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Research Article

Advancing Ocular Drug Delivery: Sulfoxy Amine Xanthan Gum-Based Inserts

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ABSTRACT

Xanthan gum, a natural polysaccharide, is commonly used in pharmaceutical sciences for its biocompatibility and its mucoadhesive property. Recent modification in adding sulfoxy amine groups to xanthan gum have demonstrated potential activity in improving its efficacy in ocular drug delivery systems. The objective of this research is to develop and assess ocular inserts containing sulfoxy amine xanthan gum for sustained release of ciprofloxacin as a drug. Objectives: The objective of this study is to formulate and assess ocular inserts made with sulfoxy amine-modified xanthan gum, focusing on their properties, drug release pattern, and compatibility with the body. Methods: Xanthan gum is modified and successfully converted into sulfoxy amine xanthan gum. Ocular inserts films of Ciprofloxacin have been successfully formulated by solvent casting technique. The prepared films were evaluated in terms of physical appearance, surface pH, uniformity, and folding endurance. The method of preparation of ocular inserts is reproduced, and ocular inserts ensure excellent quality with uniformity of patch characteristics with minimum variability. Results: Xanthan gum-based ocular inserts containing sulfoxy amine demonstrated an appropriate film thickness and suitable folding endurance. The surface pH and weight uniformity of the ocular inserts also within acceptable ranges, supporting their suitability for sustained release of drug ciprofloxacin. Conclusion: The sulfoxy amine xanthan gum-based ocular inserts exhibited superior physiological properties, sustained drug release, and excellent biocompatibility, making them a promising candidate for ocular drug delivery systems. Further studies are needed to explore their potential in clinical settings.

INTRODUCTION

Administering drugs through the eye is a difficult task in pharmaceuticals due to the eye's anatomical and physiological barriers, including tear turnover, nasolacrimal secretions, and corneal permeability, resulting in low bioavailability for topical

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medications. Traditional eye drops usually only deliver less than 5% of the medication to the intended location, requiring patients to take them often in order to keep levels of treatment high. This can result in patients adherence as directed and an increased chance of experiencing side effects or adverse effects. As a result, there is an increasing demand for innovative ODDS (ocular drug delivery systems) that can offer extended drug retention, enhance bioavailability, and improve patient compliance.[1] Ocular inserts are becoming a optimistic approach for prolonged drug delivery, as campared to traditional forms of medication. These firm or partially firm implants are meant to be inserted into the conjunctival sac, where they can slowly release the medication for a prolonged period, reducing the need for frequent dosing and enhancing treatment results.[2] Polysaccharides from natural sources like xanthan gum are particularly intriguing for developing ocular inserts because of their biocompatibility, mucoadhesive properties, and ability to gel in water.[3] Research on the use of xanthan gum, a bacterial polysaccharide, in pharmaceutical formulations such as ODDS has been thorough.[4] Xanthan gum's mucoadhesive characteristics enable it to stick to the eye's surface, extending the time drugs remain in contact and enhancing drug bioavilability. Nevertheless, the original xanthan gum form has drawbacks, including weak mechanical strength and varying drug release patterns[5].In order to overcome these limitations, researchers have investigated chemical alterations of xanthan gum. One alteration includes adding sulfoxy amine groups, known to enhance the polymer's mechanical properties, swelling behavior, and binding affinity.[6] A new variation called sulfoxy amine-modified xanthan gum (SAXG) has been developed, providing better physicochemical properties specifically for ocular inserts. Adding sulfoxy amine groups improves the ability of xanthan gum to swell and its mechanical strength, which helps in regulating drug release rates and prolonging the bioavailability of drugs in the eye.[7] The objective of this research is to create and assess ocular inserts using modified xanthan gum for extended drug delivery.[8,9] The drug ciprofloxacin were evaluated for identification, melting point determination, UV spectroscopy, IR spectroscopy, calibration curve whereas inserts were evaluated for physical appearance, surface pH, uniformity, and folding endurance.

It is anticipated that the results of this research will help in the advancement of enhanced ophthalmic drug delivery systems, presenting novel treatment options for chronic eye conditions that need continuous medication administration.

Materials and Methods:

Xanthan gum, Pyridine, and Methanol were acquired from Sd. Chemical Laboratory located in Mumbai with pin code 40002. Cipla Pvt. Ltd., located in Goa, gifted Ciprofloxacin. Thionyl Chloride, Ammonia, Ethanol were bought from Pallav Chemicals & Solvents Pvt Ltd, located in Andheri (W) Mumbai – 400053. Glycerin and Propylene Glycol were acquired from Loba Chemical Pvt. Ltd in Mumbai, India. All remaining substances were of analytical quality.

Polymer Preparation:

Five grams of xanthan gum powder were precisely measured and deposited into an iodine flask. A quantity of 20 ml of pyridine was measured out and poured into the flask. The xanthan gum and pyridine mixture was blended completely. Following that, 3-4 ml of thionyl chloride was slowly added while continuously shaking the solution. The blend was exposed to microwave radiation for 2 minutes and subsequently allowed to sit undisturbed for 24 hours. Following this time frame, the remedy was strained with a suction pump and rinsed with 50 ml of ethanol to eliminate any extra pyridine. The filtered product was then dried at room temperature and weighed. give

scientific reference for this data The resulting mixture was returned to the iodine flask, where 20 ml of ethanol, 5 g of modified xanthan gum, and 5 ml of ammonia were added with continuous shaking. The solution was again set aside for 24 hours. Finally, the mixture was filtered using a suction pump, washed with ethanol, dried at room temperature, weighed, and its melting point was determined.[10]

Polymer Characterization:

FTIR Study:

The FTIR study was conducted to investigate the interaction between the drug ciprofloxacin and the polymers. Modified xanthan gum disks containing ciprofloxacin and formulation blends were prepared manually using a press method. Approximately 1 mg of the drug was triturated with 10 mg of dry modified xanthan gum and then manually pressed into a pellet form for analysis. This method allowed for the detection of potential interactions between the components of the formulation via FTIR spectra.[11]

DSC Study:

The possible interactions between the drug Ciprofloxacin and the polymer were analyzed using Differential Scanning Calorimetry (DSC) thermograms. These thermograms were obtained from both the pure drug and a physical mixture of the drug with the polymer (Drug + MXG). For the analysis, the pure drug and the physical mixture were each weighed separately and placed in aluminum pans. These pans were then covered with aluminum lids and hermetically sealed using a pan press to ensure isolation from the environment.[12]

Identification of Drug:

The Ciprofloxacin drug was determined for its physiochemical properties, such as color and smell, along with its physicochemical properties. The objective of the study was to evaluate the physical appearance, which includes examining the shape, color, smell of the drug and compared to the standard requirements. Furthermore, its melting point, UV spectroscopic analysis, IR spectroscopic analysis and calibration curve were evaluated to compare with the standard values of marketed product.[13]

Melting point of Drug:

The melting point of drug, ciprofloxacin was determined by using a small amount of the sample into a capillary tube attached to a thermometer. The capillary tube was then placed in a Thiele's tube containing a paraffin, and continuous heat was provided to the assembly and accurate melting point was recorded. This method ensures precise control over heating, allowing accurate measurement of the drug's melting point, which is a critical parameter for assessing its purity and thermal stability.

UV Spectroscopy:

The absorption maximum (λmax) of the standard drug solution in water was determined by scanning the solution between 278 nm using a UV spectrophotometer. This method allowed for the precise identification of the wavelength at which the drug exhibits peak absorbance, providing critical information about its electronic transitions. The λmax is essential for ensuring accurate quantitative analysis of the drug in further studies, as it reflects the optimal wavelength for its detection in UV spectroscopy.[14]

IR Spectroscopy:

Infrared (IR) spectroscopy is a precise analytical technique which is used to detect chemical interactions. This method uses functional groups within a compound for idebtification. The IR spectrum of Ciprofloxacin was recorded using a Fourier Transform Infrared (FTIR) Spectrophotometer, which allows for precise detection of vibrational transitions in the molecular structure.[15,16,17,18]

Calibration Curve:

Accurately measured 100 mg of Ciprofloxacin was dissolved in 10 ml of water. Prepared solution

transferred into a 100 ml volumetric flask, and made up the 100 ml with water concentration of (1000 µg/Ml). 10 ml solution was taken out from prepared solution and transferred into 100 ml volumetric flask, and made up to 100 ml with water. Furthermore, 1 ml of the solution was transferred into a 10 ml volumetric flask and adjusted with water up to 10 ml, resulting in a concentration of 100 µg/ml.
To prepare different concentrations, the solution was diluted by transferring the appropriate volumes into a 10 ml flask and make up with water to reach 2.5, 3.0, 3.5, 4.0, 4.5, and 5.0 µg/ml. The UV spectrophotometer was used to measure the absorbance of each solution at 278 nm. A graph was recorded as absorbance against concentration to determine quantify Ciprofloxacin in further studies. This dilution and absorbance measurement method is often used in pharmaceutical analysis to assure precise and required quantification of drug concentrations.[19]

Preparation of ocular inserts:

Sulfoxy amine modified xanthan gum (MXG) solution was prepared and used as polymer. Nine batches of different amount of ciprofloxacin ocular inserts were prepared (Table 1). Solvent casting method was used with propylene glycol as a plasticizer at different amount. The required amount of polymer and drug was dissolved in various beakers in the required quantity of distilled water (20ml) and stirred on a magnetic stirrer until completely dissolved both solution. Then plasticizer (Propylene glycol) was added to the solution under stirring condition. Then solution of polymer was sonicated for 30 min to remove the air bubbles. After proper mixing, casting the solution in poured in a clean Teflon plate. The dried films thus, obtained were cut into circular pieces of definite size (5.5 mm diameter). The ocular inserts were wrapped in aluminum foil and were stored in an airtight container.[20,21,22]

Code	Drug (Mg)	MXG(%W/W)	Propylene Glycol (ml)	Distilled Water (ml)
F1	100	0.8	0.5	20
F2	100	0.9	0.5	20
F3	100	1.0	0.5	20
F4	100	0.8	0.6	20
F5	100	0.9	0.6	20
F6	100	1.0	0.6	20
F7	100	0.8	0.7	20
F8	100	0.9	0.7	20
F9	100	1.0	0.7	20

Evaluation of ocular inserts:

a) Folding Endurance:

The folding endurance of ocular inserts were evaluated by repeatedly folding the film of ocular inserts at the same position until an audible creak was produced. The number of folds required to induce this creak was recorded as a measure of folding endurance. This test was conducted on multiple sets of ocular inserts to ensure the reliability and consistency of the results.[23,24]

b) **Uniformity of Thickness:**

The thickness of the ocular inserts was measured using a micrometer gauge at five random points on each insert. The average thickness was then calculated to provide a representative value for each sample. This method ensures accuracy and consistency in measuring the physical dimensions of the inserts, which is crucial for their performance and compatibility in ocular applications.[25,26]

C) Surface pH:

The surface pH of the ocular inserts was determined by allowing the inserts to swell in distilled water within a Petri dish at room temperature for 30 minutes. After this swelling period, pH paper was placed on the surface of the inserts, and after one minute, the developed color was compared to a standard color scale to ascertain the pH value. This method provides a simple and effective means of evaluating the biocompatibility of ocular inserts, as surface pH can significantly affect the performance and safety of these formulations in ocular applications.[27]

d) Weight Variation:

For the determination of film weight uniformity, six films from each formulation were randomly selected and weighed individually using an electronic balance. The mean weight of the inserts for each formulation was recorded. This assessment of weight uniformity is essential for ensuring consistent dosing and performance of ocular inserts, as variations in weight can impact drug release and therapeutic efficacy. [28,29,30]

RESULT AND DISCUSSION:

Sulfoxy amine xanthan gum-based ciprofloxacin ocular inserts were prepared and evaluated individually. The prepared ocular inserts were found in milky white color along with smooth texture in a round shape. Thickness was found to be 0.12 to 0. 15 mm. Folding endurance of prepared ocular inserts performed in ranges between 07 to 10 times which displays the strength of an insert. Surface pH was found to be within the range 6.5 to 6.8. The weight of the ocular inserts of all formulation was found to be value varied between 0.583 to 0.783 mg. (Table 2) The nelting point of pure drug ciprofloxacin was found to be 315-318 ℃.

Table 2: Evaluation parameters of Ciprofloxacin ocular inserts:

Formulation code	Thickness (mm)	Folding endurance	Surface Ph	Weight Uniformity(mg)
F1	0.15±0.012	7±1.52	6.5±0.05	0.583±0.19
F2	0.12±0.017	10±1.52	6.5±0.08	0.733±0.08
F3	0.15±0.011	6±1.50	6.8±0.05	0.683±0.29
F4	0.12±0.011	7±0.57	6.5±0.05	0.65±0.28
F5	0.14±0.015	8±1.52	6.6±0.06	0.783±0.11
F6	0.14±0.017	7±1.52	6.7±0.06	0.616±0.29
F7	0.15±0.017	7±1.10	6.5±0.05	0.783±0.24
F8	0.15±0.015	9±2.64	6.6±0.04	0.65±0.27
F9	0.14±0.018	7±2.51	6.8±0.03	0.683±0.30

The prepared solutions were analyzed for UV absorption within the range of 200–400 nm. The recorded UV spectrum exhibited a maximum absorbance (λmax) at 278 nm in the water-based solution, as shown in Table 3. The highest drug absorbance wavelength peak was recorded which is required for further quantitative analysis (Table 4 & Figure 4).

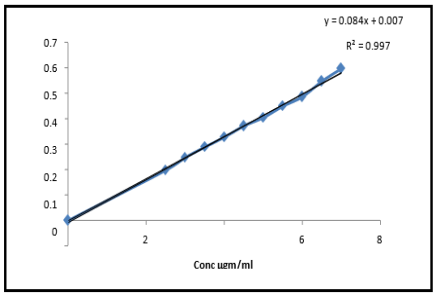

Figure 3: Calibration curve of ciprofloxacin

Table 3: Observation for Standard Calibration Curve of Ciprofloxacin

Concentration	Absorbance
0	0
2.5	0.198
3	0.248
3.5	0.289
4	0.328
4.5	0.372
5	0.405
5.5	0.45
6	0.487
6.5	0.548
7	0.598

Table 4: Standard Curve Statistics:

Sr.no	Parameter	Observation
1	Absorbance Maximum	278
2	Slope	0.084
3	Intercept	0.007
4	Coefficient of correlation	0.997

The DSC (Differential Scanning Calorimetry) analysis of the pure drug ciprofloxacin was determined. The thermogram of pure ciprofloxacin showed two peaks one at 154°C and another at 168°C, corresponding to its melting points. (Fig.5)

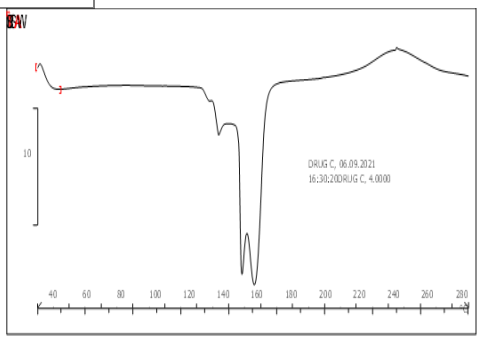

Figure 4: DSC Spectra of Ciprofloxacin

The FTIR (Fourier Transform Infrared) spectra of the pure drug ciprofloxacin and its physical mixture with the polymer were compared to detect appearance of characteristic peaks. The FTIR spectrum of pure ciprofloxacin showed prominent absorption bands, with a major peak observed for NH stretching at 3540.67 cm^{-1}, indicating the presence of the amine group. The comparison between the spectra of the pure drug and the physical mixture revealed no significant changes in these characteristic peaks, suggesting no chemical interaction between ciprofloxacin and the polymer. (Fig. 6,7,8)

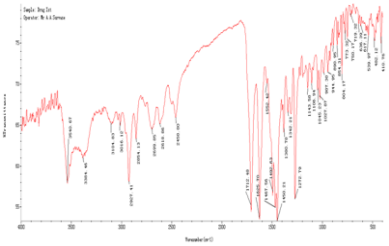

Figure 5: FTIR of Ciprofloxacin

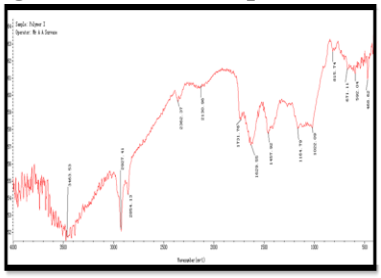

Figure 6: FTIR of Modified Xanthan Gum

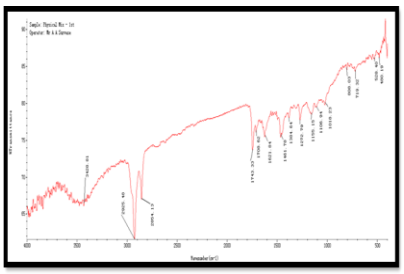

Figure 7: FTIR of Physical Mixture

CONCLUSION:

In this study, xanthan gum was successfully modified using a chemical method involving treatment with thionyl chloride and ammonia in the presence of pyridine. The modified xanthan gum demonstrated enhanced gelling, viscosity, and film-forming properties compared to its unmodified counterpart. Characterization using FTIR and DSC confirmed the successful conversion into sulfoxy amine xanthan gum. Ciprofloxacin ocular inserts were formulated using a solvent casting technique, with the films showing excellent physical properties, uniformity, and folding endurance, ensuring minimal variability and high quality in the final product

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