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FORMULATION AND EVALUATION OF PROPRANOLOL LOADED BIO FLEXI OCUSERT USING SORGHUM FLOUR BIOPOLYMER

Deepika Kunwar[1], DEEPTI DWIVEDI[2], BHARAT MISHRA*[3]

Institute of Pharmacy, Dr Shakuntala Misra National Rehabilitation University, Lucknow.

Corresponding Author
Bharat Mishra

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ABSTRACT

Delivering propranolol hydrochloride via conventional eye drops often results in poor bioavailability. This is mainly due to rapid precorneal drainage and tear turnover, which quickly eliminate the drug from the ocular surface, requiring frequent administration. Such repeated dosing can reduce patient compliance and therapeutic effectiveness. Ocuserts, which are thin ocular inserts designed to provide sustained drug release, offer a promising alternative. They can maintain therapeutic drug levels for extended periods, improving patient convenience. The use of natural biopolymers in ocular drug delivery is particularly attractive because they are biodegradable, biocompatible, economical, and environmentally friendly. This study aimed to develop and evaluate propranolol-loaded bio-flexi ocuserts using sorghum flour biopolymer as a natural film-forming matrix for sustained ocular drug delivery. Bio-flexi ocuserts were prepared using the solvent casting method by incorporating different concentrations of sorghum flour polymer along with appropriate plasticisers to enhance flexibility. The prepared inserts were evaluated for various physico-mechanical properties, including thickness uniformity, weight variation, folding endurance, surface, pH, and drug content uniformity. In vitro drug release studies were carried out using a diffusion cell to examine the release profile of propranolol over time. The release data were further analysed using mathematical models to determine the mechanism of drug release. All the formulated ocuserts showed satisfactory physico-mechanical characteristics. The thickness and weight variation were uniform, and the surface pH was found to be compatible with ocular tissues. Folding endurance values ranged from 98 to 120, demonstrating good flexibility and mechanical strength. The results of this study suggest that sorghum flour biopolymer can serve as an effective, natural, biodegradable, and cost-efficient matrix for the development of bio-flexi ocuserts. Propranolol-loaded sorghum flour ocular inserts demonstrated promising potential for sustained ocular drug delivery and may be beneficial in the management of glaucoma.

Keywords: *Propranolol hydrochloride, Bio-flexi ocuserts, Sorghum flour biopolymer, Sustained ocular drug delivery, Ocular inserts, Glaucoma.*

INTRODUCTION

Delivering drugs to the eye is one of the most fascinating yet difficult tasks for pharmaceutical scientists. Traditional eye medications such as drops, suspensions, and ointments are no longer fully effective for treating many of today's more aggressive eye diseases. The eye is the most easily accessible site for topical corneal contact, with a contact time of only about 1-2 minutes in humans when administering a medication [1]. Drugs are typically administered in a solution, usually at a concentration of less than 10%. As a result, when applied to the ocular system for localised action, only a small amount of the drug actually penetrates the corneal surface or enters the interior of the eye, which ultimately reaches the intraocular tissue [2]. Because of these factors, the eye presents unique drug disposition limitations. Controlled drug delivery to the eye remains a significant challenge due to its distinct anatomical and physiological barriers, which impose effective restrictions on topical treatments for ocular illnesses [3].

Conventional ophthalmic formulations such as eye drops and ointments exhibit poor bioavailability, typically less

than 5%, primarily due to rapid precorneal elimination, nasolacrimal drainage, tear turnover, and limited corneal permeability [4]. These limitations necessitate frequent dosing, which often leads to poor patient compliance and reduced therapeutic efficacy, particularly in chronic ocular conditions such as glaucoma. Propranolol hydrochloride, a non-selective β-adrenergic blocker, has been reported to reduce intraocular pressure (IOP) and may be useful in the management of glaucoma and ocular hypertension. Propranolol is a type of medicine known as a non-selective beta-blocker [5]. This means it works by blocking the effects of stress hormones like adrenaline (epinephrine) and noradrenaline (norepinephrine) on both beta-1 and beta-2 receptors in the body. By doing this, it helps slow the heart rate, reduce blood pressure, and lower the heart's workload. However, it does have a strong membrane-stabilising effect, which helps regulate abnormal electrical activity in the heart [6].

However, its conventional ocular delivery is hindered by short residence time on the ocular surface and low drug absorption, resulting in suboptimal therapeutic outcomes. Therefore, the development of a sustained ocular drug delivery system for propranolol is of considerable clinical interest [7].

Ocuserts are controlled-release ocular inserts designed to deliver drugs at a predetermined rate for an extended period. Compared to conventional eye drops, Ocuserts offer several advantages, including prolonged precorneal residence time, reduced dosing frequency, minimised systemic absorption, and improved patient compliance. The success of an Ocusert system largely depends on the selection of an appropriate polymer that provides adequate mechanical strength, flexibility, biocompatibility, and controlled drug release characteristics [8].

Sorghum polymer, derived from *Sorghum flour*, is a natural polysaccharide-based material that has gained attention for its film-forming ability, swelling characteristics, and potential mucoadhesive properties. Sorghum flour is valued for its nutritional benefits and is often used as a staple food in many regions. On average, whole sorghum flour contains About 11.5% protein, Around 2.7% fat, Nearly 1.3% fibres and Approximately 72% carbohydrates [9].

Additionally, sorghum polymer is cost-effective and readily available, making it an attractive alternative to commonly used synthetic polymers such as hydroxypropyl methylcellulose (HPMC) and polyvinyl alcohol (PVA), which may present limitations related to cost and biodegradability [10].

Sorghum is a highly versatile crop. It is not only used as food for humans but also as animal feed. In many parts of the world, especially in dry and drought-prone areas, sorghum serves as a staple food because it can survive harsh growing conditions where crops like maize or sugarcane may fail [11]. In addition to food uses, sorghum can be processed to produce ethanol fuel. It is also traditionally used to make corn brooms. Due to its ability to grow in challenging environments and provide essential nutrients, jowar remains an important crop for food security and sustainable agriculture [12].

Despite the promising attributes of sorghum polymer, its application in ocular drug delivery systems, particularly in the formulation of Ocuserts, has not been extensively explored. The development of a **bio-flexi ocuserts** using sorghum polymer could provide a sustained release platform for propranolol while ensuring ocular compatibility and patient comfort [13].

Therefore, the present study aims to formulate and evaluate propranolol-loaded bio-flexi ocuserts using sorghum polymer as a natural film-forming agent. The study focuses on the preparation, physico-mechanical characterisation, in vitro drug release behaviour, and release kinetics of the developed ocuserts, to establish a sustained and effective ocular drug delivery system for improved management of ocular conditions such as glaucoma [14].

MATERIAL AND METHOD

Jowar, also known as sorghum, is a widely grown cereal crop that belongs to the grass family. There are about 30 different species of sorghum. Some are cultivated mainly for grain, while others are grown as fodder for animals. This crop grows well in warm climates and is especially suited to tropical and subtropical regions. It originally comes from parts of Africa and Asia, though one variety is native to Mexico, and today it is grown in many countries around the world.15 Sorghum is a highly valued cereal crop recognised for its high nutritional value. Sorghum grains have become a major food crop in Africa and India, Sorghum contains 8–18 % protein, 70–80 % carbohydrates, 19 % dietary Fiber, about 3 % Fiber, and various minerals. Sorghum is a rich source of carbohydrates, providing around 70–80 % of the daily recommended intake in one serving. Sorghum grain also contains fructose, a trisaccharide that adds to its carbohydrate composition. Sorghum is harder than other food grains due to its higher prolamin concentration (3.6 to 5.1 %) and lysine content (1.06 to 3.64). Its proteins, mainly composed of albumins, globulins, glutelins, and kafirins, are unique as they lack gliadin and glutenin - the two components of gluten; hence, making sorghum an excellent grain source for those following a gluten-free diet [16].

Physicochemical and Pharmacokinetic Properties of Propranolol

Propranolol is characterised by the chemical formula $C_{16}H_{21}NO_2$ with a molecular weight of 259.34 g/mol. propranolol appears as a white crystalline powder and exhibits a melting point of approximately 96 °C, indicating its stable crystalline nature. The drug exhibits

good solubility in ethanol, facilitating its formulation into various delivery systems [17].

Pharmacokinetically, propranolol demonstrates a relatively low oral bioavailability of approximately 26%, primarily due to extensive first-pass metabolism. It exhibits a high degree of plasma protein binding (>90%), contributing to its distribution characteristics. The reported volume of distribution is approximately 4 L/kg, indicating extensive tissue distribution. Propranolol undergoes predominant hepatic metabolism, and its elimination half-life ranges between 4 and 6 hours, supporting the need for controlled or sustained drug delivery systems to maintain therapeutic plasma concentrations [18].

Isolation of polymer from sorghum flour

0.5kg of jowar seeds were weighed & grinded in a mixer. Powder was mixed with water & kept overnight. The mixture was filtered through muslin cloth, centrifuged & divided into two parts. Acetone was added to one part, while ethanol was added to another. Both mixtures were then placed in the refrigerator overnight. The next day, the mixtures were centrifuged at 3000 rpm for about 5–10 minutes to collect the solid biomaterial. After centrifugation, the collected material was carefully separated and dried in a desiccator for 20–30 hours to remove any remaining moisture. Finally, the dried material was passed through a #120 mesh sieve to obtain a fine and uniform powder [19].

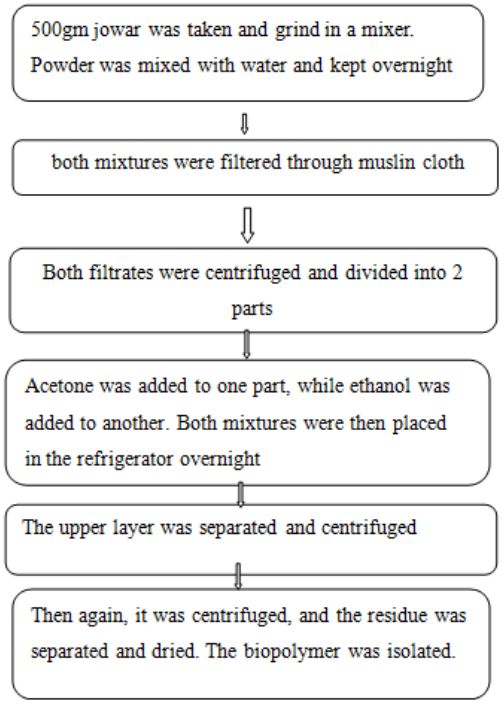


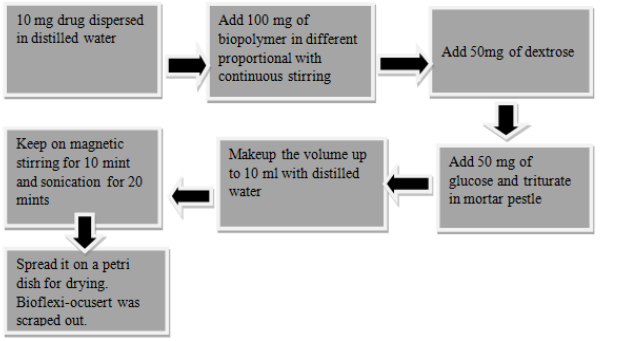
Figure 01: Isolation of Biopolymer from Sorghum Flour

Formulation of Bioflexi Ocuserts

The bio-flexi ocuserts were prepared using a simple and systematic solvent casting method. Different formulations were developed by changing the ratio of biopolymer (from 1:1 to 1:10) to study how varying concentrations affect the final product. First, the required amount of biopolymer was taken in a mortar and pestle and ground thoroughly until a fine, smooth powder was obtained. Then, 50 mg of dextrose and 50 mg of glucose were added, followed by 100 mg of nanosized propranolol. All the ingredients were mixed carefully to ensure even distribution. After this, 10ml of distilled water was added slowly, and the mixture was triturated continuously in the same direction to form a uniform and smooth dispersion. To further improve mixing, the preparation was subjected to magnetic stirring for 45 minutes. Sonication was then carried out for three cycles to remove any trapped air bubbles and to achieve better uniformity. Finally, the prepared mixture was poured evenly onto a Petri dish and allowed to dry at room temperature. Once completely dried, a thin and flexible bio-flexi film was formed. The same procedure was followed for all formulations, with only the concentration of the biopolymer being varied [20, 21].

Table 01: formulation of propranolol loaded bio flexi ocusert by using sorghum flour (jowar) biopolymer

formulation	FJ1(1:1)	FJ2(1:2	JF3(1:3)	JF4(1:4)	FJ5(1:5)	FJ6(1:6)	JF7(1:7)	FJ8(1:8)	FJ9(1:9)	FJ10(1:10)
Propranolol(mg)	10	10	10	10	10	10	10	10	10	10
jowar	1%	2%	3%	4%	5%	6%	7%	8%	9%	10%
dextrose	50	50	50	50	50	50	50	50	50	50
glucose	50	50	50	50	50	50	50	50	50	50
Distilled water	10	10	10	10	10	10	10	10	10	10



Fourier Transform Infrared (FTIR) Spectroscopy

FTIR analysis was performed to investigate possible drug–excipient interactions and to identify functional groups present in the formulation. The spectra of pure drug, biopolymer, and optimised formulation were recorded using an FTIR spectrophotometer. 22 Samples were prepared by the KBr pellet method, where a small quantity of sample was finely triturated with dry potassium bromide and compressed into a transparent pellet under hydraulic pressure. The spectra were scanned over a range of 4000–400 cm^{-1} at a resolution of 4 cm^{-1}. The obtained spectra were analysed for characteristic peaks and any significant shifts or disappearance of peaks indicating interactions [23].

Scanning Electron Microscopy (SEM)

The surface morphology and microstructural characteristics of the prepared bio-flexi ocuserts were examined using scanning electron microscopy. The samples were mounted on aluminium stubs using double-sided adhesive tape and coated with a thin layer of gold under vacuum using a sputter coater to render them electrically conductive. The coated samples were observed under SEM at an appropriate accelerating voltage. Micrographs were recorded at different magnifications to evaluate surface uniformity, porosity, and drug distribution within the polymeric matrix [24].

Differential Scanning Calorimetry (DSC)

DSC analysis was carried out to evaluate the thermal behaviour and compatibility of the drug with the selected biopolymers. Accurately weighed samples of pure drug, polymer, and formulation were sealed in aluminium pans and analysed using a differential scanning calorimeter. The samples were heated over a temperature range of 25°C to 300°C at a constant heating rate of 10°C/min under a nitrogen atmosphere to prevent oxidative degradation. Thermograms were recorded, and characteristic transitions such as melting point (Tm) and glass transition temperature (Tg) were analysed for any shifts indicating interaction or difference in crystallinity [25].

Nuclear Magnetic Resonance (NMR) Spectroscopy

NMR spectroscopy was employed to confirm the structural integrity of the drug and to assess any possible chemical interactions with the biopolymer. The samples were dissolved in a suitable deuterated solvent (such as D_2O or $CDCl_3$) and transferred to NMR tubes. The spectra were recorded using a ^1H NMR spectrometer operating at an appropriate frequency (e.g., 400 MHz). Chemical shifts (δ) were expressed in parts per million (ppm) relative to an internal standard such as tetramethylsilane (TMS). The obtained spectra were analysed for characteristic proton signals and any changes indicating molecular interactions 26].

Zeta Potential Analysis

Zeta potential measurements were carried out to determine the surface charge and stability of the nanosized propranolol-loaded system. The samples were appropriately diluted with distilled water and analysed using a zeta potential analyser based on dynamic light scattering (DLS) principles. Measurements were performed at room temperature, and each sample was analysed in triplicate to ensure reproducibility. The zeta potential values were recorded in millivolts (mV), and the results were interpreted to assess colloidal stability, where higher absolute values indicate better stability of the system [27].

Evaluation Methods for Bio-Flexi Ocuserts

Physical Appearance

The prepared bio-flexi ocuserts were evaluated for physical appearance by visual inspection. The films were examined under normal illumination for colour, transparency, smoothness, and flexibility. The presence of any surface imperfections, such as air bubbles, cracks, or non-uniformity, was also noted [28].

Weight Uniformity

Weight uniformity was determined by randomly selecting three to five ocuserts from each formulation. Each ocusert was individually weighed using a calibrated digital analytical balance. The mean weight and standard deviation were calculated to assess uniformity among the formulations.

Thickness Measurement

The thickness of the ocuserts was measured using a digital vernier calliper. Measurements were taken at three different points on each film, and the average thickness was calculated to ensure uniformity of film casting [29, 30].

Drug Content Uniformity

Drug content was determined by cutting a 1 mm^2 section of the Ocusert and dissolving it in a known volume of methanol (10 mL). The solution was suitably diluted, and the absorbance was measured at 290 nm using a UV-visible spectrophotometer. The drug concentration was calculated using a previously prepared calibration curve of propranolol. The experiment was performed in triplicate, and the average drug content was calculated [31].

Folding Endurance

Folding endurance was determined by repeatedly folding the ocusert at the same point until it broke. The number of times the film could be folded without breaking was recorded as the folding endurance value. This test was performed to evaluate the mechanical strength and flexibility of the films [32].

Surface pH Study

The surface pH of the ocuserts was measured to assess their compatibility with ocular tissues. Each ocusert was placed in a Petri dish and moistened with 0.5 mL of

distilled water. After allowing the film to swell for approximately 30 seconds, the surface pH was measured using a calibrated pH meter. The electrode was allowed to equilibrate for 1 minute, and readings were recorded. The measurements were performed in triplicate, and the mean pH was calculated [33].

In Vitro Drug Release Study

The in vitro drug release study was carried out using a modified M.S. diffusion apparatus (static method). The ocusert was placed in the donor compartment, and the receptor compartment was filled with phosphate buffer (pH 7.4) maintained at physiological conditions. The system was kept at a constant temperature (37 ± 0.5°C). At predetermined time intervals, samples were withdrawn from the receptor compartment and replaced with an equal volume of fresh dissolution medium to maintain sink conditions. The amount of drug released was analysed using a UV-visible spectrophotometer at 290 nm. The cumulative percentage drug release was calculated [34].

Drug Release Kinetics

The release data obtained from the in vitro studies were fitted into various kinetic models, including zero-order, first-order, Higuchi, Korsmeyer–Peppas, and Hixson–Crowell models. The correlation coefficient (R^2) was calculated for each model to determine the best-fit release mechanism. Additionally, parameters such as t_{50}% and t_{80}% were calculated from the release data [35].

RESULT AND DISCUSSION

The biopolymer was extracted using a simple and cost-effective method. To optimise the isolation process, the procedure was repeated six times, and the percentage yield was calculated each time. The results were consistent, showing very little variation, which indicates that this method is reliable and can be scaled up for bulk production.

The percentage yield of the biopolymer obtained from sorghum flour (jowar) was around **2%**. The resulting biomaterial had a **greenish colour**, a **distinctive odour**, and a **sweet taste**. Its texture was smooth, and it displayed a **colour-changing point between 220–260°C**. The material was **sparingly soluble in water** and **insoluble in acetone and methylene chloride**.

SPECTRAL STUDIES OF THE ISOLATED BIO-MATERIALS

(I) IR Spectroscopy: Selected

The Fourier Transform Infrared (FTIR) spectrum of sorghum flour exhibited several characteristic absorption bands corresponding to its major biochemical constituents. A prominent peak observed at 3132 cm^{-1} is attributed to the stretching vibration of =C–H bonds, indicating the presence of unsaturated compounds, possibly derived from lipid components.

A strong absorption band at 2924 cm^{-1} corresponds to aliphatic C–H stretching vibrations (–CH_2 and –CH_3 groups), which are characteristic of long-chain hydrocarbons present in carbohydrates and fatty acids.

The peak at 1734 cm^{-1} is assigned to C=O stretching of ester functional groups, confirming the presence of lipid constituents such as triglycerides in the sorghum flour matrix.

Additionally, a significant band at 1146 cm^{-1} is attributed to C–O stretching vibrations, commonly associated with alcohols, ethers, and polysaccharides. This peak strongly supports the presence of starch and other carbohydrate structures, which are the main components of sorghum flour.

Overall, the FTIR spectral profile confirms that sorghum flour is primarily composed of carbohydrates (starch) along with lipid fractions, with minor contributions from unsaturated compounds.

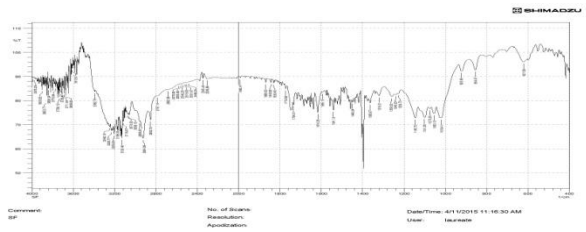


Figure 01: IR Spectra of sorghum flour (jowar)biomaterial

Characterisation of Biopolymer Isolated from Sorghum Flour Scanning Electron Microscopy (SEM)

The surface morphology of the biopolymer isolated from sorghum flour was analysed using SEM. The micrographs revealed an **irregular, smooth, and polycrystalline structure** at a magnification of **3500×**. The absence of visible cracks or large pores indicates a uniform and compact structure, which is advantageous for drug incorporation and controlled release. The smooth surface further confirms the good film-forming ability of the biopolymer.

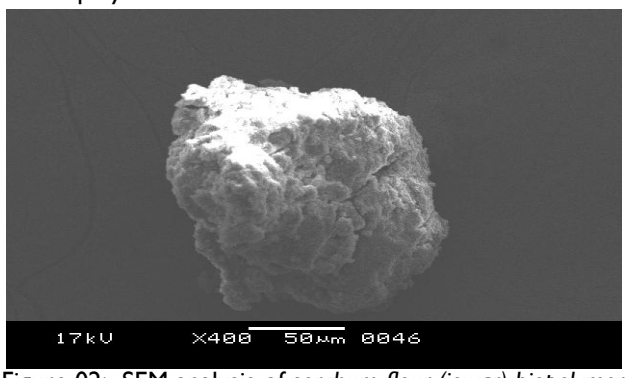


Figure 02: SEM analysis of *sorghum flour (jowar) biopolymer*

Differential Scanning Calorimetry (DSC)

The DSC thermogram of the isolated biopolymer showed a **sharp endothermic peak at approximately 170°C**, corresponding to its melting point. This sharp transition indicates the **semi-crystalline nature** of the polymer and confirms its thermal stability. The absence of additional peaks suggests purity of the material and suitability for pharmaceutical applications.

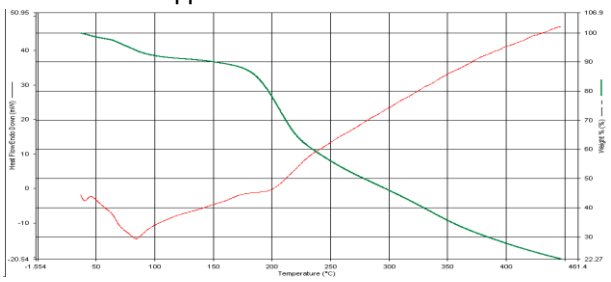


Figure 03: DSC report of sorghum flour (jowar) biopolymer

Nuclear Magnetic Resonance (NMR) Spectroscopy

The NMR spectrum of the sorghum-derived biopolymer exhibited characteristic peaks at **33.430 ppm**, indicating the presence of **C–C bonds**. Peaks at **61.203 ppm, 73.338 ppm, and 75.731 ppm** were attributed to **C–O functional groups**, confirming the presence of polysaccharide structures. Additionally, a peak at **93.249 ppm** suggests the presence of **unsaturated carbon (C=C)**. These results confirm the carbohydrate-rich composition of the biopolymer.

Zeta Potential Analysis

The zeta potential of the biopolymer was found to be **+5.48 mV**, with a standard deviation of **±4.82 mV**. This relatively low zeta potential indicates moderate colloidal stability, suggesting a tendency for slight aggregation. However, it remains acceptable for incorporation into a polymeric drug delivery system.

Evaluation of Bio-Flexi Ocuserts

Physical Appearance

All prepared bio-flexi ocuserts were visually uniform, exhibiting acceptable colour, clarity, smooth surface, and flexibility. No visible defects, such as air bubbles or cracks, were observed, indicating successful formulation using the solvent casting method.

Weight Uniformity

The weight of ocuserts ranged from **16.8 mg to 25.7 mg**, with minimal variation among formulations. This indicates uniform distribution of the polymer and drug within the films, ensuring consistent dosing.

Table 02: Weight uniformity of propranolol loaded bio flexi ocuserts

S.No	Formulation	Weight Uniformity
1	FJ1	16.8
2	FJ2	18.5
3	FJ3	23.6
4	FJ4	21.6
5	FJ5	19.8
6	FJ6	16.8
7	FJ7	25.7
8	FJ8	14.6
9	FJ9	16.8
10	FJ10	18.7

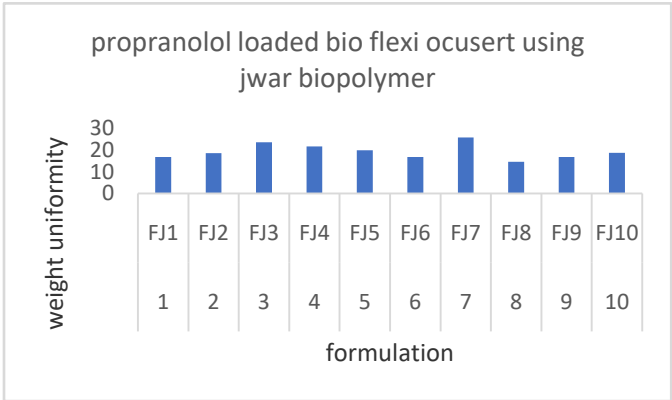


Figure 04: Weight uniformity of propranolol loaded bioflexi ocusert using jowar biopolymer

Thickness

The thickness of the ocuserts was found to be in the range of **0.21 mm to 0.32 mm**, demonstrating uniform film formation. Consistent thickness is essential for achieving reproducible drug release profiles.

Table 03: Thickness of bio-flexi ocusert using sorghum flour biopolymer

S.No	Formulation	Thickness
1	FJ1	0.23
2	FJ2	0.28
3	FJ3	0.23
4	FJ4	0.21
5	FJ5	0.32
6	FJ6	0.22
7	FJ7	0.24
8	FJ8	0.31
9	FJ9	0.32
10	FJ10	0.24

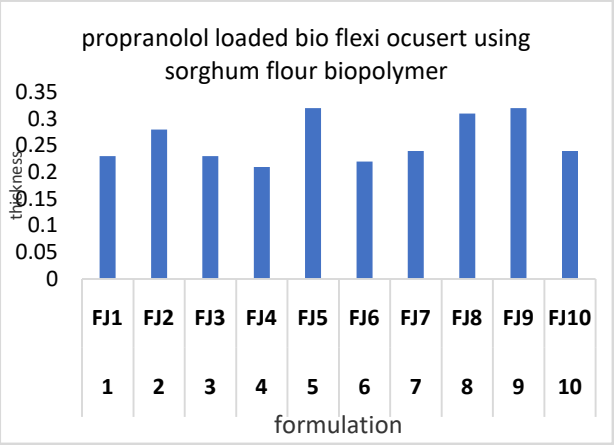


Figure 05: Thickness Of Bioflexi Ocuserts Using Sorghum Flour Biopolymer

Drug Content Uniformity

Drug content analysis confirmed uniform distribution of propranolol within the ocuserts. The consistent absorbance values obtained at **290 nm** indicate efficient drug loading and minimal variation between samples, which is critical for therapeutic consistency.

Table 04: Content Uniformity of Propranolol Loaded Bio Flexi Ocusert Using Sorghum Flour Biopolymer

s.no	formulation	%drug content uniformity
1	FJ1	71.41
2	FJ2	92.29
3	FJ3	94.52
4	FJ4	71.64
5	FJ5	76.86
6	FJ6	79.10
7	FJ7	70.89
8	FJ8	91.53
9	FJ9	88.05
10	FJ10	87.31

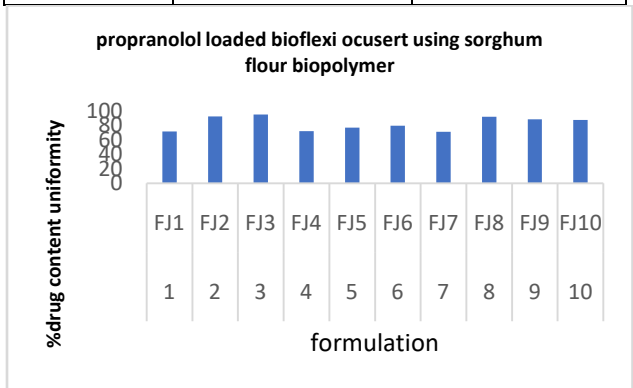


Figure 06: Content Uniformity Of Propranolol Loaded Bio Flexi Ocusert Using Sorghum Flour Biopolymer

Folding Endurance

The folding endurance values ranged from **98 to 120 folds**, indicating good mechanical strength and flexibility. This ensures that the ocuserts can withstand handling during administration without breaking.

Table 05: Folding endurance of propranolol loaded bio flexi ocusert using sorghum flour biopolymer

s.no	formulation	Folding endurance
1	FJ1	98
2	FJ2	112
3	FJ3	98
4	FJ4	120
5	FJ5	118
6	FJ6	101
7	FJ7	106
8	FJ8	112
9	FJ9	120
10	FJ10	114

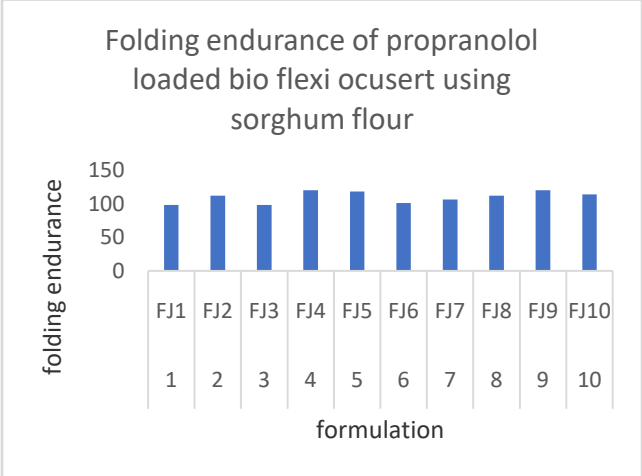


Figure 07: folding endurance of propranolol loaded bio flexi ocusert using jowar biopolymer

Surface pH

The surface pH of the ocuserts was found to be between **7.0 and 7.5**, which is close to the physiological pH of tear fluid. This indicates that the formulations are non-irritant and suitable for ocular application.

In-Vitro Drug Release Study

The in vitro drug release studies revealed that all developed formulations exhibited a **sustained release profile of propranolol** over an extended period. The cumulative drug release data indicated a **controlled and gradual diffusion of the drug from the polymeric matrix**, which is desirable for prolonged ocular drug delivery.

Based on the **t_{80}% values** (time required for 80% drug release), the formulations demonstrated the following release order:

FJ3 (1:3) > FJ5 (1:5) > FJ7 (1:7) > FJ6 (1:6) > FJ10

(1:10) > FJ9 (1:9) > FJ8 (1:8) > FJ4 (1:4) > FJ1 (1:1) > FJ2 (1:2).

Among all the formulations, **FJ3 (1:3)** exhibited the most optimal drug release behaviour, indicating an ideal balance between polymer concentration and drug diffusion, thereby making it the most promising formulation for sustained ocular delivery of propranolol.

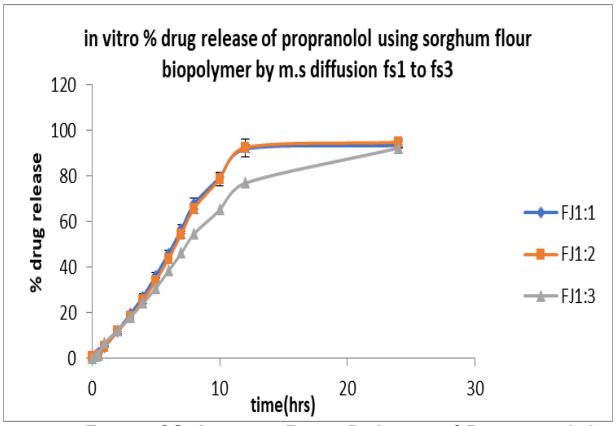


Figure 08: In vitro Drug Release of Propranolol using *sorghum flour* by modified M.S Diffusion (FJ1 to FJ3)

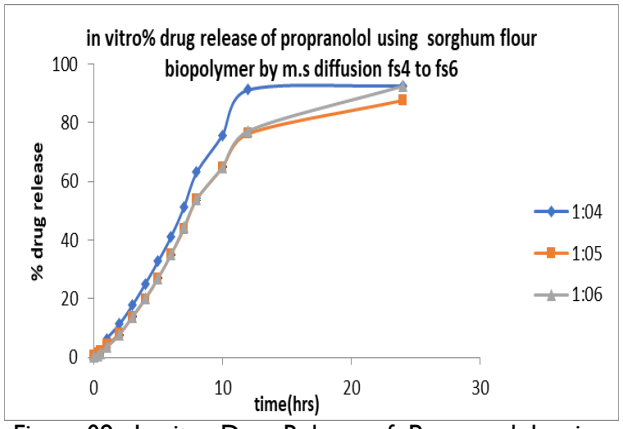


Figure 09: In vitro Drug Release of Propranolol using *sorghum flour* by modified M.S Diffusion (FJ4 to FJ6)

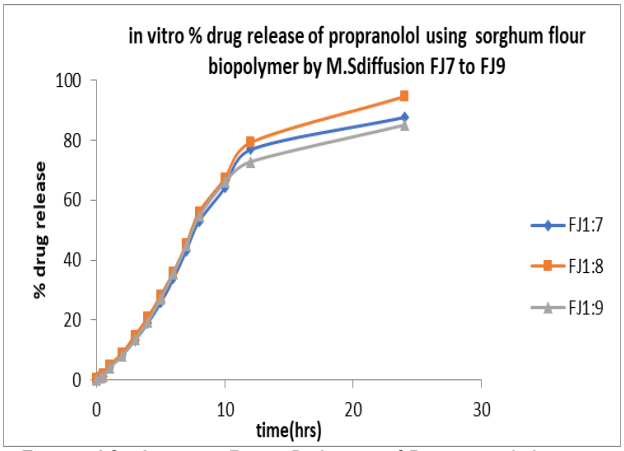


Figure 10: In vitro Drug Release of Propranolol using *sorghum flour* by modified M.S Diffusion (FJ7 to FJ9)

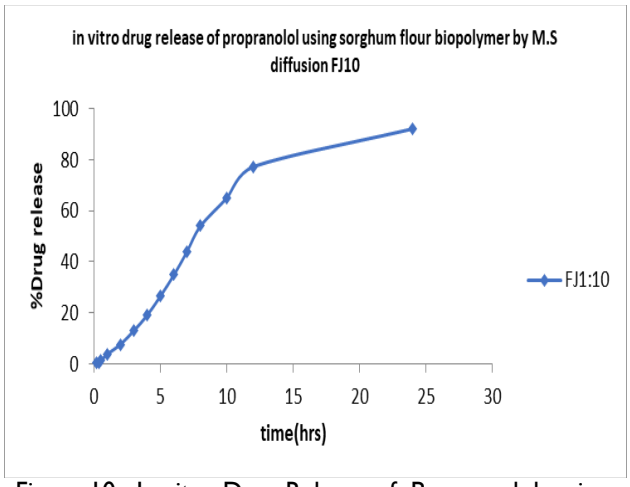


Figure 10: In vitro Drug Release of Propranolol using *sorghum flour* by modified M.S Diffusion (FJ10)

Drug Release Kinetics

The release data were fitted to various kinetic models. The optimized formulation **FJ3 (1:3)** showed:

- **R^2 = 0.9905**
- **t_{50}% = 4.4 hours**
- **t_{80}% = 22 hours**

The high R^2 value indicates that the release data best fit the **Higuchi matrix model**, suggesting that the drug release is primarily governed by diffusion through the polymer matrix. Furthermore, the release mechanism followed **Super Case II transport**, indicating that drug release is controlled by a combination of polymer relaxation, swelling, and erosion processes.

Table 6- T50% and T80% values of propranolol loaded bio-flexy films of *sorghum flour* Biopolymer

JOWAR **Ratio**	**T50 % (hrs.)**	**T80 % (hrs.)**
FJ1 (1:.1)	13.53	18.04
FJ2 (1:2)	13.44	17.92
FJ3 (1:3)	**15.22**	**20.29**
FJ4 (1:4)	13.78	18.38
FJ5 (1:5)	15.20	20.26
FJ6 (1:6)	14.91	19.88
FJ7 1:7	14.97	19.96
FJ8 1:8	14.60	19.47
FJ9 1:9	14.76	19.68
FJ10 1:10	14.76	19.68

Kinetic Release of *Jowar*

Release kinetics analysis, dynamic method formulation of ***SORGHUM FLOUR***							
formulation	R^2					Best fit model	Mechanism of action
	Zero order	1st order	Higuchi Matrix	Peppas	Hixon Crowell		
FJ1 (1:.1)	0.9365	0.9789	0.9395	0.9769	0.9873	Hixon Crowell	Super case II transport.
FJ2 (1:.2)	0.9494	0.9705	0.9355	0.9648	0.9891	Hixon Crowell	Super case II transport.
FJ3 (1:3)	0.9701	.9337	0.9257	0.9785	0.9779	Peppas Korsmeyer	Super case II transport.
FJ4 (1:4)	0.9575	0.9689	0.9332	0.9770	0.9874	Hixon Crowell	Super case II transport.
FJ5 (1:5)	0.9760	0.9469	0.9343	0.9751	0.9814	Hixon Crowell	Super case II transport.
FJ6 (1:6}	0.9762	0.9292	0.9312	0.9802	0.9753	Peppas Korsmeyer	Super case II transport.
FJ7 (1:7)	0.9806	0.9228	0.9282	0.9805	0.9729	Zero order	Super case II transport.
FJ8 (1:8)	0.9767	0.9136	0.9304	0.9852	0.9722	Peppas kerseymere	Super case II transport.
FJ9 (1:9)	0.9762	0.9280	0.9306	0.9784	0.9757	Peppas kerseymere	Super case II transport.
FJ10 (1:10)	0.9762	0.9280	0.9306	0.9784	0.9757	Peppas kerseymere	Super case II transport.

SUMMARY AND CONCLUSION

The present investigation successfully established the design and development of nanosized propranolol-loaded bio-flexi ocuserts as an advanced ocular drug delivery system utilising naturally derived biopolymers. The selected biopolymers demonstrated favourable physicochemical and biological characteristics, including the highest biodegradability, biocompatibility, non-toxicity, and non-irritancy, thereby confirming their suitability for ophthalmic applications.

Detailed physicochemical characterisation revealed that the isolated biopolymers possess significant macromolecular composition, including proteins, polysaccharides, and carbohydrates. **Fourier Transform Infrared (FTIR) spectroscopy** confirmed the absence of any significant chemical interaction between propranolol and the polymeric matrix, indicating drug excipient compatibility and structural integrity of the formulation.

Surface morphology and nanoscale characteristics of the formulated ocuserts, as evaluated by **Scanning Electron Microscopy (SEM)**, demonstrated uniform dispersion of drug particles within the polymeric network and a smooth, homogeneous surface, which is critical for controlled drug release and ocular comfort. Thermal analysis using **Differential Scanning Calorimetry (DSC)** further confirmed the stability of the drug within the formulation, with no significant shifts in main thermal transitions, indicating the absence of drug degradation or incompatibility.

The bio-flexi ocuserts were successfully fabricated using the solvent casting method, yielding films with uniform thickness, good mechanical strength, and flexibility. In vitro drug release studies revealed a sustained and controlled release profile of propranolol over an extended period. The release kinetics followed established mathematical models such as the **Higuchi diffusion model** and **Korsmeyer–Peppas model**, suggesting that the drug release mechanism is predominantly diffusion-controlled with possible contribution of polymer relaxation (non-Fickian transport).

Overall, the developed nanosized bio-flexi ocuserts exhibit significant potential as a controlled ocular drug

delivery system, offering enhanced precorneal residence time, improved bioavailability, and better patient compliance. However, further in vivo pharmacokinetic, pharmacodynamic, and ocular irritation studies are essential to validate the clinical efficacy and translational feasibility of the developed system.

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