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Development of Ocular Delivery System for Glaucoma Therapy Using Natural Hydrogel as Film Forming Agent and Release Modifier

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Abstract

Background. Glaucoma is characterized by increased intraocular pressure, which results in damage to the optic nerve. The existing therapy with conventional eye drops is inefficient due to nasolachrymal drainage, resulting in a reduced corneal residence of the drug.

Objectives. The objective was to develop controlled-release ocular films of timolol maleate using natural hydrogel from *Tamarindus indica* seeds as a sustaining and film-forming agent, to overcome the problems associated with eye drops.

Material and Methods. The hydrogel was isolated using hot aqueous extraction followed by precipitation with ethanol. Six batches of ocular films were prepared and evaluated for drug content, weight variation, thickness, diameter and in vitro release profile. The ideal batch of the films was subjected to stability, pharmacodynamic and ocular safety studies.

Results. The yield of the hydrogel was 58.29%. The thickness of the ocular films was in the range of 0.17 to 0.25 mm and the weight of the films was found to increase with the increase in polymer content. The drug release from the films was found to be controlled over a period of 8 h. The films were found to be stable and were able to reduce the intraocular pressure for 24 h in a more efficient manner than the eye drops. The films were found to be practically non-irritating to the eye.

Conclusions. It can be concluded that the hydrogel from tamarind seeds can be used as a film-forming and release-controlling agent for the development of an ocular drug delivery system for the effective therapy of glaucoma (**Polim. Med.** 2016, 46, 1, 25–33).

Key words: polysaccharide, pharmacodynamics, ocular safety, tamarind seed, timolol maleate.

Glaucoma is the second leading cause of blindness. Worldwide, it is estimated that about 66.8 million people have visual impairment from glaucoma, with 6.7 million suffering from blindness. Glaucoma is characterized by increased intraocular pressure (IOP), followed by slow and progressive degeneration of retinal ganglion cells (RGC) and optic nerve axons leading to deterioration of the visual field. If untreated, the condition can lead to irreversible blindness [1].

Reduction of elevated intraocular pressure is the primary goal in the management of glaucoma. Beta blockers such as timolol maleate are the drugs of choice

for the therapy of glaucoma. Medications used to lower IOP act by increasing the outflow of aqueous humor or by reducing the production of aqueous humor [2]. The therapy involves administration of a drug by topical, oral, or parenteral routes. The conventional ocular delivery systems used in glaucoma management include solutions, suspensions and ointments. The most commonly-used dosage form is the eye drop, which is an aqueous solution of the drug.

The intraocular bioavailability of the drug through conventional eye drops is very poor due to factors such as nasolachrymal drainage, lacrimation, drug dilution

with tear fluid, tear turnover and conjunctival absorption. The binding of drugs to protein also contributes to the loss of drugs through the precorneal parallel elimination loss pathway. Consequently, only a small amount (1–3%) of the drug actually penetrates the cornea and reaches the intraocular tissue [3]. The use of a controlled-release drug delivery system can improve the corneal residence time of the drug.

Today, there is renewed interest in the development of multifunctional excipients from natural sources. Natural polymers are easy to isolate, cheap, non-toxic and biocompatible. Among the natural polymers, polysaccharide hydrogels are of importance as they are found as common ingredients in the cosmetics, food and pharmaceutical industries as binders, disintegrants, suspending agents, emulsifying agents and sustaining agents [4, 5].

Tamarind seed polysaccharide (TSP) is a galactoxyloglucan, obtained from the kernels of *Tamarindus indica* (Family: Leguminosae). It possesses properties like high viscosity, broad pH tolerance and adhesivity. Recently, its non-carcinogenicity, mucoadhesivity, biocompatibility, high drug-holding capacity and high thermal stability have been reported [6, 11]. Due to these properties, it is being used as stabilizer, thickener, gelling agent and binder in the food industry. It is also reported as a sustaining agent in the formulation of spheroids [5].

Consequently, in the present work, an attempt has been made to develop controlled-release matrix films containing timolol maleate, using the polysaccharide isolated from the seeds of *Tamarindus indica* (tamarind) as a film-forming and sustaining agent in the development of an ocular delivery system.

Materials and Methods

Materials

Tamarind seeds were purchased from the market of Belgaum (Karnataka, India). Timolol maleate was obtained from Centaur (Mumbai, India). All other ingredients used in the present study were of AR grade and were purchased from Ranbaxy Fine Chemicals (New Delhi, India).

Methods

Isolation of Polysaccharide From Tamarind Seeds [4, 11]

The seeds were washed thoroughly with water to remove the adhering materials. Then, the reddish testa of the seeds was removed manually and the seeds were crushed lightly and used for isolation of mucilage. The crushed seeds of *Tamarindus indica* were soaked in water for 24 h, boiled for 1 h, and kept aside for 2 h for the release of the polysaccharide into water. The soaked

seeds were taken and squeezed in a muslin bag to remove marc from the filtrate. Then, an equal quantity of ethanol was added to the filtrate to precipitate the polysaccharide, which was separated by filtration. The marc was not discarded but it was sent for multiple extractions with a decreasing quantity of extracting solvent, *i.e.*, water, with the increase of the number of extractions. The isolation was continued until the material was free of polysaccharide. The separated polysaccharide was dried in an incubator at a temperature of 40°C. The dried hydrogel was powdered and stored in airtight containers at room temperature.

Characterization of Polysaccharide

The purity of the polysaccharide was determined by using tests for different phytoconstituents [12]. The pH of 1% w/v solution was determined using a digital pH meter. The swelling index of the polysaccharide was determined using the WHO method [13], which is described below.

The swelling index is the volume (in mL) taken up by the swelling of 1 g of test material under specified conditions. An accurately weighed quantity of the polysaccharide (1 g) – previously reduced to the required fineness – was introduced in a 25 mL glass-stoppered measuring cylinder. Twenty-five mL of water was added and the mixture was shaken thoroughly every 10 min for 1 h. It was then allowed to stand for 3 h at room temperature. Then the volume occupied by the polysaccharide, including any sticky mucilaginous portion, was measured. The same procedure was repeated thrice and the mean value was calculated.

Drug-Polysaccharide Compatibility

The compatibility between timolol maleate and TSP was determined using a FTIR peak-matching method using a Shimadzu FTIR spectrophotometer [14].

Preparation of Ocular Films

Matrix type ocular films containing timolol maleate were prepared using a molding technique. The dose of the drug was kept at 1 mg per film (of a diameter 0.4 cm and area 0.5 cm²). A glass mold of 7.6 cm diameter (57.6 cm² area) was used for the preparation of films. Timolol maleate (316 mg) was dissolved in 10 mL purified water, to which the required quantity of polysaccharide was added as per the formula shown in Table 1 and mixed using a stirrer (Yamato, Japan) at 800 rpm for 30 min. This mixture was subjected to sonication for a period of 30 min to remove the air bubbles and then transferred into the glass mold. The inner surface of the glass mold had been previously coated with 2–3 drops of glycerin. It was dried at 45°C for 24 h in a hot air oven. After complete drying, the film was removed from the mold and cut into small circular films of 0.4 cm diameter using a previously cleaned cork borer. Six batches of films were prepared as per the details given in Table 1.

Table 1. Composition of various batches of ocular films

Ingredient	Batch 1	Batch 2	Batch 3	Batch 4	Batch 5	Batch 6
TSP (mg/10 mL)	500	600	700	800	900	1000
Timolol maleate	316	316	316	316	316	316

Evaluation of Ocular Films

The developed films were evaluated for various physicochemical properties like drug content, weight variation, average thickness, diameter and in vitro release profile. The optimized batch of ocular films developed was subjected to optimization of the sterilization technique and stability studies as per ICH guidelines. The thickness of the films was determined using a digital micrometer (Mutotoya, Japan). For the determination of average weight, six films from each batch were weighed accurately by using digital balance (Shimadzu, Japan).

Average weight of the six films was calculated and the deviation from the average weight was determined. The diameters of six randomly selected films were recorded with the help of digital calipers (Mutotoya, Japan) and the average diameter and standard deviation were calculated.

To determine the drug content, five ocular films were crushed into powder form, the powder was dissolved in 25 mL of simulated tear fluid (pH 7.2) and the solution was sonicated for 30 min and centrifuged. The supernatant was filtered and the absorbance was measured after suitable dilution at 294 nm. The drug content was determined in triplicate. The same procedure was followed for all of the six batches.

In Vitro Release Behavior

The *in vitro* release behavior of the developed ocular films was determined by a method reported earlier [15]. In vitro release behavior of the developed formulation was performed by taking the 5 mL simulated tear fluid (pH 7.2) in a glass vial, in which the ocular film was placed. The glass vial was shaken on the mechanical shaker cum water bath at 20 rpm and the temperature was maintained at $37 \pm 0.1^\circ\text{C}$. The sampling was done for a period of 8 h at various time intervals. The sampling volume at each time interval was 0.5 mL, which was replaced each time by an equal volume of the dissolution medium (simulated tear fluid with pH 7.2). The samples were then analyzed spectrophotometrically at 294 nm.

To determine the release kinetics of the drug from the ocular film, the drug release data was fitted according to a zero order equation. The release mechanism was determined according to Peppas' equation.

The drug release data was statistically analyzed by two-way ANOVA. The *p* value of < 0.0001 was considered statistically significant. All the calculations were performed using GraphPad Prism v5 (GraphPad Prism Software Inc., San Diego, USA).

Optimization of Sterilization Method

Ideal batch of films were packed in polythene sheets using heat sealing and were sterilized using two different methods, viz., autoclaving at 121°C (15 lb pressure) for 25 min and exposure to UV radiation for 5, 10, 15, 20, 25, 30, 35 and 40 min. For sterility testing, two media, namely fluid thioglycolate medium and nutrient agar medium, were used to investigate the presence/absence of the aerobic, anaerobic bacteria and fungi in the formulated sterilized delivery system [16]. All the samples were inoculated separately in the fluid thioglycolate medium and nutrient agar medium, and were incubated for 7 days at 37°C . One unsterilized sample was also used in the test.

Stability Studies

To assess the stability of an ideal batch of films, a study was carried out as per ICH guidelines for Zone-III/IV countries (MKT: 40°C , 75% RH) in a stability chamber for a period 45 days after packing the films in polythene packs by heat sealing, followed by sterilization [17]. Sampling was done after 30 and 45 days and the films were evaluated for physical appearance, drug content, and in vitro drug release by adopting the procedures mentioned earlier.

Pharmacodynamic and Ocular Safety Studies

Pharmacodynamic and ocular safety studies were carried out after obtaining the approval from the animal ethics committee (No. MIET/IAEC/MPh/PhCeutics/001/2008-2009, dated 03.05.2008). For the study, three albino rabbits of either sex weighing approximately 750 g were selected. The animals were housed in the animal house in clean individual cages. The animals were maintained under 12 h day and night cycles with temperature ranging between $24\text{--}26 \pm 2^\circ\text{C}$. The animals were allowed free access to food and water at all the times during the duration of the study. The rabbits were thoroughly examined for any ophthalmological abnormalities prior to use. The study was planned in two phases in overnight fasted rabbits with a wash over a period of 10 days. In the first phase, marketed eye drops (3 drops \approx 1 mg drug) were tested (Brand: Glaucomol, Mfd: Allergan) and in the second phase the developed ocular films were tested (one film \approx 1.01 mg drug). The test delivery system was administered to the lower conjunctival sac and its IOP reducing potential and ocular safety was evaluated. The potential of the formulated delivery system in controlling the IOP was evaluated by adopting a tonometric technique [18]. IOP measurements were done at 0.5, 1, 2, 3, 4, 6, 8, 12

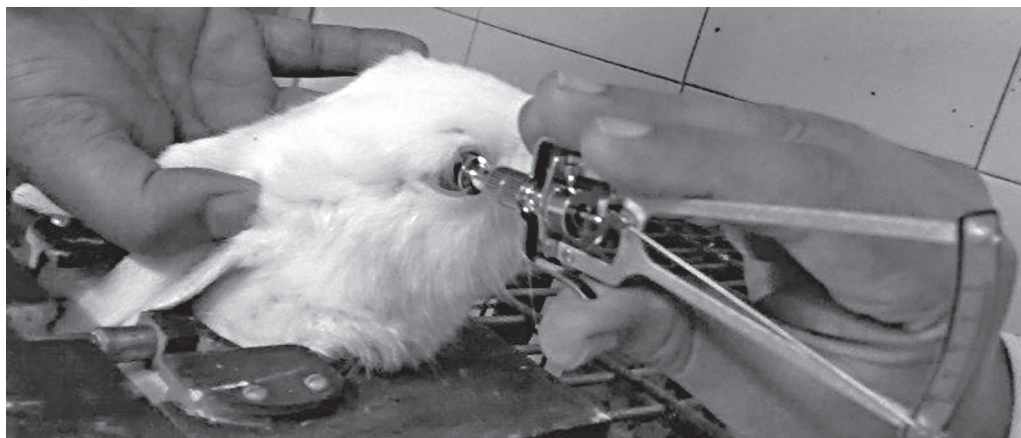


Fig. 1. Measurement of intraocular pressure in rabbits using Schiotz tonometer

and 24 h post administration. A Schiotz tonometer was used for this purpose. The tonometer was cleaned with alcohol and placed in a convex test block to assure the position of the pointer. The weight marked 10 g was always on the plunger. For measuring the IOP, rabbits were placed in restraining boxes and their eyelids were retracted gently with one hand, without exerting pressure on the eyeball, and the tonometer was placed in the horizontal position on the center of the cornea (Fig. 1).

The handle was midway between the top and foot plate of the cylinder, thereby the instrument might cut independently with its own weight. The position of the pointer was noted and the tension in mmHg was determined from the calibration scale. The various scale readings for various IOP are shown in Table 2.

The pharmacodynamic study was performed for the developed timolol maleate ocular films, and the results were compared to the brand of marketed eye

drops. The observations were tabulated and the changes in IOP were calculated. The IOP-reducing potential of individual delivery systems were compared based on the area under the curve (AUC) of the change in IOP vs. the time curve adapting the trapezoidal rule [19]. The ocular safety of the delivery system administered was observed between each phase of the pharmacodynamic evaluation over a period of one week [20, 21]. The Draize scoring approach was followed, where the cornea, iris and conjunctiva were observed, scored and evaluated by following Tables 3 and 4, which show the scoring scale and evaluation chart which demonstrates the ocular safety after formulation administration.

To test the significant difference in IOP among the treated animal groups, a t test was applied. The p value of < 0.001 was considered statistically significant. All the calculations were performed using GraphPad Prism v5 (GraphPad Prism Software Inc., San Diego, USA).

Table 2. Intraocular pressure scale for use with Schiotz tonometer

Scale	9	9.5	11.5	12	13	13.5	14.5	15	15.5	16	16.5	17
Corresponding IOP (mmHg)	19.6	18	12.6	11.5	9.5	8.6	7.1	6.4	5.8	5.2	4.7	4.2

Table 3. Ocular safety scoring and calculation

Ocular tissue	Scoring scale	Calculation	Total
Cornea: Opacity (O) Area involved (A)	0, 1, 2, 3, 4 0, 1, 2, 3, 4	$O \times A \times 5$	80
Iris: Values for congestion and hemorrhage (I)	0, 1, 2	$I \times 5$	10
Conjunctiva: Redness (R) Chemosis (C) Discharge (D)	0, 1, 2, 3 0, 1, 2, 3, 4 0, 1, 2, 3	$(R + C + D) \times 2$	20
	Total maximum		110

Score of 0 is normal, 1 is trace, 2 is mild, 3 is moderate and 4 is severe in the case of O, R, C and D.

Score of 0 is none, 1, 2, 3 and 4 is the extent of the cornea covered for A.

Score of 0 is normal, 1 is moderate and 2 is severe in the case of I.

Table 4. Draize scoring evaluation chart for ocular safety

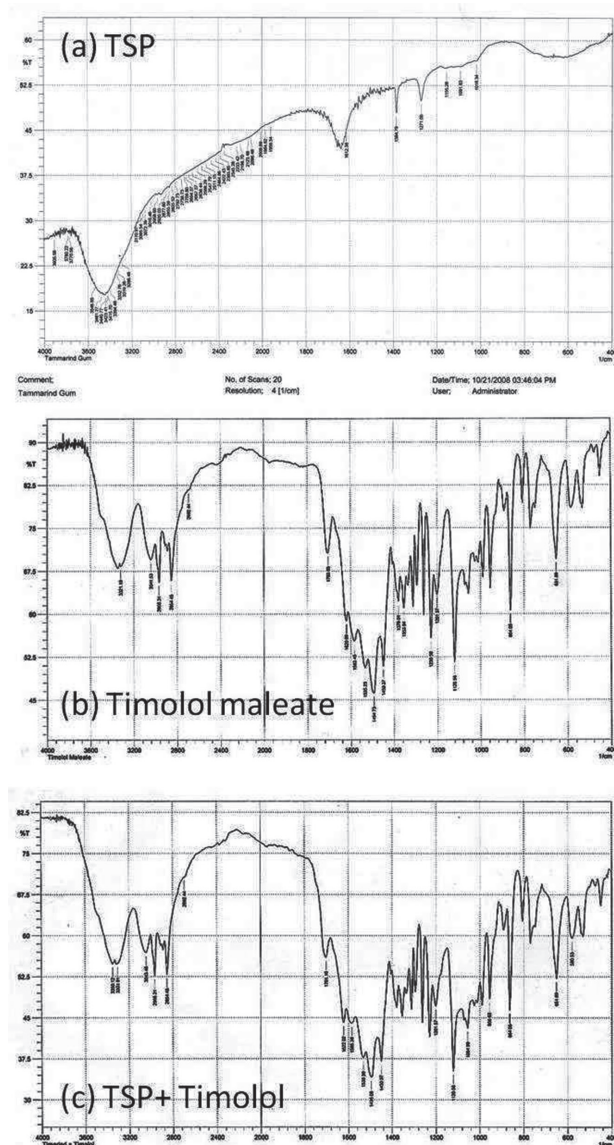
Score	Rating
0.5	Non-irritating
0.5–2.5	Practically non-irritating
2.5–15.0	Minimally irritating
15.0–25.0	Mildly irritating
25.0–50.0	Moderately irritating
50.0–80.0	Severely irritating
80.0–110.0	Extremely irritating

Results and Discussion

After hot water extraction and acetone treatment, the Tamarind seeds yielded 58.29% w/w of polysaccharide. The results of the purity tests showed the presence of carbohydrates. Other phytoconstituents such as alkaloids, flavonoids, steroids, amino acids, terpenes, glycosides, oils-fats, phenols and tannins were absent in the isolated powder. This can be considered as proof for the purity of the isolated polysaccharide.

The pH of the 1% solution of the polysaccharide was 6.85, which was slightly acidic/near neutral. This indicated that the polysaccharide was non-irritating to the eye. The TSP was found to swell to 18.26 mL, which is an indication of good water absorption, and hence, the formation of a hydrated three-dimensional network, from which the drug release might follow diffusion. In the compatibility study, the mixture of timolol maleate and TSP did not show any physical changes such as discoloration and caking. No significant changes were found when an IR spectrum of the physical mixture was compared to the IR spectrum of the pure drug and polysaccharide (Fig. 2). Even though it is a crude method, this indicates the absence of any possible interaction between the drug and polymer.

The results of the various physical properties and drug content of the prepared ocular films are given in Table 5. The thickness of different batches of the ocular films was found to be in the range of 0.17 to

**Fig. 2.** FTIR spectra of TSP, timolol, and physical mixture

0.25 mm. The films were considered to be non-irritating to the eye due to their low thickness. The average weight of the films was found to increase with an increase in polymer content. The highest weight variation was

Table 5. Physical properties and drug content of different batches of ocular films

Batch Code	Thickness* (mm)	Weight* (mg)	Diameter* (mm)	Drug content per film (mg)	
				Theoretical	Practical**
Batch 1	0.19 ± 0.03	2.28 ± 0.31	0.4 ± 0.00	1.00	0.98 ± 0.01
Batch 2	0.18 ± 0.03	2.88 ± 0.77	0.4 ± 0.00	1.00	0.98 ± 0.01
Batch 3	0.21 ± 0.02	3.20 ± 0.28	0.4 ± 0.00	1.00	0.99 ± 0.01
Batch 4	0.17 ± 0.04	3.50 ± 0.68	0.4 ± 0.00	1.00	1.00 ± 0.00
Batch 5	0.25 ± 0.04	3.15 ± 0.48	0.4 ± 0.00	1.00	0.99 ± 0.00
Batch 6	0.24 ± 0.04	3.95 ± 0.27	0.4 ± 0.00	1.00	1.01 ± 0.01

*Average of six determinations ± SD; ** Average of three determinations ± SD.

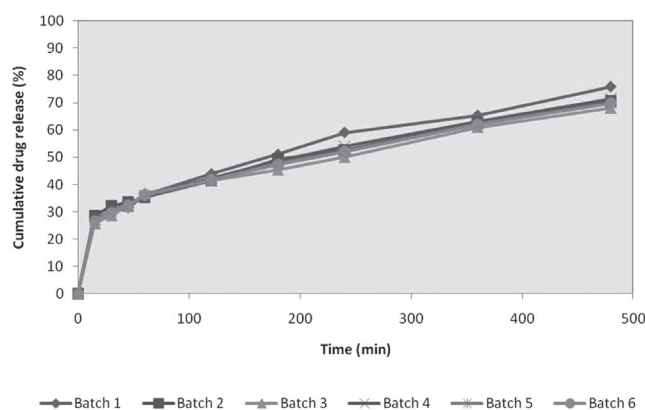


Fig. 3. *In vitro* release of timolol maleate from various batches of ocular films

found to be $\pm 33\%$ in Batch 2. The drug content variation was found to be within $\pm 5\%$ in all the batches.

The *in vitro* release behavior of the drug from the different batches of ocular films is shown in Figure 3. From the results, it is observed that the drug release is controlled by polymer concentration. The release of the drug was significantly decreased with the increase in the polymer concentration ($p < 0.0001$).

The release pattern was found to be linear with correlation coefficients in the range of 0.951 to 0.992 (Table 6). This indicated that the release might be following zero order kinetics. Hence, in order to determine the mechanism of drug release from the films, Peppas' model of data fitting was applied [22]. In this model, the log-cumulative percentage of the drug released is plotted against log time.

According to Peppas' equation, the rate of drug release can be expressed as:

$$\log Q = \log K + n \log t$$

Where Q is the amount of drug released, ' t ' is the time and ' n ' is the slope of the linear plot. If the value of n is less than or equal to 0.5, the mechanism of release is diffusion without swelling. If the value is greater than 0.5 and less than 1, the mechanism is anomalous diffusion, not conforming to any of Fick's laws (non-Fickian) [23].

The correlation coefficient (r) and diffusion coefficient (n) values for the various batches of ocular films are shown in Table 6. The ' n ' values indicated that the release mechanism of timolol maleate from the developed ocular films in simulated tear fluid was diffusion without swelling.

Upon application of two-way analysis of variance (ANOVA), a significant difference was observed in *in vitro* release profiles among the developed ocular films at a 95% confidence interval ($p < 0.0001$), as the calculated F value was higher than the tabulated value. This substantiates the role of polysaccharide in controlling the drug release (Table 7).

Based on the physicochemical properties and release behavior, Batch 6 was selected as the ideal batch and was used for further studies like optimization of the sterilization technique, stability studies, *in vitro* pharmacodynamic and ocular safety studies. The ideal batch of the developed formulation was sterilized using surface sterilization by UV exposure and autoclaving. Among these, exposure to UV radiation was found to be an ineffective method of sterilization for the developed formulation, as microbial growth was observed the samples exposed to UV radiation for a maximum period of 40 min. After autoclaving, there was no microbial growth in the nutrient agar as well as the fluid thioglycolate media. Hence, autoclaving was considered as an ideal method for sterilization of the developed ocular films.

Table 6. Correlation coefficients and diffusion coefficients of dissolution data and Peppas' plots

Formulation Code	Correlation coefficient (r) of cumulative release plots	Correlation coefficient (r) of Peppas' plots	Diffusion coefficient (n) of Peppas' plots
Batch 1	0.983	0.978	0.311
Batch 2	0.992	0.961	0.262
Batch 3	0.986	0.977	0.277
Batch 4	0.971	0.985	0.301
Batch 5	0.951	0.987	0.342
Batch 6	0.986	0.987	0.340

Table 7. Results of ANOVA on the release profiles of timolol maleate from different formulations

Source of variation	Sum of square	Degree of freedom	Mean square	Calculated F	Tabulated F
Column factor	57.15	5	11.43	6.439	1.91
Row factor	11 150	8	1394	785.5	1.96
Residual	71.01	40	1.775		

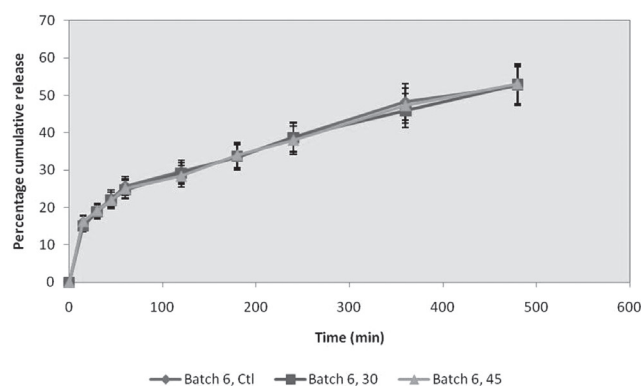


Fig. 4. *In vitro* release profile of ocular films after 0, 30 and 45 days of stability study

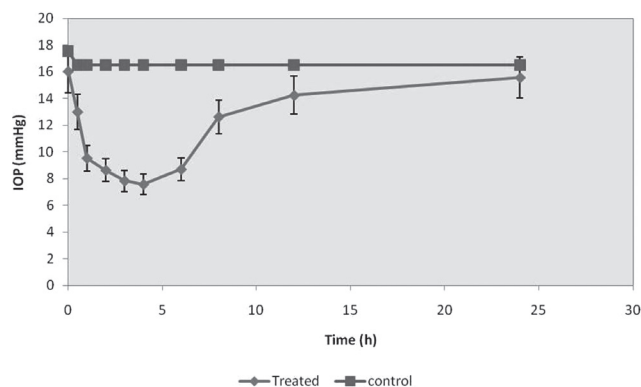


Fig. 5. Reduction of IOP after administration of eye drops

Table 8. Stability of the ocular films after storage at 40°C/75% RH for 45 days

Property	Control	30 days	45 days
Physical appearance	X	NC	NC
Weight (mg)**	3.58 ± 0.231	3.47 ± 0.150	3.55 ± 0.44
Thickness (mm)**	0.245 ± 0.043	0.245 ± 0.043	0.243 ± 0.038
Diameter (cm)**	0.4	0.4	0.4
Drug content (mg)*	1.003 ± 0.005	1.004 ± 0.013	1.001 ± 0.008

* Average of three determinations ± SD; ** Average of six determinations ± SD; NC – no significant change; X – brown colored ocular films.

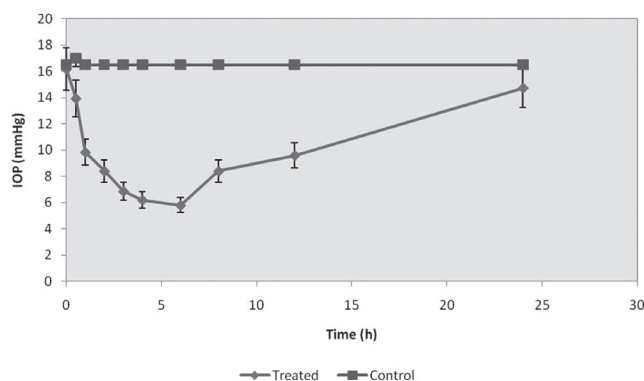


Fig. 6. Reduction of IOP after administration of ocular films

The results of the stability studies are shown in Table 8 and Figure 4. There were no changes in the appearance, physicochemical properties or *in vitro* drug release behavior of the film. Hence, the formulation was considered to be stable at 40°C/75% RH (conditions for zone III/IV countries as per ICH guidelines). On application of one-way ANOVA, no significant difference was observed in the *in vitro* drug release profiles at various study points (0, 30 and 45 days) at 5% confidence interval ($p < 0.05$), as the table F value was higher than the calculated F value.

The results of the comparative pharmacodynamic evaluation of the developed timolol maleate ocular films and marketed timolol maleate eye drops are given

in Figures 5 to 7. The reduction in IOP after administration of eye drops was found to be rapid (Fig. 5). The maximum reduction in IOP was observed at 4 h, after which the pressure started increasing. This might be due to limited absorption and rapid elimination of the drug from the precorneal area. After application of the ocular films, a similar decrease in IOP was observed. The maximum reduction in IOP was found to be at 6 h, which was further extended up to 12 h (Fig. 6).

The IOP reducing potential of the ocular film was initially slow but the reduced IOP was maintained for 24 h, whereas eye drops had a sharp IOP-reducing potential as compared to the films but the reduction in IOP was not maintained for a long period as compared to the films. This can be observed clearly in the change in IOP vs time curve (Fig. 7).

The area under the IOP change vs time curve for eye drops was found to be 88 mmHg h, whereas for the developed films, it was 148.425 mmHg h, which is 1.69 times higher than that of the eye drops (Table 9). This indicates the better corneal residence and availability of the drug at the site of action.

Compared to the eye drops, there was a significant difference ($p < 0.001$) between the intraocular pressure of the animals upon ocular film administration suggested by the 1.68-fold enhanced AUC (mmHg h) values.

The results of the ocular safety study are given in Table 10. The ocular safety score for the conventional

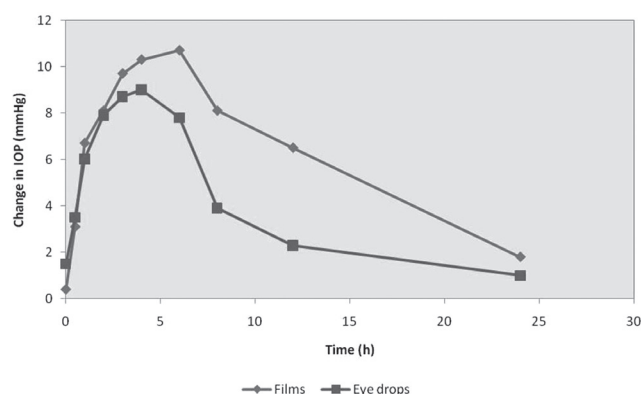


Fig. 7. Change in IOP at different time intervals after administration of eye drops and ocular films

Table 9. Area under the curve (AUC) for change of IOP vs time plot

Time (h)	AUC (mmHg h)	
	eye drops	ocular films
0–0.5	1.25	0.875
0.5–1	2.38	2.45
1–2	6.97	7.4
2–3	8.3	8.9
3–4	8.9	10.0
4–6	16.8	21.0
6–8	11.2	18.8
8–12	12.4	29.2
12–24	19.8	49.8
Total	88	148.425

Table 10. Ocular safety scoring and calculation for eye drops and ocular films

Ocular tissue	For eye drops			For ocular films		
	Scoring scale	Calculation	Total	Scoring scale	Calculation	Total
Cornea: Opacity (O) Area involved (A)	0 0	$0 \times 0 \times 5$	0	0 0	$0 \times 0 \times 5$	0
Iris: Values for congestion and hemorrhage (I)	0	0×5	0	0	0×5	0
Conjunctiva: Redness (R) Chemosis (C) Discharge (D)	0 0 0	$(0 + 0 + 0) \times 2$	0	1 0 0	$(1 + 0 + 0) \times 2$	2
Total maximum score			0			2

eye drops was 0, and hence, eye drops were considered totally non-irritating. In the case of ocular films, there was no corneal opacity, congestion or hemorrhage in the iris.

Only slight redness was observed in the conjunctiva, for which a score of 2 was given. This score of 2 can be considered insignificant when compared to the maximum score of 110, and therefore categorized as practically non-irritating.

Conclusion

In conclusion, it can be stated that the developed ocular films can reduce the dose intake, dose frequency and dose-related adverse effects of timolol maleate and ultimately, improve the pharmacotherapy of glaucoma. The natural polysaccharide from the seeds of *Tamarindus indica* can be used as a film-forming and release-controlling agent for the development of an ocular drug delivery system, which can be a cheaper alternative to synthetic polymers. Ocular pharmacokinetic studies in glaucomatous subjects are, however, needed to establish the potential of the ocular films developed.

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