International Journal of Pharmaceutics and Drug Research
ISSN: 2347-6346
Available online at http://ijpdr.com

Original Research Article

FORMULATION AND EVALUATION OF POLYMERIC OPHTHALMIC DRUG DELIVERY SYSTEM CONTROLLED RELEASE OF SELECTED ANTIBACTERIAL DRUG

Akash Kumar, Akansha Verma, Aman Pawar, Aman Verma, Manisha Verma*
Oriental College of Pharmacy, Bhopal (M.P.)

***Correspondence Info:**
Manisha Verma
Oriental College of Pharmacy, Bhopal (M.P.)
Email:
manishaverma25@gmail.com

***Article History:**

Received: 02/02/2025
Revised: 19/02/2025
Accepted: 10/03/2025

ABSTRACT

The present study focuses on the formulation and evaluation of a polymeric in situ gel system for the controlled ocular delivery of Tobramycin, an antibacterial drug commonly used to treat eye infections. In situ gels offer advantages such as enhanced ocular residence time, sustained drug release, and improved patient compliance compared to conventional eye drops. Formulations were prepared using Pluronic F127 in combination with Carbopol 934 and HPMC 15 cps, and evaluated for clarity, drug content, pH, gelling capacity, viscosity, and in vitro drug release. All formulations (F1, F2, and F3) were found to be clear and had drug content ranging from 96.65% to 99.28%. The pH of the formulations was adjusted to 5.0 ± 0.1 to ensure ocular compatibility. Among the three, formulation F2 demonstrated optimal performance with the highest gelling capacity (+++), appropriate viscosity after gelation (2374 cps), and sustained drug release, reaching 99.14% over 5 hours. These findings suggest that the developed in situ gel system has the potential to enhance the therapeutic efficacy of Tobramycin by providing controlled and prolonged drug delivery in the ocular environment.

Keywords: In situ gel, Tobramycin, Ocular drug delivery, Pluronic F127, Controlled release, Ophthalmic formulation, Gelling capacity, Carbopol, HPMC, Viscosity, Antibacterial.

INTRODUCTION

Ocular drug delivery remains a significant challenge in pharmaceutical research due to the eye's unique anatomy and physiology, which limit the bioavailability of topically administered drugs. Conventional ophthalmic formulations like eye drops and ointments often result in poor therapeutic outcomes due to rapid precorneal elimination, nasolacrimal drainage, and low corneal permeability, leading to less than 5% of the administered dose reaching intraocular tissues (Mandal *et al.*, 2017).

To overcome these limitations, advanced drug delivery systems such as in situ gelling systems have gained increasing attention. These systems are liquid upon instillation but undergo a phase transition to a gel upon exposure to physiological stimuli such as temperature, pH, or ionic strength (Kandimalla and Donovan, 2005). In situ gels offer several advantages over conventional eye drops, including prolonged corneal contact time, improved patient compliance, sustained drug release, and reduced dosing frequency.

Tobramycin, an aminoglycoside antibiotic, is widely used in the treatment of ocular infections caused by *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and other

Gram-negative organisms. However, due to its hydrophilic nature and short residence time in the ocular cavity, frequent administration is required to maintain therapeutic levels (Varela-Garcia *et al.,* 2015). Incorporating tobramycin into an in situ gelling system could significantly enhance its ocular bioavailability by sustaining drug release and improving therapeutic efficacy.

Various polymers such as poloxamers, carbopol, hydroxypropyl methylcellulose (HPMC), and gellan gum are used to formulate these in situ gels. These polymers exhibit sol-gel transition properties under specific physiological conditions. For example, poloxamer-based gels transition at physiological temperatures, while carbopol responds to pH changes, and gellan gum reacts with cations present in the tear fluid (Srividya *et al.,* 2001). The combination of such polymers can optimize gelation time, viscosity, and drug release profiles, thereby improving formulation performance.

This study focuses on the formulation and evaluation of a polymer-based in situ gelling system containing tobramycin, aiming to achieve controlled drug release, enhanced ocular retention, and improved antibacterial efficacy. The developed system was characterized for various physicochemical properties, including gelling capacity, pH, viscosity, drug content, and in vitro drug release behavior.

MATERIALS AND METHODS

Formulation development of *In-situ* gel

All ingredients were passed through sieve no. 44. Tobramycin (0.5% and 0.1%) was dissolved in acetate buffer (pH 5.0), and the solution was cooled in an ice bath. Pluronic F127 was slowly added with continuous stirring and kept at 4°C for 24 hours to ensure complete dissolution. Afterward, Carbopol 934, HPMC 15 cps, and other excipients were added gradually with continuous stirring for 2–3 hours to avoid lump formation. The formulation was then sonicated to remove air bubbles and stored in sterile LDPE bottles under refrigeration for further use.

Evaluations of formulations

Appearance

Clarity is one of the most important characteristic features of ophthalmic preparations. All developed formulations were evaluated for clarity by visual observation against a black and white background (Saxena and Kushwaha, 2013).

Drug content

The assay of drug Tobramycin was performed by UV method. The calculation was based on calibration curve method using regression equation (Y=mx+c) (Viram and Lumbhani, 2012).

pH

pH is one of the most important parameter involved in the ophthalmic formulation. The two areas of critical importance are the effect of pH on solubility and stability (Shankar and Kalikonda, 2014). The pH of ophthalmic formulation should be such that the formulation will be stable at that pH and at the same time there would be no irritation to the patient upon administration of the formulation. Ophthalmic formulations should have pH range in between 5 to 7.4.

The developed formulations were evaluated for pH by using calibrated digital pH meter. For *In situ* gel pH 5.0 should be optimum because both the drug is stable at pH 3.5-5.0. Lowering the pH from 5.0 can causes irritation to eye and on raise the above 5 will

result in gelation of formulation due to presence of carbopol.

***In-situ* gelling capacity**

In situ gelling capacity determined by visual inspection. The formulation has been exposed to the physiological conditions of temperature and pH. Simulated tear fluid (STF) was prepared and warm up to 37^0C. Formulations were introduce into STF in a ratio of 1:2 Change in consistency of Formulations were visually inspected.

***In-vitro* drug diffusion study**

The *in vitro* release of drugs from the formulations was studied through cellophane membrane. The dissolution medium used was artificial tear fluid freshly prepared (pH 7.4). Cellophane membrane, previously soaked overnight in the dissolution medium, was tied to one end of a specifically designed glass cylinder (open at both ends and of 5 cm diameter).

A 1-ml volume of the formulation was accurately pipetted into this assembly. The cylinder was attached to the metallic driveshaft and suspended in 50 ml of dissolution medium maintained at 37±1°C so that the membrane just touched the receptor medium surface. The dissolution medium was stirred at 50 rpm using magnetic stirrer. Methodology Aliquots, each of 1-ml volume, were withdrawn at hourly intervals and replaced by an equal volume of the receptor medium (Costa and Lobo, 2001).

RESULTS AND DISCUSSION

The present study aimed to develop and evaluate Pluronic F127-based in situ gel formulations for the controlled ocular delivery of Tobramycin. The formulations were assessed for clarity, drug content, pH, gelling capacity, viscosity, and *in vitro* drug release to ensure suitability for ophthalmic application.

Clarity is a critical parameter for ophthalmic preparations, as visual transparency is essential for patient acceptability. All three formulations (F1, F2, and F3) were found to be clear (Table 2), indicating successful formulation without particulate matter or turbidity.

Drug content analysis showed that the formulations contained Tobramycin within acceptable limits, with values ranging from 96.65% to 99.28% (Table 3). F2 exhibited the highest drug content (99.28 ± 0.12%), reflecting uniform drug distribution and minimal loss during processing.

The pH of all formulations was initially slightly acidic (Table 4) but was successfully adjusted to approximately 5.0 ± 0.1, making it compatible with the physiological pH of the eye and thus minimizing irritation upon application.

The in situ gelling capacity (Table 5) varied among formulations. F2 showed the best gelling response ("+++") upon contact with simulated tear fluid, indicating optimal polymer concentration for gel formation. F1 and F3 showed weaker gelation ("+" and "++", respectively), suggesting suboptimal polymer ratios.

Viscosity measurements (Table 6) demonstrated a direct correlation between the concentration of Pluronic F127 and gel strength. F2, with 14% Pluronic F127, had the highest viscosity post-gelation (2374 cps), indicating effective gel formation at physiological conditions. The increase in viscosity after gelation is critical for prolonged ocular retention and sustained drug release.

In vitro drug release studies for formulation F2 (Table 7) revealed a sustained release profile, with nearly complete release (99.14%) achieved over 5 hours. This controlled release behavior supports the potential of the formulation to reduce dosing frequency and maintain therapeutic drug levels in the eye.

Table 1: Composition of different formulations of *In-situ* gel

S. No.	Ingredient (%)	Formulations		
		F1	F2	F3
1.	Tobramycin	0.3%	0.3%	0.3%
2.	Pluronic F127	10	12	14
3.	Carbopol 934	0.2	0.2	0.2
4.	HPMC 15cps	1.0	1.0	1.0
5.	EDTA	0.1%	0.1%	0.1%
6.	Benzalkonium Chloride	0.010%	0.010%	0.010%
7.	NaCl	q.s.	q.s.	q.s.
8.	Poly ethylene glycol	0.1%	0.1%	0.1%
9.	Acetate Buffer (pH 5.0)	50 ml	50 ml	50 ml

Table 2: Clarity test of *in situ* gel formulations

Formulation code	Clarity
F1	Clear
F2	Clear
F3	Clear

Table 3: Drug content analysis

Formulation	Drug Content (%)*
F1	98.12±0.25
F2	99.28±0.12
F3	96.65±0.16

Table 4: pH Determination

Formulation	pH	Adjust to
F1	4.5	5.0 ±0.1
F2	4.3	5.0 ±0.1
F3	4.7	5.0 ±0.1

Table 5: *In situ* gelling capacity of *In situ* gel formations

Formulation code	*In situ* gelling capacity
F1	"+"
F2	"+++"
F3	"++"

Table 6: Comparative viscosity* of *In situ* formulation

Formulation code	% of Pluronic F 127	Viscosity of solution (in cps)	Viscosity after galation
F1	10	658	2250
F2	14	798	2374
F3	12	698	2310

Table 7: *In vitro* drug release profile of Tobramycin from *in situ* formulation F2

Time (h)	Cumulative% Drug Release
0.5	13.25
1	29.98
1.5	49.98
2	72.23
2.5	83.32
3	91.15
4	96.65
5	99.14

CONCLUSION

Among all formulations, F2 was found to be optimal, showing superior clarity, highest drug content, excellent gelation ability, appropriate viscosity, and sustained drug release. These findings suggest that a Pluronic F127-based in situ gel system can serve as an effective ocular drug delivery platform for Tobramycin, improving patient compliance and therapeutic outcomes.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

REFERENCES

- Bauer, A.W., Kirby, W.M., Sherris, J.C. & Turck, M. (1966) Antibiotic susceptibility testing by a standardized single disk method. *American Journal of Clinical Pathology*, 45, 493–496.
- Bhalerao, S.A., Kelkar, T.S. & Bhalerao, K.S. (2013) Phytochemical and pharmacological profile of *Cassia auriculata* Linn: An overview. *International Journal of Pharmacy and Pharmaceutical Sciences*, 5, 33–36.
- Devi, B.P., Boominathan, R. & Mandal, S.C. (2003) Evaluation of antipyretic potential of *Cleome viscosa* Linn. (Capparidaceae) extract in rats. *Phytomedicine*, 10, 521–524.
- Kokate, C.K.E. (1994). *Practical Pharmacognosy*, 4th edn, *Vallabh Prakashan*: 112,120.
- Kokilavani, R. et al. (2009) Hepatoprotective and antioxidant activity of *Cassia auriculata* flowers against paracetamol-induced liver injury in rats. *Journal of Ethnopharmacology*, 123, 292–296.
- Mishra, A.G., Singh, R., Meha, P. & Parkhe, G. (2017) Determination of total phenolic, flavonoid content, antioxidant and antimicrobial activity

of *Gloriosa superb* seed extract. *Asian J. Pharm. Educ. Res*, 6, 12–17.

- Mukherjee, P.K. (2007). "Quality Control of Herbal Drugs", 2nd edn, Business Horizons, 2007, 2–14.
- Nadkarni, K.M. (2002). *Indian Materia Medica*, Vol. 1. Popular Prakashan.
- Rajagopal, K. & Sasikala, C. (2004) Antihyperglycemic and antihyperlipidemic effects of *Nymphaea stellata* flowers in alloxan-induced diabetic rats. *Ancient Science of Life*, 24, 55–61.
- Ravikumar, V., Shivashangari, K.S. & Devaki, T. (2005) Effect of *Cassia auriculata* leaf extract on lipids in rats with alcoholic liver injury. *Asia-Pacific Journal of Clinical Nutrition*, 14, 366–373.