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EVALUATION OF AN OCULAR DRUG DELIVERY SYSTEM FOR ANTIVIRAL DRUGS USING NANOPARTICLE-BASED FORMULATIONS

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Abstract

The results of this study demonstrate that chitosan nanoparticles (CS NPs) may be used as carriers for the efficient delivery of acyclovir, which can be used to treat a wide range of ocular viral diseases. The current study did include the in-vivo absorption characteristics of the developed acyclovir (ACV) CS NPs in an animal model. In order to investigate the role of CS NPs in the ocular disposition of acyclovir, two different formulations were tested. These formulations were ACV-loaded CS NPs and a solution of pure ACV in phosphate buffer (pH 7.4). This was determined by measuring the corneal drug level. The lowest amount of drug release was observed in F-1 (70.2%), while the greatest amount was recorded in F-9 (90.10%). Because of the desirable drug release in twenty-four hours, formulation F-9 was chosen as the optimal formulation out of all the possible formulations. Based on the findings of the in vitro drug release tests for formulations F1 through F15, it was discovered that an increase in the polymer concentration slows the drug release. This is because the larger particle size results in a smaller surface area that is available for drug release.

Keywords: Acyclovir,Antiviral drugs, Nano technology, Ocular drug delivery system

Introduction

In the last decade, nanotechnology has been vital in the development of delivery systems for tiny molecules, proteins, and DNA. As a result, whole new and perhaps unanticipated sectors have emerged as a result of this technology's application. Innovative drug delivery systems (DDSs) are a strategic instrument for increasing drug markets, which represents their value to the pharmaceutical business [1]. The technique could solve problems that are caused by existing medications by prolonging the product's shelf life, or it could enhance the performance and acceptability of existing pharmaceuticals in one of three ways: by boosting efficacy, improving safety, or raising patient compliance. Because of this

technology, it is now possible to distribute medicines that have a very low solubility in water or that are unstable in their natural biological setting [2, 3].

The objective of the research is to compare in vitro drug release analysis carried out with the utilisation of optimised ACV-loaded CS NPs and a formulation of ACV that is available for purchase in the marketplace.

Methodology

2.1. IN-VIV AND IN VITRO DRUG RELEASE STUDIES

For the objective of the study, a total of six healthy albino rabbits weighing between 1.5 and 2.2 kg that showed no evidence of ocular inflammation were chosen. The procedures were carried out in accordance with the CPCSEA rules. On the basis of the results of the in vitro drug release investigation, formulation F-9 was chosen for the in vivo study out of a total of 15. The control consisted of unadulterated ACV that had been dissolved in a phosphate buffer solution with a pH of 7.4. The left eye of rabbits was utilised for the control preparation of the F-9 formulation, and the right eye of rabbits was utilised for the prepared formulation of the F-9 formulation. After nanoformulation (F-9) and a control were injected into the conjunctival sac, the levels of ACV in the aqueous humour of the test subjects were measured at 1, 4, 8, 16, 20, and 24 hours later. During the allotted amount of time, the rabbits were rendered unconscious by intravenous application of ketamine at a dose of 25 mg/kg and then 150 L of aqueous humor. It was extracted from the limbus region of the rabbits using a heparin-rinsed glass syringe linked to a needle with a 27-gauge. The samples were denatured by adding an equivalent amount of a sol containing 2% zinc sulphate. After the samples were centrifuged, the liquid in the supernatant was filtered using a millipore membrane with a 0.2-micron pore size. A similar experiment was performed on the second set of rabbits, yet this time with pure ACV that was suspended in phosphate buffer with a pH of 7.4. A high-performance liquid chromatography run at a wavelength of 253 nm was utilised to conduct the analysis on the samples.

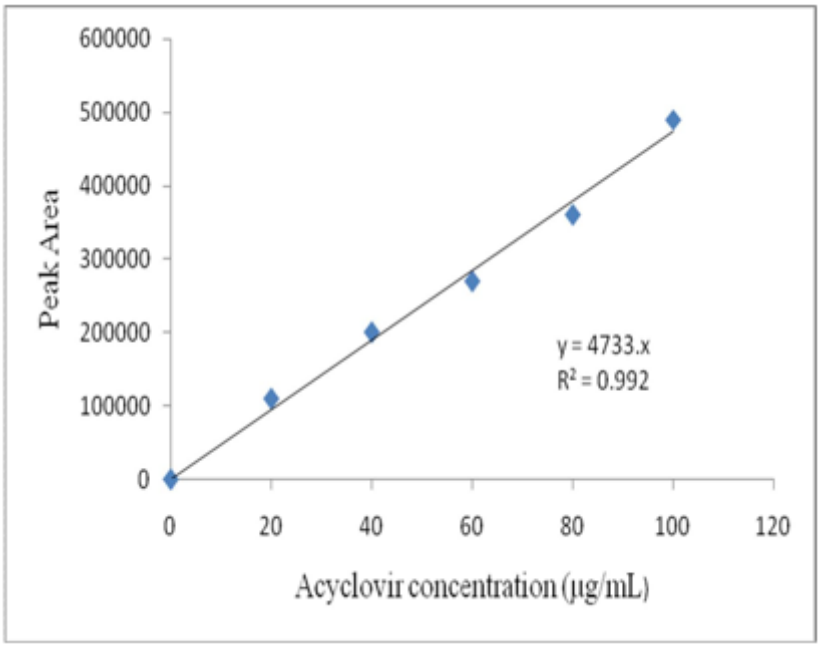


Figure 1: The Reverse phased-HPLC calibration curve for ACV in aqueous humour

Result and discussion

As can be seen in Figure 2, the diffusion of ACV from the CS NPs, also called drug leakage, was measured for a period of twenty-four hours. Based on the findings of the in vitro drug release tests for formulations F1 through F15, it was discovered that an increase in the polymer concentration slows the drug release. This is because the larger particle size results in a smaller surface area that is available for drug release. After 10 minutes of sonication, it was discovered that an increase in drug release occurred in conjunction with an increase in polymer concentration. On the basis of this information, the in vitro drug release study will focus on five different formulations: F-3, F-6, F9, F12, and F-15. Within the first hour, the amount of medication that was released was 12.0%, 12.5%, 12.8%, 13.8%, 14.71%, 16.62%, 14.56%, and 15.85%, correspondingly, for F-3, F-6, F-9, F-12, and F-15. Following a period of 24 hours, the cumulative percentage of medicine that was released from F3, F6, F9, and F15 was 76.14%, 85.28%, 90.10%, 82.30%, and 80.40%, correspondingly.

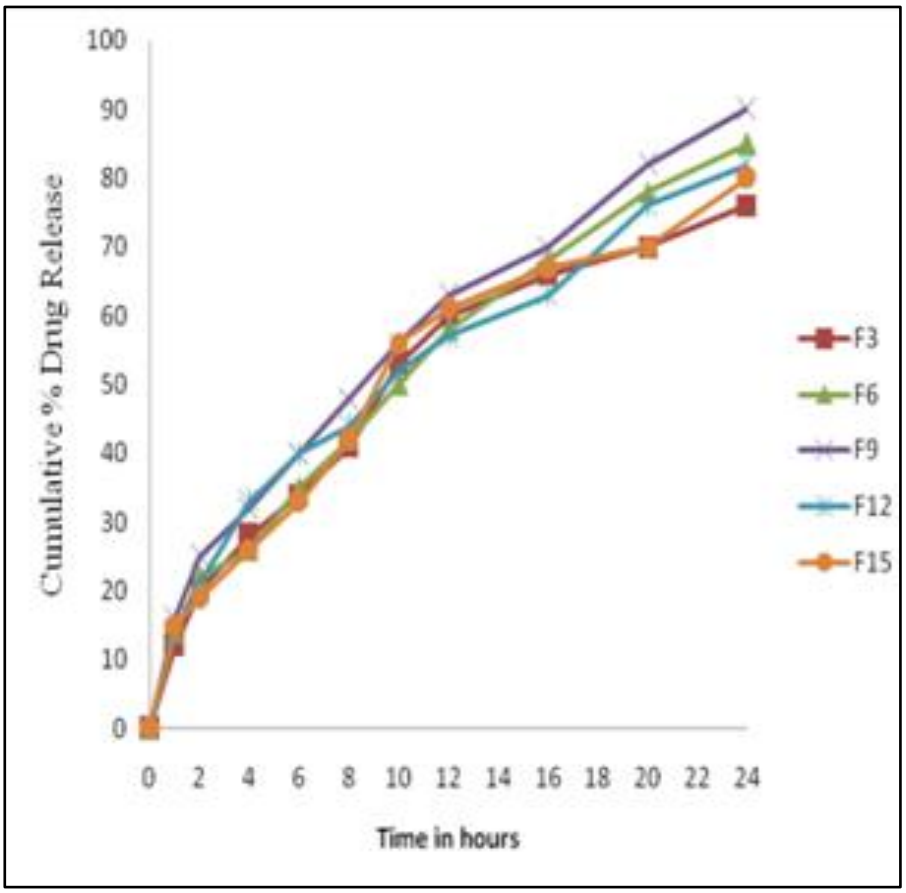


Figure 2: Comparative in vitro drug detail of F3, F6,F9,F12,F15

The lowest amount of drug release was observed in F-1 (70.2%), while the greatest amount was recorded in F-9 (90.10%). Because of the desirable drug release in twenty-four hours, formulation F-9 was chosen as the optimal formulation out of all the possible formulations.

An in-vitro analysis contrasting the produced NPs with the commercially available formulation

A phosphate buffer with a pH of 7.4 was utilised to study the in vitro drug release behaviour of optimised ACV-loaded CS NPs (F-9) and a commercial formulation of ACV (Acivir Eye 3% w/w ointment) for a period of twenty-four hours. Ointment with a 3% water-to-wax ratio of ACV can be purchased and applied to the affected eye five times a day, using a 1 cm ribbon each time. The weight of these five ribbons is roughly 66 milligrammes of the ointment, which has approximately 2 milligrammes of ACV every day.

1.

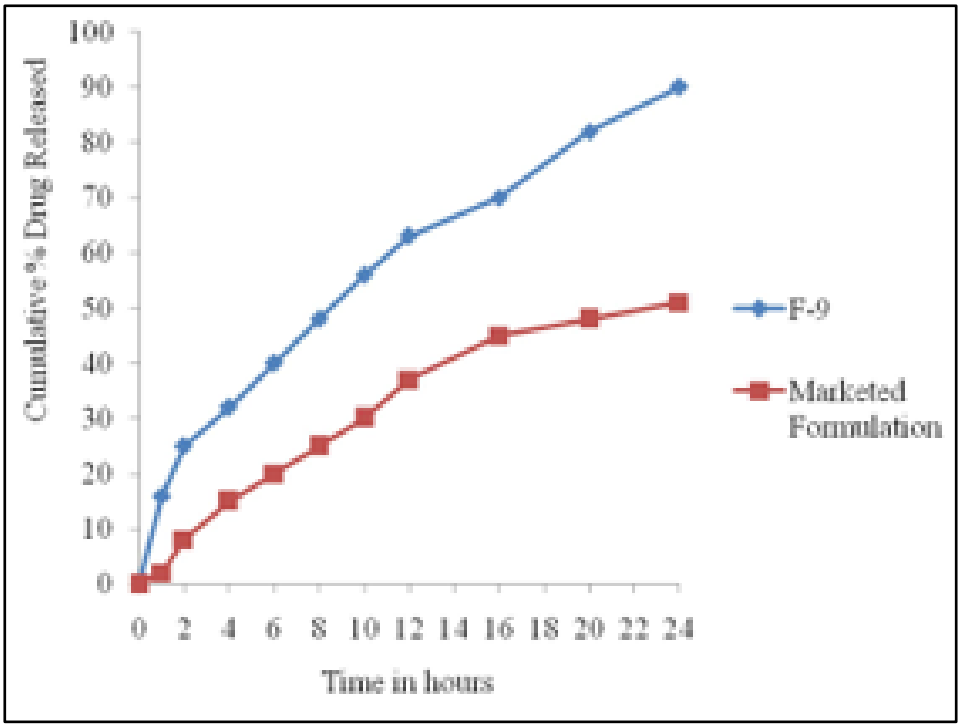
2. 

Figure 3: Comparative in vitro drug release of F9

Table 1: In vitro release of ACV

Time in hrs.	Peak area	Control (µg/mL)	Peak area	Formulation F-9 (µg/mL)
1	131651±1.56	18.231±1.70	169088±1.07	25.49±1.54
4	149782±2.61	22.10±2.78	229876±2.90	35.71±2.80
8	221456±1.28	33.65±2.45	308764±1.98	48.36±2.50
16	267352±2.98	40.12±2.87	514520±1.54	78.59±3.67
20	187003±1.21	28.18±1.58	348976±2.62	54.92±2.01
24	138786±1.78	20.13±1.34	270752±1.38	40.54±2.16

For the in vivo pharmacological tests, formulation F-9 was chosen since it showed satisfactory results in in vitro release. The HPLC method was utilised in order to ascertain the drug concentration. The controlled preparation showed a concentration of 33.65 g/mL, whereas the maximum concentration was found to be

78.59 g/mL in the F-9 sample at the eighth hour. ANOVA was performed on the drug concentrations that were obtained from aqueous humours utilising formulation F-9 and a controlled preparation. The results showed that the P value was 0.0879.

The in-vitro drug release behaviour of optimised ACV-loaded CS NPs (F-9) was compared with the marketed formulation of acyclovir, and the results showed that at the end of 24 hours, the drug release was 90.68% for F9, whereas it was only 28.45% for the marketed product. When compared with the cumulative drug release of a commercially available ACV ophthalmic solution, it was discovered that the cumulative drug release of the selected ACV-loaded CS NPs was greater than that value. The release pattern indicated that the medicine from the ACV NPs was being released at each point in time at an extremely slow rate. An earlier study showed that CS NPs boosted the rate of ACV absorption in rabbits eyes in comparison to commercially available formulations.

Conclusion

The findings of the current research have shown that in order to study the in vitro diffusion of ACV from the NPs, the drug leakage was monitored for a period of twenty-four hours. The release profile of ACV from CS NPs is distinguished by an initial fast release, followed by a steady release of the medication over the course of a period of twenty-four hours. The burst effect that results from the release of the drug fraction that is encapsulated near the surface of the nanospheres may be responsible for the initial rapid release. The subsequent slow release of ACV from the CS NPs may be the result of the release of the drug fraction that is encapsulated in the core of the nanospheres. Following a period of 24 hours, the cumulative percentage of medicine that was released from F3, F6, F9, and F15 was 76.14%, 85.28%, 90.10%, 82.30%, and 80.40%, respectively. The lowest amount of drug release was observed in F-1 (70.2%), while the greatest amount was recorded in F-9 (90.10%). Out of all the formulations, F-9 was chosen as the optimal formulation because it provided the desired level of drug release over the course of 24 hours.

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