RESEARCH ARTICLE

DESIGN AND EVALUATION OF POLYMERIC OCULAR DRUG DELIVERY SYSTEM FOR CONTROLLED DELIVERY OF CIPROFLOXACIN HYDROCHLORIDE

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ABSTRACT

The field of Ocular drug delivery is one of the interesting and challenging endeavors facing the pharmaceutical scientist. The most frequently used dosage forms i.e. ophthalmic solutions and suspensions are compromised in their effectiveness by several limitations, leading poor ocular bioavailability. Ocuserts (or) Ophthalmic inserts are sterile preparations containing drug as dispersion or as solution in the polymeric support. Ocusert helps to improve ocular bioavailability by increasing the duration of contact with corneal tissue, thereby reducing the frequency of administration. Ciprofloxacin is a fluoroquinolone antibacterial drug effective in the treatment of bacterial conjunctivitis. The ciprofloxacin hydrochloride ocuserts were then evaluated for their physicochemical parameters like uniformity of thickness, weight, drug content and in vitro release pattern. It can be concluded that this ocular inserts formulation can be a promising for controlled release formulation.
Keywords: Ocusert, Ciprofloxacin hydrochloride, In vitro release pattern, controlled release.

INTRODUCTION

Eye is most interesting organ due to its drug disposition characteristics. Generally, topical application of drugs is the method of choice under most circumstances because of its convenience and safety for ophthalmic chemotherapy.[1] A significant challenge to the formulator is to circumvent (bypass) the protective barriers of the eye without causing permanent tissue damage.[2] Development of newer, more sensitive diagnostic techniques and novel therapeutic agents continue to provide ocular delivery systems with high therapeutic efficacy. Conventional ophthalmic formulations like solution, suspension, and ointment have many disadvantages which result into poor bioavailability of drug in the ocular cavity.

The specific aim of designing a therapeutic system is to achieve an optimal concentration of a drug at the active site for the appropriate duration. Ocular disposition and elimination of a therapeutic agent is dependent upon its physicochemical properties as well as the relevant ocular anatomy and physiology. A successful design of a drug delivery system, therefore, requires an integrated knowledge of the drug molecule and the constraints offered by the ocular route of administration.[3]The various approaches that have been attempted to increase the bioavailability and the duration of the therapeutic action of ocular drugs can be divided into two categories. The first one is based on the use of sustained drug delivery drugs. The second involves maximizing corneal drug absorption and minimizing precorneal drug loss.[3] Ideal ophthalmic drug delivery must be able to sustain the drug release and to remain in the vicinity of front of the eye for prolong period of time. Consequently it is imperative to optimize ophthalmic drug delivery; one of the ways to do so is by addition of polymers of various grades, development of ocusert using erodible or non-erodible insert to prolong the precorneal drug retention.[4]

The zero order kinetics[5] characteristics a sustained release type of delivery system whereby the drug is held in a reservoir and is released into the tear film at constant rate to provide a constant concentration in the corner which provides greatly improved compliance. Ciprofloxacin ocuserts [6] were also prepared by using polymers. Hence, the present study aimed to prepare Ciprofloxacin hydrochloride ocuserts.

MATERIALS AND METHODS:

Ciprofloxacin Hydrochloride was obtained as gift sample from Dhana pharmaceuticals Pvt. Ltd, Ambarnath, India. Hydroxy Propyl Methyl Cellulose (E-50), Poly vinyl pyrrolidone (K-30), Poly vinyl alcohol, Poly ethylene glycol- 400, Glycerine were purchased from SD Fine chemicals, Mumbai, India. All other reagents and solvent used were of analytical grade. Cellophane membrane and distilled water were the other materials used.

Instruments used:

UV-spectrophotometer (shimadzu lab.), Digital oven**,** **Verinier** calliper's scale and desiccator (Bros scientifics limited) were the instruments used for this study.

Method:

Standard calibration curve: [7]

Accurately weighed 100 mg Ciprofloxacin Hydrochloride was dissolved in 0.1N HCl in 100 ml calibrated flask to get the stock solution . From this stock solution aliquots of 2, 4, 8, 10, 12, & 14 ml were withdrawn and further diluted to 100 ml with 0.02N HCl to obtain a suitable concentrations range. The absorbance of the solutions was measured at 280 nm by using UV spectrophotometer. A graph of Concentration vs. Absorbance was plotted.

Preparation of Ocusert: [7]

Ciprofloxacin hydrochloride was accurately weighed and dissolved in distilled water. Pre-determined HPMC, PVA and PVP was weighed and dissolved in distilled water separately in beaker. Then clear drug solution was poured into polymer solution with constant stirring to get a homogenous solution. Required amount of PEG-400 was added and mixed well. The resulting solution was casted over the petri plate surface.The method used here was solvent casting method.

Table no.1 Composition of Ciprofloxacin ocular inserts

Ingredients	MHF1	MHF2	MHF3	MHF4
Ciprofloxacin HCL	100 mg	100 mg	100 mg	100 mg
Poly vinyl pyrrolidone (K-30)	400 mg	600 mg	400 mg	600 mg
Hydroxy Propyl Methyl Cellulose (E-50)	600 mg	400 mg	-	-
Poly vinyl alcohol	-	-	600 mg	600 mg
Poly ethylene glycol- 400	0.5 ml	0.5 ml	0.5 ml	0.5 ml
Glycerine	25mg	25 mg	25mg	25mg

EVALUATION OF OCUSERT:

% Moisture absorption: [7]

It was carried out to check the physical stability or integrity at wet condition. The prepared ocusert was accurately weighed and placed in a dessicator containing aluminium chloride with 79.5% moisture and it was kept for 3 days. The ocusert was taken out and reweighed after 3 days. The amount of moisture absorbed by the ocusert was calculated by using the following formula.

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

% Moisture loss: [11]

The prepared ocusert was initially weighed and kept in a dessicator containing fused anhydrous calcium chloride and it was kept for 3 days. The ocusert was taken out and reweighed after 3 days. The % of moisture loss was calculated by using the following formula.

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

Uniformity of thickness: [8]

The thickness of the insert was determined using a Vernier caliper at five separate points of each insert. For each formulation, five randomly selected inserts were tested for their thickness.

Uniformity of weight: [9, 10]

From each batch, five inserts were taken out and weighed individually using digital balance (Asco, India). The mean weight of the insert was noted.

Drug content: [11]

Five films were taken from each batch and dissolved or crushed in 10 ml of 0.1N in a beaker and were filtered into 25 ml volumetric flask and the volume was made up to the mark with buffer. 1 ml of the above sample was withdrawn and the absorbance was measured by UV spectrophotometer 280 nm after suitable dilutions.

In vitro drug release studies: [12, 13]

The in vitro drug release from the different ocular insert was studied using the classical standard cylindrical tube fabricated in the laboratory (bi-chambered donor receptor compartment model). A simple modification of glass tube of 15 mm internal diameter and 100 mm height. The diffusion cell membrane (prehydrated cellophane) was tied to one end of open cylinder, which acted as a donor compartment. An ocular insert was placed inside this compartment. The diffusion cell membrane acted as corneal epithelium. The entire surface of the membrane was in contact with the receptor compartment comprising of 12 ml of isotonic phosphate buffer (pH 7.4) in a 100 ml beaker. The content of receptor compartment was stirred continuously using a magnetic stirrer and temperature was maintained at 37±0.5°C. At specific intervals of time, 1 ml aliquot of solution was withdrawn from the receptor compartment and replaced with fresh buffer solution. The aliquot was analyzed for the drug content using UV spectrophotometer at 280 nm after appropriate dilutions against reference using isotonic phosphate buffer pH 7.4 as blank.

Results and Discussion:

Uniformity of thickness

The thickness of ocular inserts (MHF1 to MHF4) was found to be in range of 0.148 mm to 0.154 mm as shown in (Table 2). The measured thickness of all the four formulations ensured uniformity in thickness.

Uniformity of weight

The weight ocular inserts were found to be in the range of 12.61 to 12.95 mg (Table 2). The uniformity of the weights of the films indicates good distribution of the drug, polymer and plasticizer.

Drug content

For the various formulations (MHF1 to MHF4), drug content was found to vary between 0.969 mg to 0.988 mg (Table 2). The estimation of drug content was found to be almost same.

% Moisture absorption:

For the various formulations (MHF1 to MHF4), % Moisture absorption was found to vary between 31.95 to 33.15 (Table 2). The % moisture absorption was more in formulation I.

% Moisture loss:

For the various formulations (MHF1 to MHF4), % Moisture loss was found to vary between 30.18 to 32.83 (Table 2). % moisture loss was more in formulation IV.

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Table 2: Physicochemical characteristics of various batches of ocular inserts

Formulation code	Weight* (mg)	Thickness* (mm)	Drug content* (mg)	Drug Content (%)	% Moisture absorption	% Moisture loss
MHF1	12.71	0.148	0.980	98.00	33.15	30.18
MHF2	12.95	0.162	0.988	98.80	32.44	30.32
MHF3	12.61	0.165	0.978	97.80	32.11	31.67
MHF4	12.76	0.154	0.969	96.90	31.95	32.83

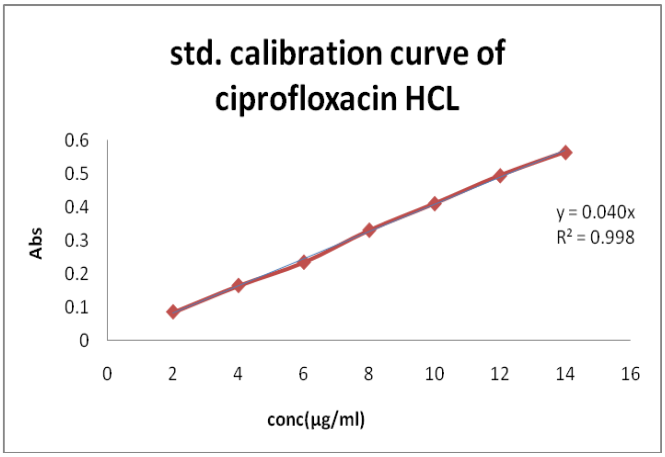

Figure 1: Standard calibration curve of ciprofloxacin

Table 3: In-vitro drug release studies

Time (hrs)	Cumulative drug release(MHF1)	Cumulative drug release (MHF2)	Cumulative drug release (MHF3)	Cumulative drug release (MHF4)
1	12.32	14.22	11.90	11.14
2	14.28	18.31	13.65	13.58
3	16.28	19.2	16.72	14.92
4	17.82	21.56	18.64	16.11
5	19.20	24.32	20.73	18.57
6	21.22	27.23	22.45	19.76
7	24.55	29.76	24.22	20.11
8	26.42	31.85	25.34	22.29
9	27.65	33.22	26.62	24.64
10	28.64	34.18	27.35	25.13
11	30.10	37.12	28.12	25.93
12	31.39	38.95	28.95	27.11

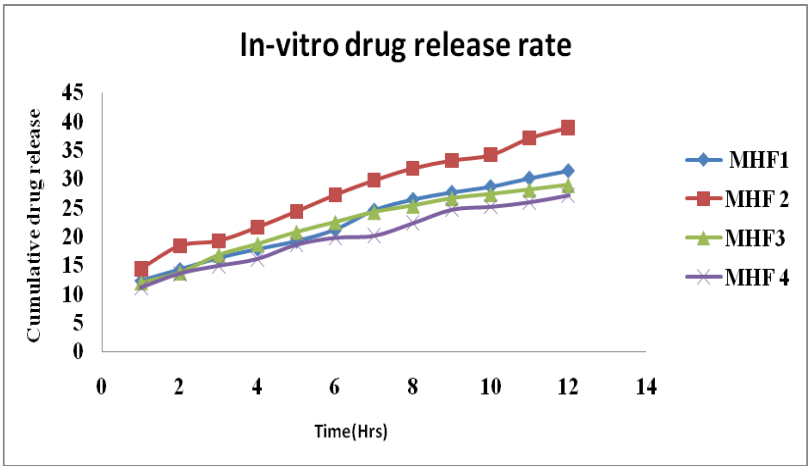

Figure 2: In-vitro drug release rate of all formulation

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The results indicate formulation II has better drug release through an artificial membrane over an extended period of 12 hours.

CONCLUSION

Various batches of Ciprofloxacin ocular inserts were prepared by solvent casting method and characterized. The formulation (MHF2) containing HPMC and PVP as polymer satisfied required pharmaceutical characteristics of ocular inserts and was found promising. The Ciprofloxacin ocusert is bio-degradable and would be able to offer benefits such as i.e., increasing residence time, prolonging drug release, reducing frequency of administration, and there by may help to improve patient compliance. The results indicate formulation II has better drug release through an artificial membrane over an extended period of 12 hours. However, their potential to improve ocular bioavailability in humans needs to be investigated further.

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