carbopol® 940 (F6) and Carbopol® 934 (F10) in combination with HPMC (2% w/v). These two formulations were found to be highly clear viscous solutions with no flow which might be due to high

concentration of both Carbopol® and HPMC. Hence, formulations were not prepared with further increase in the concentrations of both polymers. The pH of formulations were found to be in the range of 5.97 to 6.71. The combination of water soluble polymeric system i.e. Carbopol®/HPMC aided to reduce the acidity of the solution. The pH of formulation would raise instantly to pH 7.4 (an ideal ocular pH) after instillation into eye due to pH of lacrimal secretion. Thus, the formulations were considered to be suitable for ocular administration and may not cause any irritation to ocular tissues upon administration.^{2,28} The drug content of all the formulations was found to be in the acceptable range of 98.63% to 99.63% and results demonstrated the uniform distribution of drug in the prepared formulations.

Viscosity

Viscosity of formulations is an important factor in determining residence time of drug in the eye as the low viscosity solutions may drain faster after instillation into eye and high viscosity solutions would be difficult for instillation and also have poor spreadability in the eye. Viscosity of all the formulations was found to be in the range of 64.8 to 1857 cP. The viscosity was directly dependent on the polymeric content of the formulations and increase in the polymer concentration caused to increase in viscosity of the formulations. Formulations consisting of Carbopol® 940 showed higher viscosity compared to Carbopol® 934. It might be due to differences in their crosslinking density as Carbopol® 940 has high crosslinking density and Carbopol® 934 has low

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

Formulation	Clarity	pH	Drug content (%)	Viscosity (cP)	Gelling capacity
F1	Transparent and Clear	6.71	99.13 ± 0.35	64.80 ± 0.71	-
F2	Transparent and Clear	6.27	99.07 ± 0.51	86.05 ± 0.64	+
F3	Transparent and Clear	5.97	99.27 ± 0.15	259.20 ± 7.07	++
F4	Transparent and Clear	6.03	98.63 ± 0.23	1023.00 ± 63.64	++
F5	Transparent and Clear	6.02	98.67 ± 0.21	1209.00 ± 28.28	+++
F6	Clear and Viscous	6.27	98.87 ± 0.32	1857.00 ± 82.02	NS**
F7	Transparent and Clear	6.20	99.63 ± 0.15	685.10 ± 12.59	+
F8	Transparent and Clear	6.19	98.90 ± 0.20	726.50 ± 0.00	++
F9	Transparent and Clear	6.08	99.00 ± 0.40	1063.75 ± 7.14	++
F10	Clear and Viscous	6.19	98.80 ± 0.20	1572.50 ± 68.59	NS**

“-” no gelation, “+” gelation immediate but dissolves rapidly (1-2 h), “++” gelation immediate and remain for few h (3-4 h), “+++” stiff gel is formed immediately and remain for extended period (more than 6-8 h).

**Not Studied for gelling capacity.

crosslinking density.^{9,29} Remarkable increase in the viscosity of formulations from 64.8 to 259.2 cP with the increase in the concentration of Carbopol® 940 from 0.3 to 0.8 %w/v. The same phenomena was observed with the formulations consisting of Carbopol®/HPMC polymeric mixture i.e. increase in the concentration of HPMC E4M from 0.6 to 2 % w/v (F3 to F6) while maintaining the Carbopol® 940 concentration constant at 0.8 %w/v. The similar findings was observed with Carbopol® 934 (0.6-0.8 %w/v) and HPMC E4M (1-2 %w/v) in formulations F7 to F10. The results are well in correlation with the Nanjwade *et al.*⁵ and Pandey *et al.*³⁰ where the researchers used a combination of Carbopol® 934/HPMC E4M and Carbopol® 940/HPMC E4M at various concentrations to formulate pH triggered *in situ* gels containing ketorolac tromethamine and levobunolol hydrochloride, respectively.

Formulations, F1 to F5 and F7 to F9 were found to be free flowing in nature. However, formulations F6 and F10 were not pourable in nature as they exhibited higher viscosity due to higher content of polymeric system. Hence, these two formulations were not considered for further studies.

Gelling capacity

An optimal *in situ* gelling formulation should have the balanced gelling capacity and viscosity which enables easy administration to the eyes with good gel formation by undergoing rapid sol to gel transition upon contact at the affected site. Besides, enhancing the residence time of drug at pre-corneal surface dependent on the viscosity of the formulations.³¹

Formulation F1 containing 0.3 %w/v Carbopol® 940 and 0.6 %w/v HPMC E4M was assigned with ‘-’ sign as it is not having gelling ability at the pH of STF (pH 7.4) due to the low viscosity of solution and hence were abandoned for further studies. With increase in the concentration of Carbopol® and HPMC, the formulations retained their liquid state at room temperature and at the formulated pH and increased the gelling capacity of the formulations upon exposure to pH of STF due to increase in the viscosity of formulations. Among all, formulation F5 demonstrated excellent gelling capacity and assigned with ‘+++’ sign. They formed stiff gel immediately and remained for extended period of time (more than 6-8 h).

The formation of stiffer gel might be due to hydrophobic nature of Carbopol® backbone and with increasing in the concentration, large amount of polymeric chains develop hydrophobic interchain aggregation. Also, due to increased ionization of functional groups present in Carbopol® as a result of increasing pH, leading to

an increased repulsion of negative charges along the polymer backbone and the subsequent expansion of polymeric network. Furthermore, by increasing the concentration of Carbopol®/HPMC in the aqueous environment, they form a stable three dimensional viscoelastic network.^{32,33} The formulation of such *in situ* gels facilitates the sustained drug release locally by preserving their integrity without dissolving and eroding for prolonged period of time.

In-vitro drug release studies

The results of *in-vitro* drug release study was shown in Figure 1. The reference product released about 99.27% of drug within 2 h. However, the selected formulations F3, F4 and F5 released 90% of drug within 4, 6 and 8 h, respectively. These three formulations had same concentration of Carbopol® 940 (0.8% w/v) but the concentration of HPMC E4M as a viscosity enhancer increased from 0.6 to 1.5 %w/v. Similarly, the formulation F8 and F9 released 90% of drug within 3 and 4 h, respectively. The formulation F8 and F9 contained same amount of Carbopol® 934 (0.8 %w/v) but the concentration of HPMC E4M increased from 1 to 1.5 %w/v. Therefore, the *in vitro* drug release results demonstrated that higher viscosity with stronger gelling ability plays an important role in sustaining the drug release from the formulations for prolonged period of time.

The $T_{50\%}$ of reference formulation (Albucid®10%), F3, F4, F5, F8 and F9 were 0.28, 0.48, 0.93, 2.86, 0.56 and 0.76 h, respectively. As the formulation F3 had an initial burst release at an initial hour, no statistically significant difference was observed between reference and F3. However, a statistically significant difference was observed

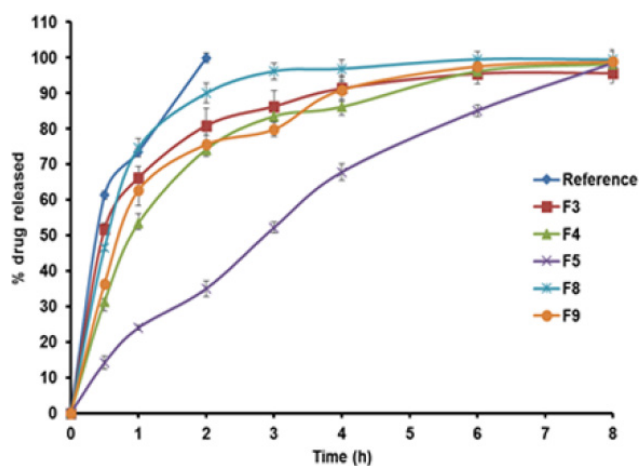


Figure 1: *In-vitro* release profile of sulfacetamide sodium from Reference (Albucid®10%), Carbopol®940/HPMC *in situ* gels (F3: 0.8/0.6%w/v, F4: 0.8/1.0%w/v, F5: 0.8/1.5%w/v) and Carbopol®934/HPMC *in situ* gels (F8: 0.8/1.0%w/v, F9: 0.8/1.5 %w/v).

between reference, F4 and F5 as the initial burst release was decreased and exhibited sustained drug release with an increasing the concentration of HPMC E4M. The formulation F5 (2.86 h) had better sustained release profile compared to other *in situ* gel formulations and marketed eye drops. It could be due to the higher viscosity and excellent gelling capacity of the formulation which supported to immediate transition of solution to gel at ocular pH and remained in the gel form for a prolonged period of time to sustain the sulfacetamide sodium release for 8 h. This phenomenon eliminates the aforementioned disadvantages of eye drops i.e. rapid precorneal elimination of formulation caused by blinking of eyes and tear secretion and frequency of dosing frequency of currently available sulfacetamide sodium eye drops (every 2-3 h). Therefore, the *in situ* gel formulation achieves the improved patient compliance and convince with the dosing administration of every 8 h. Formulation F5 was selected as the best among the prepared formulations and evaluated for sterility testing and antimicrobial efficacy studies.

In order to find out the kinetic of drug release, the *in-vitro* drug release data was fitted into different release kinetic models. The best fit model of release pattern was considered with highest regression value (r^2) of zero and first order. The regression values of Higuchi model which indicate diffusion mechanism and Hixon-crowell model which indicate erosion mechanism were compared to identify the release mechanism. The release mechanism can be further confirmed by the release exponent (n) value in Korsemeyer-peppas model. The release kinetic results of *in situ* gels are presented in Table 3. The formulation F5 and conventional eye drops showed identical kinetic of drug release which was followed zero order release pattern and non-fickian diffusion (combination of diffusion and erosion) mechanism (n value was in between 0.43-0.85).

Sterility testing

The results of the sterility test on the formulation F5 (Carbopol® 940/HPMC-0.8/1.5 %w/v) is shown in Figure 2. The results indicated that there is no evidence of microbial growth on the fluid thioglycolate medium during the incubation period of 14 days at 35°C. Therefore, the formulation was found to be clear without appearance of turbidity which confirmed the sterility of formulation.

Antimicrobial efficacy studies

The zone of inhibition results from antimicrobial efficacy studies are shown in Table 4 and depicted in Figure 3. The zone of inhibition results demonstrated that

Table 3: Release kinetics of *in situ* gel formulations. Mean±SD, n=3.

Formulation	Zero order		First order		Higuchi r^2	Hixon-crowell r^2	Korsemeyer-peppas		Release pattern and release mechanism
	r^2	Slope	r^2	Slope			r^2	Release exponent (n)	
Reference	0.9226±0.006	0.5763±0.016	0.8347±0.069	0.0158±0.004	0.9789±0.002	0.9482±0.021	0.9983±0.003	0.5895±0.030	Zero order and combination of diffusion and erosion
F3	0.7209±0.05	5.1584±0.322	0.9283±0.029	0.1512±0.039	0.8680±0.037	0.8587±0.007	0.9753±0.039	0.2312±0.047	First order and Fickian diffusion
F4	0.7509±0.007	7.7425±0.398	0.9738±0.022	0.2069±0.054	0.9369±0.004	0.8813±0.028	0.9542±0.022	0.3552±0.031	First order and Fickian diffusion
F5	0.9690±0.007	11.4303±0.219	0.8919±0.033	0.2178±0.023	0.9887±0.007	0.9758±0.012	0.9500±0.049	0.6885±0.063	Zero order and combination of diffusion and erosion
F8	0.5421±0.067	5.2937±0.516	0.7756±0.152	0.2012±0.037	0.7585±0.062	0.7008±0.200	0.9400±0.014	0.2956±0.033	First order and Fickian diffusion
F9	0.7489±0.030	7.0767±0.178	0.9584±0.022	0.2437±0.041	0.9416±0.026	0.8716±0.022	0.9740±0.009	0.2542±0.062	First order and Fickian diffusion

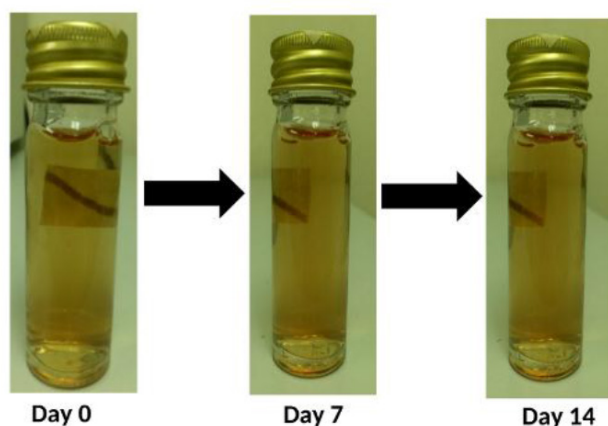


Figure 2: Sterility testing of formulation F5 from 0 to 14 days.

Table 4: Results of antimicrobial efficacy studies.

Bacterial strains	Zone of inhibition (mm), n=3	
	Reference (Albucid®10%)	F5
<i>Staphylococcus aureus</i>	41.33 ± 1.15	39.67 ± 1.53
<i>Escherichia coli</i>	41.33 ± 1.15	39.67 ± 0.58
<i>Klebsiella pneumoniae</i>	35.00 ± 1.00	33.33 ± 1.15

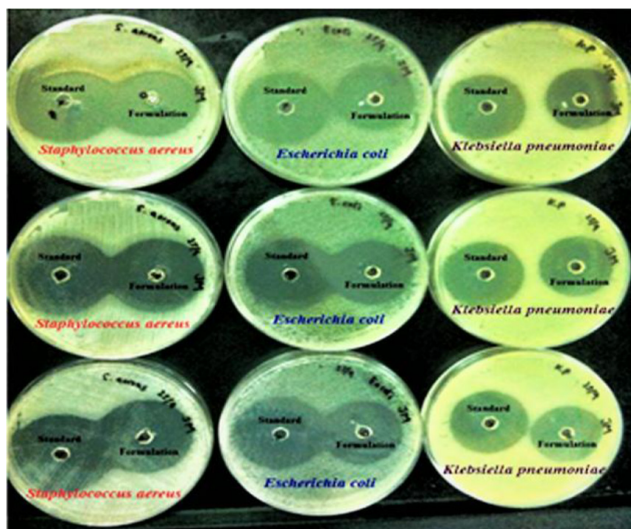


Figure 3: Antimicrobial efficacy: Zone of inhibition of Reference (Albucid®10%) and Formulation F5.

in situ gel formulation showed prominent antimicrobial efficiency against *Staphylococcus aureus*, *Escherichia coli* and *Klebsiella pneumonia* micro-organisms and the results were in comparable with the marketed product. It was statistically confirmed that there was no significant difference ($p > 0.05$) in antimicrobial activity of the marketed product and the selected formulation (F5) against the micro-organisms responsible for conjunctivitis and other superficial ocular infections. As described by

Pundir and Jain³⁴ when the diameter of zone of inhibition is more than 18 mm, it is considered that formulations have very active antimicrobial activity. Thus, it indicated that sulfacetamide sodium retained its very active antimicrobial efficiency even after being formulated in an *in situ* gelling system.

CONCLUSION

Sulfacetamide sodium was successfully formulated as pH dependent *in situ* ocular gel using Carbopol®/HPMC as a polymeric system. All the formulations were clear and free flowing solutions other than F6 and F10. The formulation F5 was found to be sterile and showed excellent gelling capacity. It also demonstrated a good viscosity and sustained the drug release over a period of 8 h. The antimicrobial efficacy of selected formulation was similar to commercial eyes drops (Albucid®10%). Therefore, it was concluded that *in situ* gelling formulation with Carbopol®/HPMC would invariably improve the patient's compliance by minimising the frequency of drug administration and could be a viable alternative to the conventional commercial product.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

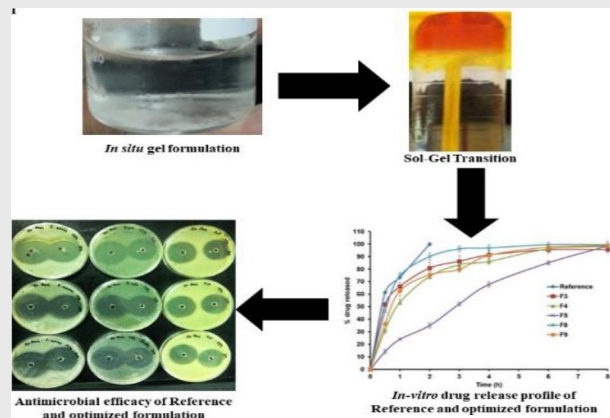
NaCl: Sodium chloride; **STF**: Simulated tear fluid; **NaHCO₃**: Sodium bicarbonate; **HPMC**: Hydroxypropyl methylcellulose; **CaCl₂ · 2H₂O**: Calcium chloride dihydrate.

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PICTORIAL ABSTRACT



SUMMARY

In-situ gels has received extensive attention over the past few years as they are capable of undergoing rapid solution-to-gel transformation due to physico-chemical changes occurring in the eye. Hence the developed sulfacetamide sodium *in situ* gel formulation is a better alternate to existing conventional eye drops by virtue of improved precorneal residence time of dosage form at the site of administration, sustained action, better therapeutic efficiency and consequently reduces the dosing frequency with improved patient compliance and convenience.

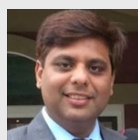
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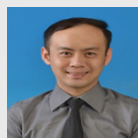
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