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# FORMULATION AND CHARACTERIZATION OF A NOVEL PH-TRIGGERED *IN-SITU* GELLING OCULAR SYSTEM CONTAINING AMOXICILLIN

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***Abstract***

*The present research work deals with the formulation and evaluation of in-situ gelling system based on sol-to-gel transition for ophthalmic delivery of an antibacterial agent amoxicillin, to overcome the problems of poor bioavaila-bility and therapeutic response exhibited by conventional formulations based a sol-to-gel transition in the cul-de-sac upon instillation. Carbopol 934 was used as the gelling agent in combination with HPMC and HPMC E15 which acted as a viscosity enhancing agent. The prepared formulations were evaluated for pH, clarity, drug content, gelling capacity, bioadhesive strength and in-vitro drug release. In-vitro drug release data of optimized formulation (F6) was treated according to Zero, First, Korsmeyer Peppas and Higuchi kinetics to access the mechanism of drug release. The clarity, pH, viscosity and drug content of the developed formulations were found in range 6.0-6.8, 10-570cps, 82-98% respectively. The gel provided sustained drug release over an 8 hour period. The developed formulation can be used as an in-situ gelling vehicle to enhance ocular bioavailability and the reduction in the frequency of instillation thereby resulting in better patient compliance.*

***Key Words:*** *In-situ gelation; Gatifloxacin; Carbopol 934; HPMC K15M.*

**INTRODUCTION:**

Ophthalmic drug delivery is one of the most attrac-tive and challenging field facing the pharmaceutical scientist. A significant challenge to the formulator is to circumvent the protective barriers of the eye without causing permanent tissue damage (Mitra, 2003). Most of the ocular treatments call for the topi-cal administration of ophthalmically active drugs to the tissues around the ocular cavity (Gorle and Gat-tani, 2009). The most conventional ocular dosage forms for the delivery of drugs are eye drops (solu-tion, suspension) and ophthalmic ointments. Short residence time, pulsed dosing of drug, frequent in-stillation, and large drainage factor are the limitation associated with conventional ocular do-sage form. Newer ocular drug delivery systems are being explored to develop extended duration and controlled release strategy (Rathore and Nema, 2009). Formulation of *in-situ* ocular gel of gatiflox-acin is a fourth generation fluoroquinolone deri-vative used to treat external infections of the eye, using biodegradable polymers is the approach to overcome the drawbacks of conventional eye prepa-rations (Zhidong *et al.,* 2006; Mishra *et al.,* 2008; Pundir *et al.,* 2009; Kalam *et al.,* 2009). Carbopols are mainly used in liquid or semisolid pharmaceutical formulations as suspending or viscosity increasing agents. Formulations include creams, gels and ointments for use in ophthalmic, rectal and topical preparations. HPMC is widely used in oral and top-ical pharmaceutical preparations as coating agent, film formers, rate controlling polymers for sustained release, stabilizing agents, viscositifier etc. (Ray-mond *et al.,* 2004; Edsman *et al.,* 1996).

**MATERIALS :**

Amoxicillin was obtained as a gift sample from Ranbaxy labs. Ltd., Guargon (India). Hydroxypropylmethyl cellulose (HPMC) and HPMC E15 were obtained from SD Fine Chemi-cals Limited, Mumbai, India and Carbopol 934 was obtained from Himedia Laboratories Pvt. Ltd., Mumbai, India. All other chemicals/reagents used were of analytical grade, available commercially and used as such without further processing. A UV/Vis spectrophotometer was used for drug analysis.

| Composition | F1 | F2 | F3 | F4 | F5 | F6 |
|---|---|---|---|---|---|---|
| **Amoxicillin** | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 |
| **Hpmc** | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 |
| **Hpmc e15** | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 |
| **Carbopol 934** | 1% | 1.2% | 1.4 % | 1.6% | 1.8% | 2.0% |

Each formulation contains 0.407g of citric acid; 1.125g of disodium hydrogen phosphate; 0.02g of benzalkonium chloride, 100ml purified water; all values are expressed in gram.

**Preparation of Formulations:**

Accurately weighed 0.1g of HPMC was dispersed in 50ml of purified water, HPMC e15 was added, carbopol 934 was sprinkled over this solution and allowed to hydrate overnight. The solution was stirred with an overhead stirrer and buffer salts were dissolved in the solution. amoxicillin was dissolved in small quantity of water, benzylkonium chloride (BKC) was added to this solution; the drug solution was added to the polymer solution. Purified water was then added to make up the volume to 100ml and the prepared formulations were sterilized in an autoclave at 121°C for 20 min . Formulation ingredients of formulation F1 to F6 was represented.

**Evaluation parameters:**

**Physical appearance and pH:**

The formulations were light yellowish in color and clear. The pH value of all the prepared formulations ranged from 6.0 to 6.8, which is considered acceptable to avoid the risk of irritation upon application to the eye. Physicochemical data shows pH, clarity, viscosity and gelation capacity of the prepared gels.

**Viscosity & gelling capacity :**

The two main fundamentals of gelling system are viscosity and gelling capacity. The viscosity of the different formulations was compared. The viscosity was directly dependent on thepolymeric content of the formulations. The data indicated that the viscosity increased with increase in concentration of HPMC e15 and carbopol 934 (1 to 2%). F6 showed the maximum viscosity of 510cps at 100rpm (HPMC:HPMC e15M:Carbopol 934 was 1:1:2) whereas the minimum viscosity at 100 rpm was shown by F1(HPMC:HPMC e15: Carbo-pol 934 was 1:1:1). Except for the formulations F1, F2, F4, all the formulations gelled instantaneously on addition to the simulated tear fluid and extended for few hours. The *in-situ* formed gel should preserve its integrity without dissolving or eroding for prolonged period to facili-tate sustained release of drugs locally.

| Formulation | pH | Clarity | Viscosity in cps at 100 rpm | Gelation Capacity |
|---|---|---|---|---|
| **F1** | 6.8 | Clear | 10 | + |
| **F2** | 6.4 | Clear | 30 | + |
| **F3** | 6.2 | Clear | 75 | ++ |
| **F4** | 6.1 | Clear | 220 | ++ |
| **F5** | 6.5 | Clear | 30 | + + |
| **F6** | 6.3 | Clear | 60 | + |

**Drug content and in-vitro release studies :-**

On the basis of physicochemical properties (viscosi-ty and gelation capacity) nine formulations (F3, F4, F5) were selected and evaluated for drug content and *in-vitro* dissolution. The drug content of all the formulations was in range (82-98%). the cumulative amount of amoxicillin released versus time profiles for different drug-containing solutions. In the case of formulation F6, approximately 74% of drug was released from the solution (1% HPMC, 1% HPMC e15, 2% Carbopol 934 1:1:22) after 90 min. This indicates that formulation 6 has a better ability to retain drugs than the individual polymer solution. These results also suggest that the HPMC. HPMC e15, Carbopol 934 aqueous system can be used as an *in-situ* gel-forming system for ophthalmic drug delivery systems. The release of drug from these gels was characterized by an initial phase of high release (burst effect). However, as gelation proceeds, the remaining drug was released at a slower rate followed by a second phase of moderate release.

**Kinetics of release :**

The *in-vitro* release profiles were fitted to various kinetic models in order to find out the mechanism of drug release. The rate constants were calculated from the slope of the respective plots. High correlation (R2=0.9031) was observed in the Higuchi plot rather than first-order (R2=0.3273) and zero-order (R2=0.6485) models. The drug release was proportional to square root of time, indicating that the drug release from *in-situ* gel was diffusion con-trolled. The data obtained was also fit in Korsmeyer-Peppas model in order to find out n value, which describes the drug release mechanism. The n value (0.8029) obtained from Korsmeyer-Peppas was more than 0.5, which indicated that the mechanism of the drug release was Anomalous and Non Fickian diffusion controlled.

**CONCLUSION:**

HPMC, HPMC e15, Carbopol 934 ocular *in-situ* gel of amoxicillin showed appreciable gel forming properties on application in eye. The gels were found to be uniform, clear, viscous and bioadhesive. On the basis of *in-vitro* drug release, drug content and gelation capacity studies, it could be concluded that amoxicillin could be successfully administered through gel forming controlled release ocular formulation for treatment of eye infections and also important is the ease of ad-ministration afforded and decreased frequency of administration resulting in better patient acceptance.

**REFERENCES :**

1 Doijad, R.C., Manvi, F.V. Malleswara Rao, V.S.N. Alase, P. Sustained Ophthalmic Delivery of Gatifloxacin from insitu Gelling System. Indian Journal Pharmaceutical Sciences, 68; 2006:814-818.

2 Edsman, K., Carlfors, J. Harju, K. (1996). Rheological evalua-tion and ocular contact time of some carbomer gels for ophthalmic use. International Journal of Pharmaceutics, 137;1996: 233-241.

3 Gorle, A.P., Gattani, S.G. Design & Evaluation of po-lymeric ocular drug delivery system. Chemical & Pharmaceutical Bulletin, 57; 2009: 914-919.

4 Mohan, E.C., Kandukuri, J.M. Allenki, V. Preparation and Evaluation of In-Situ-Gels for Ocular Drug Delivery, Journal of Pharmacy Research. 2(6);2009: 1089-1094.