IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

# Ciprofloxacin Ocuserts: Design, Formulation and Evaluation

**[1]Prajwal D. Shrirao, [2]Navnath S. Rathod, [3]Ajwita S. Kale, [4]Nikita P. Aware,**
[1]Lecturer, [2] Lecturer, [3] Lecturer, [4]Head of Department,
[1]Department of Pharmacology
[1]Advika college of pharmacy and research centre, Ansing, Washim, India

**ABSTRACT:**

The main aim of the present study is to formulate an effective ocusert of Ciprofloxacin (an anti-biotic drug), which can produce a better ocular therapy against ocular bacterial infections. Conjunctivitis, keratitis, and keratoconjunctivitis are just a few examples of the eye infections that can be treated with ciprofloxacin hydrochloride, a fluoroquinolone antibiotic. By using different polymers in various ratios and combinations, including Poly Vinyl Alcohol (PVA), Hydroxy Propyl Methyl Cellulose (HPMC), Methyl Cellulose (MC), and Hydroxy Ethyl Cellulose (HEC), Ciprofloxacin Hydrochloride Ocuserts were made with the goal of extending the contact time, achieving sustained release, reducing the frequency of administration, improving patient compliance, and enhancing therapeutic efficacy. Here, I'm using hydroxyl methyl cellulose, which is 15cps grade, low viscosity methyl cellulose, and warm water soluble poly vinyl alcohol. The prepared ocuserts' physico-chemical properties were assessed for sterility testing, ocular irritation studies, moisture absorption, moisture loss, thickness, weight variation, folding endurance, and surface pH. Using a bovine cornea (semi permeable membrane) Franz diffusion cell, the in vitro drug release was investigated, and the maximum absorbance at 274 nm was checked. A zero order release formulation FB2 is sterilized by exposing UV radiation and subjected to *In vivo* studies. Ocular toxicity was also carried out for the formulation FB2. IR spectral observation show there is no interaction of drug with polymer which indicates the intactness of drug in formulation.

**KEYWORDS:** Ciprofloxacin, ocuserts, bovine cornea, Franz diffusion cell, keratoconjunctivitis.

**INTRODUCTION:**

To reduce the potential of eye injury from high blood concentrations of the medicine, which is not intended, local therapy is typically employed instead of systemic therapy. The eye's particular architecture, physiology, and biochemistry make it immune to outside chemicals, making it a continuing struggle for formulators to get beyond the eye's protective barriers without causing long-term tissue damage..[1]

Traditionally, eye drops and eye ointments have been used as ocular dose forms. Both of these dosage forms have drawbacks, such as frequent administration, low absorption, and medicine drainage through tears and nasal lachrymal fluid. Patient compliance is increased by including the medication into ocuserts because frequent administration is reduced and the drug's bioavailability is increased. In order to increase the bioavailability of medications, various innovative ocular drug delivery systems were created. In situ gelling polymer, microspheres, nanoparticles, liposomes, and ocular inserts are some of these formulations. Ocular inserts, which are solid devices inserted in the eye's cul-de-sac, have many advantages over liquid formulations.[2]

Ciprofloxacin hydrochloride (HCl) is a new 8-methoxy derivate of fluoroquinolones with enhanced activity *invitro* against gram positive bacteria and maintenance of activity against gram negative bacteria. It is an antiinfective agent useful in the treatment of eye infection such as bacterial conjunctivitis, keratitis and keratoconjuctivitis.

The eye drop dosage form is convenient to use, but the majority of the drug is diluted by tears and quickly washed out of the sac by continuous tear flow. This can be prevented by using an insert, which can significantly increase the therapeutic efficacy of ophthalmic drugs. [3,4] Researchers have tried using polyvinyl alcohol, hydroxy ethyl cellulose, hydroxypropyl methylcellulose (HPMC), and methylcellulose (MC) to prepare ophthalmic inserts using the solvent casting method. [5]

In the present study, an attempt has been made to formulate ophthalmic insert of ciprofloxacin hydrochloride using hydroxypropyl methylcellulose (HPMC), methylcellulose (MC) and polyvinyl alcohol (PVA) and hydroxy ethyl cellulose (HEC) as polymers and glycerol as plasticizer by solvent casting method.[6]

## MATERIAL AND METHODS:

### Materials

Ciprofloxacin hydrochloride, Hydroxypropyl methylcellulose (HPMC), methylcellulose (Low viscosity) and polyvinyl alcohol were obtained from Kamalprakash Pharmacy College and Research Centre, Kherda. All other reagents and solvent used were of analytical grade.

Table 1: Composition of ingredients

| Ingredients | $FA_1$ | $FA_2$ | $FA_3$ | $FB_1$ | $FB_2$ | $FB_3$ | $FC_1$ | $FC_2$ | $FC_3$ | $FD_1$ | $FD_2$ | $FD_3$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ciprofloxacin (mg) | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| Glycerol (mg) | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 |
| HPMC (gm) | 0.75 | 1 | 1.25 | - | - | - | - | - | - | - | - | - |
| HEC (gm) | - | - | - | 0.75 | 1 | 1.25 | - | - | - | - | - | - |
| PVA (gm) | - | - | - | - | - | - | 0.75 | 1 | 1.25 | - | - | - |
| MC (gm) | - | - | - | - | - | - | - | - | - | 0.75 | 1 | 1.25 |
| Water (ml) | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

**The preparation ocuserts involved three steps**

**1. Preparation of the drug containing reservoir film of hydrophilic polymers:**

For the formulation of the reservoir film containing the medication, ciprofloxacin and respected polymers were dissolved in 10 ml of distilled water to create a polymeric solution. In a Teflon-coated petri dish, the solutions were poured into a glass ring. The solvent was placed inside an oven and allowed to evaporate.

**2. Preparation of rate controlling films:**

To prepare the rate controlling films, In an ethanol/acetone mixture, plasticizer and hydrophobic polymer were dissolved. In a Teflon-coated petri plate, a glass ring containing the solutions was placed.

**3. Placing rate controlling films around the drug reservoir and sealing them to obtain ocular inserts:**

Circular shaped ocular inserts were cut out of medicated reservoir film with the help of a cork borer. These ocular inserts were placed on a rate controlling membrane and another rate controlling membrane was kept over it. The two rate controlling membranes containing the reservoir film between them were placed over a beaker saturated with ethanol / acetone vapours for 1-2 minutes the ocusert were stored in an airtight container under ambient conditions.[6]

**Evaluation tests of ocuserts**

The formed films were cut in to circular discs and evaluated for following parameters

**1. Weight variation:**

For uniformity of the weight, 3 films from each batch were taken randomly and their weights were determined using electronic balance.

**2. Thickness:**

The thickness of the ocuserts was a screw gauge and the average of three films thickness was calculated.

**3. Content uniformity:**

Three films were taken from each batch and dissolved or crushed in 10ml of isotonic phosphate buffer (pH 7.4) in a beaker and were filtered in to 25ml volumetric flask and the volume was made up to the mark with buffer. One ml of the above sample was withdrawn and the absorbance was measured by UV-VIS spectrophotometer at 287.6nm after suitable dilutions.

**4. Percentage moisture absorption:**

Three strips were weighed accurately and placed in a desiccator having aluminum chloride the strips were reweighed after 3 days and percentage moisture absorption was calculated using the following formula

$$\% \text{ Moisture absorption} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

**5. Percentage of moisture loss:**

Some procedure as above was used but fixed anhydrous calcium chloride or silica gel was placed instead of saturated aluminum chloride

$$\% \text{ Moisture loss} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

**6. Folding Endurance:**

It is determine by repeatedly folding a small strip of the film until it breaks. The number of times it is folded before it breaks in the folding endurance.

**7. Ocular irritation test:**

The potential ocular irritation and/or damaging effects of the ocuserts under test were evaluated by observing them for any redness, inflammation (or) increased tear production. Formulation was tested on five rabbits by placing the inserts in the cul-de-sac of the left eye.

**8. Surface pH:**

The inserts were allowed to swell in closed petridish at room temperature for 30 minutes in 0.1 ml of bi distilled water. The swollen device was removed and placed under digital pH meter (Elico, India) to determine the surface pH.

**9. Sterility test:**

In the present study, all films were sterilized separately by exposing them to UV radiation for 30minutes. The irradiated ophthalmic films were tested for their sterility as per the Indian Pharmacopoeia to detect the presence of viable forms of bacteria, fungi, and yeast in or on sterilized preparations. The tests were carried out under aseptic conditions to avoid accidental contamination of the product during the test.

**10. Drug release study:**

Ocuserts were cut in to the required size and placed between the donor and receptor compound of a diffusion cell. The bovine cornea act as semi permeable membrane. That was placed as support below the ocuserts film phosphate buffer pH 7.4 was taken in a receptor compartment and rotated at 20 rpm. The set up was run for 5 hrs with sampling interval of ½ hr, 1, 2, 3,4, 5hr. all the sampling time with whole medium was replaced with fresh medium the amount released was calculated by using spectrophotometer.

## RESULTS AND DISCUSSION:

**1. Weight variation:**

Weight variation test was performed. The weights of the ocuserts were between 7mg to 17mg. Hence all ocuserts formulations passed weight variation test. Results are shown in table no.2.

**2. Thickness:**

Thickness of all the formulations was between 0.12mm to 0.27mm. Results are shown in table no.2.

Table 2: Evaluation test of formulated Ocuserts

| Formula No. | Weight variation (mg) | Thickness (mm) | Drug content (%) | % of Moisture absorption | % of Moisture loss | Folding endurance | Surface pH |
|---|---|---|---|---|---|---|---|
| FA1 | 7.9 | 0.22 | 85 | 21.43 | 22.12 | 189 | 6.4 |
| FA2 | 8.1 | 0.25 | 90 | 5.55 | 16.66 | 198 | 6.3 |
| FA3 | 10.5 | 0.26 | 100 | 15.38 | 11.11 | 198 | 6.9 |
| FB1 | 13.8 | 0.19 | 100 | 10 | 15.3 | 220 | 6.6 |
| FB2 | 14 | 0.24 | 75 | 15.38 | 14.2 | 235 | 6.7 |
| FB3 | 17 | 0.26 | 100 | 7.69 | 11.7 | 233 | 6.4 |
| FC1 | 7.8 | 0.12 | 70 | 11.11 | 14.28 | 230 | 6.3 |
| FC2 | 8.2 | 0.18 | 75 | 5.55 | 33.38 | 256 | 6.5 |
| FC3 | 8.5 | 0.22 | 80 | 12.5 | 10 | 285 | 6.5 |
| FD1 | 6 | 0.22 | 75 | 7.14 | 12.5 | 180 | 7 |
| FD2 | 7 | 0.23 | 80 | 5 | 14.2 | 185 | 6.5 |
| FD3 | 9.3 | 0.20 | 80 | 10 | 6 | 182 | 6.3 |

Table 3: Cumulative drugs release of the various formulations

| TIME IN Hrs | FA1 | FA2 | FA3 | FB1 | FB2 | FB3 | FC1 | FC2 | FC3 | FD1 | FD2 | FD3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | HPMC | | | HEC | | | PVA | | | MC | | |
| 1 | 20.8 | 16.8 | 17.2 | 13.9 | 13.2 | 15 | 4.8 | 7.2 | 18.8 | 12.4 | 21.3 | 20.4 |
| 2 | 30.8 | 24.4 | 24 | 18.9 | 19.2 | 20 | 5.6 | 9.2 | 27.2 | 15.3 | 26.1 | 24.8 |
| 3 | 38.8 | 31.2 | 32.8 | 23 | 24.4 | 25.2 | 6.8 | 14 | 30.4 | 20.16 | 3.2 | 31.2 |
| 4 | 47.2 | 42 | 42.8 | 26.9 | 29.6 | 28.4 | 8.4 | 18.8 | 36.4 | 26.6 | 40.4 | 38.4 |
| 5 | 52.4 | 49 | 49.6 | 30.2 | 34.8 | 36.76 | 10 | 20.2 | 44 | 30.7 | 46.4 | 46.4 |
| 6 | 58.4 | 57.6 | 58.6 | 34.6 | 41.6 | 42.68 | 12 | 28.4 | 50.8 | 36.4 | 54.8 | 57.2 |
| 24 | 73.2 | 75.92 | 76.4 | 47.4 | 66.1 | 57.56 | 49.28 | 58.88 | 75 | 63.40 | 79.88 | 82.4 |

**3. Drug content:**

Percentage drug content of all formulations was between 70 to 100%. The results are shown in table no.3.

**4. Percentage moisture absorption:**

Percentage Moisture absorption of all formulations was between 5% to 21.42%. Results are shown in table no. 2.

**5. Percentage moisture loss:**

Percentage Moisture loss of all the formulations was between 6% to 33.33%. Results are shown in table no.2.

**6. Folding endurance:**

Folding endurance measures the ability of a film to withstand rupture. The folding endurance is measured manually by folding the film repeatedly at a point until it broke; the breaking time were considered as the highest for $FC_3$ (285) and lowest for $FD_1$ (180) are shown in table no.2. The folding endurance values of the films were found to be optimal and therefore, the films exhibited good physical and mechanical properties.

**7. Surface pH:**

The surface pH of prepared inserts was found be in range of 6.3 to 7. This indicated that the prepared inserts would not alter the pH of the tear fluid in the eye. Results are shown in table no.2.

**8. *In vitro* drug release:**

Ocuserts were cut in to the required size and placed between the donor and receptor compound of a diffusion cell. The bovine cornea act as a semi permeable membrane was placed as support below the ocuserts film phosphate buffer pH 7.4 was used as the meadium. The set up was run for 24 hrs with sampling intervals of 1, 2, 3, 4, 5, 6 and 24hrs (20ml) at 20rpm. The amount of drug released was determined by measuring absorbance's using UV spectrophotometer. The results are shown in the table no.3.

**CONCLUSION:**

These findings show that the ciprofloxacin formulation FB2 (drug with a 1:4 hydroxy ethyl cellulose ratio) has substantially influenced the physicochemical characteristics and permeability properties of the polymer films. There is noticeable strength and safety in these films. Maintaining the initial release while reducing the frequency of administration could lead to better patient compliance. We can infer from the current study that the release rate of a drug from an ocusert can be controlled or changed by using a different polymer in the rate-regulating membrane. These films can therefore be included in ophthalmic formulations.

**REFERENCES:**

1. Sreenivas S, Hiremath S, Godbole A. Ofloxacin Ocular Inserts: Design, Formulation and Evaluation. 3 2006; 5 (2) :159-0 URL: http://ijpt.iums.ac.ir/article-1-90-en.html
2. Ramakanth S, Madhusudhana C, et al Design and evaluation of Diclofenac sodium Ocuserts. International Journal of Pharma Tech Research. 1 (4); Oct – Dec 2009: 1229 – 1223.
3. Karatas A, Baykara T. Studies on Indomethacin insert prepared by water soluble polymers: The relation between dissolution rate and swelling behavior. Ilfarmaco. 56; 2001: 197-202.
4. Patel UL, Chotai NP, Nagda CD, Patel MP, Patel KN. Formulation and in vitro evaluation of moxifloxacin hydrochloride ophthalmic inserts, International Journal of Pharmaceutical Research, 2009; 1 (1), 23-30.
5. Gadhave MV, Pawar SD, Khilari SS, Gaikwad DD, Jadhav SJ. Formulation and Evaluation of Moxifloxacin Ocusert, International Journal of Pharmaceutical and Clinical Research 2016; 8(12): 1610-1615 ISSN- 0975 1556
6. Kaushal K, Mohd F, Nida P, Preparation and Evaluation of Ocuserts for Increasing the Bioavailability of an Antifungal Drugs, Acta Scientific Pharmaceutical Sciences (ISSN: 2581-5423) Volume 6 Issue 6 June 2022DOI: 10.31080/ASPS.2022.04.0609