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Design, Optimization and Evaluation of Biocompatible Soluble Pilocarpine Loaded Drug Inserts for Glaucoma

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Abstract

Optic nerve impairment along with differences in the field of vision are defining characteristics of glaucoma, a progressive optic neuropathy. It is one of the main global causes of permanent blindness. Elevated intraocular pressure (IOP), which can be caused by overproduction or poor aqueous humor outflow, is the main risk factor for glaucoma. Even while a high IOP is a significant risk factor, some people can get glaucoma while having a normal IOP, which suggests that there may be more underlying causes such vascular insufficiency or genetic susceptibility. A thorough eye examination to evaluate the health of the optic nerve, visual field tests, and IOP measurement are usually required for the diagnosis. In order to stop the disease's progression and protect vision, treatment seeks to lower IOP. This thesis investigates the effectiveness of chitosan polymer-based sustained-release ocular medication delivery system, Pilocarpine HCl ocusert, in the management of glaucoma. Increased intraocular pressure which causes damage to the optic nerve is a sign of glaucoma, one of the major causes of permanent blindness. The Ocusert device releases pilocarpine HCl slowly over time, thereby increasing medicine absorption and retaining its therapeutic concentration in the eye. Reducing the frequency of administration while maintaining consistent treatment effects is the goal of this continuous delivery strategy. Through clinical trials and pharmacokinetic analysis, the study assesses the efficacy of the device, ocular tolerance, and patient compliance. The findings provide information for improving glaucoma treatment plans using cutting-edge medication delivery systems.

Keywords: Ocusert, glaucoma, Pilocarpine HCl, sustained release, chitosan polymer

1. INTRODUCTION

Irreversible blindness in the globe is glaucoma. In 2006, Quigley calculated that 80 million people would be impacted by the year 2020. According to Tham (2014), there will be 111.8 million glaucoma patients worldwide by 2040. Since glaucoma is primarily asymptomatic in its early stages, many people are unaware that they have the condition. About half of glaucoma patients in the industrialized world are unaware that they have the condition. As people age, glaucoma is becoming more common in a nonlinear way. There will be more patients with glaucoma in the future because to the growing senior population. A key factor is the population's growing education and digitization.

On the opposing side, patients' demands are rising as a result of the increased technological capabilities for illness detection and treatment. One aspect of managing glaucoma is having the ability to detect and treat the condition; the other aspect is patient behaviour. Like many chronic conditions, glaucoma has a low rate of adherence and persistence, which can cause the condition to worsen and ultimately cost more money. [1]

The clinical development of the central optic nerve injury during the development of glaucoma is depicted. Glaucoma in high as well as low blood pressure follows similar clinical courses. A normal optical nerve head; a significant 360 degree decrease in the follicular rim with a cylindrical visual field; and can expand vertical excavation dimension reflected in visual field defects.[2]

Specifically shaped and proportioned, ocuserts are sterilized articles with a solid or semisolid consistent behaviour, especially designed for ophthalmic use. Ocusert comprises three key components, generally: a rate-limiting membrane which ensures controlled drug release from the medicine reservoir, a protective outer ring for simplicity of handling and safe insertion, and a central drug reservoir where the drug is suspended in a polymer. Ocuserts prolong the time of corneal contact, diminish the frequency of administration, lengthen the duration of effect, and improve patient compliance. [2,3]

2. Materials and Methods

Pilocarpine HCl was purchase from Paras Engineers, New Delhi. Acetic acid and Chitosan were procured from CDH Private Limited.

2.1 Preparation of Ocular Insert

Solvent/casting technique was implemented for the preparation of insert. To create monolayer films, 3.5 millilitres of acetic acid and 10 millilitres of a pilocarpine hydrochloride water solution were combined. To ensure uniformity and stability of both the drug and polymer, 350 mg of chitosan was added to the mixture and this highly viscous dispersion was agitated with the help of magnetic stirrer over the night. The material was subsequently placed into concentric silicone-molded trays with specific 5x2 mm wells to create inserts containing pilocarpine, and it then dried at room temperature. Finally, the silicone-molded trays were carefully opened, and the inserts were stored to protect them from light and moisture in the air.

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Serial No.	Factor 1 A: Drug mg	Factor 2 B: Chitosan mg	Factor C: Acetic acid ml
1	30	300	4
2	40	300	3.5
3	30	350	3.5
4	40	350	3
5	30	350	3.5
6	30	400	4
7	30	400	3
8	30	350	3.5
9	40	350	4
10	30	300	3
11	20	350	3
12	30	350	3.5
13	30	350	3.5
14	40	400	3.5
15	20	400	3.5
16	20	300	3.5
17	20	350	4

Table 1: Formulation of ocular insert

2.2. Characterization of Insert

2.2.1. Weight Uniformity

The weight homogeneity of the ocuserts demonstrates how consistent its components are. Every batch has three ocusert weighed from it. Average weights are noted.[5]

2.2.2. Thickness

A micrometer screw gauge was used at five distinct positions on each insert to measure its thickness. Five inserts were chosen at random for thickness measurement for each formulation.

2.2.3. Folding Endurance

For the evaluation of folding endurance of the film, it was folded continuously in the same area until it was capable of being folded without breaking.[6]

2.2.4. In Vitro Drug Release

The Franz cell system was used to measure the release of Pilocarpine HCl in vitro. A membrane consisting of 0.45 μm pores made of cellulose acetate was utilized to divide the insert section from the chamber holding the receptor liquid (6.0 mL; PBS). We cultured glass cells at 37.0 ±
0.5 °C. PBS was taken out of the corresponding container at proper intervals, and an equal volume was supplied to keep the volume constant. The release of pilocarpine was measured using UV spectroscopy. Each Franz cell was given one insert, and throughout the experiment, care was taken to make sure the receptor liquid was in touch with the cellulose acetate membrane & moistened the insert.[7]

2.3. Ex Vivo Permeation Study

The goat's eyes were chosen specifically for the ex-vivo permeation investigation. For the investigation, a modified Franz diffusion cell was employed. Eyeballs of goats were obtained from a slaughterhouse and stored at 4°C in a standard saline solution (0.9% w/v). Every experiment was completed in an aseptic setting. After thoroughly cleaning the eyes with PBS, more tissue was removed. The implant was then inserted into the removed cornea, occupying up 1.5 cm of surface area, and positioned between the diffusion cell's acceptor and donor compartments. Buffer solution filled the lower compartment, and 1 mL of the samples were removed from there once the cornea from the donor compartment had permeated. The research was conducted between 37 and 50 rpm. Now, at certain intervals of time (2 hrs, 4 hrs, 6 hrs, 8 hrs, 10 hrs, and 12 hrs), The samples that had been penetrated were extracted from their acceptor compartment in a volume of 1 mL, and they were simultaneously replaced with an equal volume of PBS solution..[5]

3. RESULT

3.1. Weight Uniformity

Randomly 5 pilocarpine ocuserts were selected and stabilized at 25°C and 60% relative humidity for 24 hours. Each ocuserts were weighed individually using an analytical balance calibrated to ±0.1 mg. Average weight of the 5 ocuserts were calculated.
The uniformity of weight of pilocarpine ocuserts was found to be 21.264 mg.

3.2. Thickness

The mean thickness of these five ocuserts was discovered to be 0.212 mm, after digital vernier gauges with the minimum number of 0.01 mm have been employed to measure the ocuserts' thickness at various spots on them.

3.3. Folding Endurance

folding endurance tester specifically designed for thin, flexible materials like ocusert was used to measure and found to be 95.

3.4. In Vitro Drug Release

Here is the % drug release data in graph form for in-vitro drug release rate of Pilocarpine ocuserts developed using chitosan and acetic acid, with a cellulose acetate membrane (0.45 µm): and the data is found to be 90% of drug releases in 10 hrs.

3.5. Ex Vivo Permeation Study

Three drug-permeated samples were measured using UV at 214 nm at various times. 90% of release within 8 hours after the loaded pilocarpine insert is loaded. The percentage of the drug released and the time in hours were shown on an illustration of the average permeability research.

Figure1:

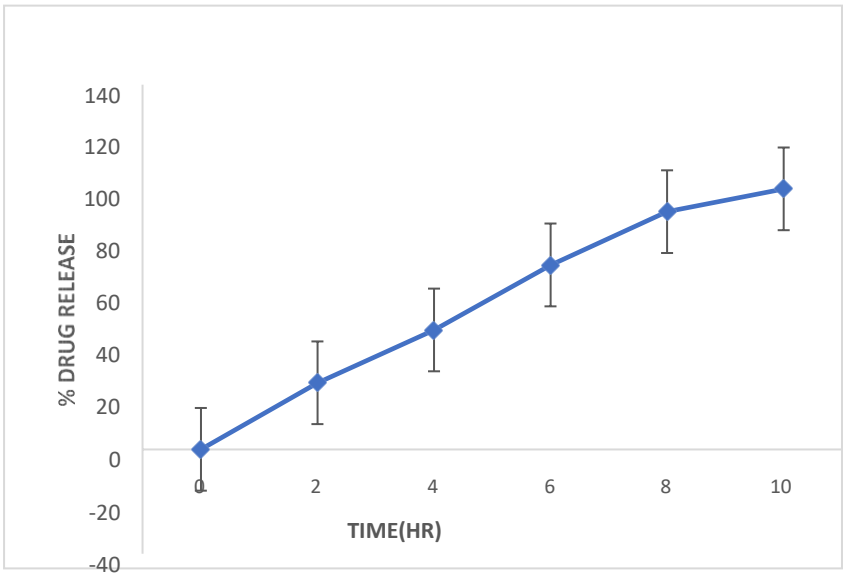
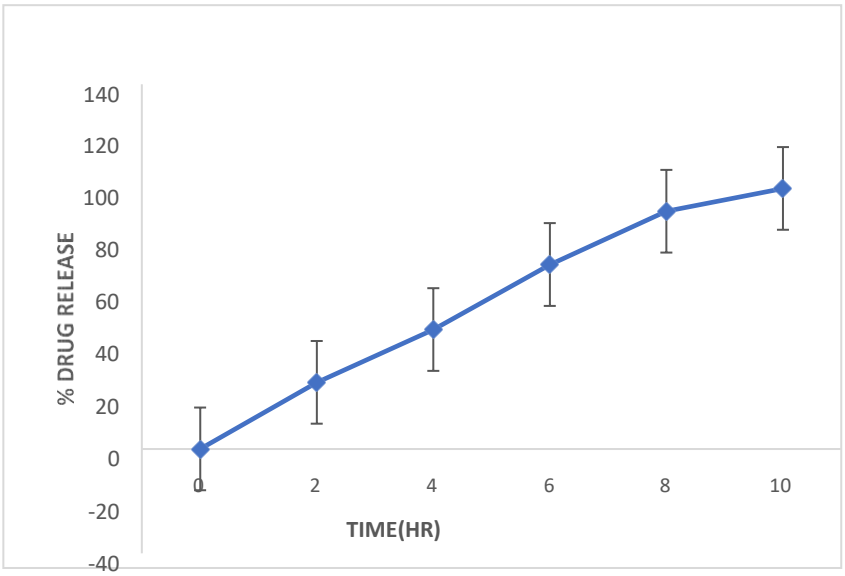


Figure 2:


140
120
100
80
60
40
20
0
-20
-40
% DRUG RELEASE
0
2
4
6
8
10
TIME(HR)

Conclusion

Prepared and analysed pilocarpine ocusert in this study exhibits stability, durability against external forces, higher pilocarpine loading, and extended pilocarpine release. These ocusert formulations are injected into the eye so that it can tolerate the shear stresses present in the eye's cul-de-sac. The In vitro drug release approaches up to 90% of its concentration within 10 hrs. The ex *vivo* results show that drug is released up to 90% within 8 hours. The ocusert formulations offer a lasting pharmacological response as indicated by a reduction in pupil diameter. The outcomes correspond with the justification for implementing pilocarpine ocusert as an ocular medication delivery method.

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