Formulation and Evaluation of Naphazoline HCl Ocular Insert

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Abstract: Ocular approach for the delivery of drug is the major challenge in the field of Pharmaceutical science. Many efforts have been done for the formulation of the ocular film so that the film can release the drug for the sustained period of time. In the present study 6 batches of ocular films (F1-F6)with drug Naphazolinewere prepared and evaluated. The evaluation parameters liketensile strength, pH, drug content estimation, weight uniformity, swelling index and *in vitro* drug release were determined. The tensile strength was found to be highest for F5 batch (5.32±0.04) and least for batch F2 (3.82±0.05). The pH of all the batches was found to be almost neutral. Swelling property of the film was observed for the period of 5hrs and *in vitro* release was determined for 4hrs. The*in vitro* results showed that the release of the drug from F5 batch after the dissolution study was 99.12%.F5 batch was found to be best as compared to other prepared batches with drug content of 90.5% and release of 99.12%.

Key words: Ocular Drug Delivery · Insert · Solvent Casting Method · Naphazoline

INTRODUCTION

Ocular drug delivery system is the most challenging part for the delivery of the medicament. Conventional dosage form suffers from the major side effect i.e. lack of retention in the eye. So novel forms ofdrugs were designed to showsustain release of medicament and better retention of drug [1]. The ideal property of the ocular drug delivery system is to release the drug for sustained period of time and to retain the drug [2]. Ocular insert isone of the examples of noveldrug delivery systemwhich has shown various advantages over conventional dosage form Kumar *et al*. [1]. Inserts are defined as the solid preparation that are sterile in nature and placed in cul-de-sac region of eye. The shape and size of the inserts are defined as per the application. They provide control drug delivery and consist of polymeric vehicle containingthe drug [3]. The retention power of the drug has been increased in the pre corneal region which is the major disadvantage of conventional dosage form Sharma and Tomar [4]. Other advantage of the insert over the conventional dosage form includes release of drug at slow and constant rate, dose accuracy and increment in the shelf-life of the drug [5].

Naphazoline HCl is a α-adrenergic agonist and hypertensive vasoconstrictor. It constricts the peripheral blood vessels. It differs from other sympathomimetic amines as it depresses central nervous system. It consists of ethylamine side chain which becomes the part of hetrocyclic ring [6]. It is a hydrophilic drug. It is used to get relief from swelling and redness of eye. It has less bioavailability so, to overcome this problem ocular insert of Naphazoline HCl has been formulated by using different polymers. Very few inserts of Naphazoline HCl are available in market. Hence in present study, an attempt is made to formulate the ocular insert of Naphazoline HCl using suitable polymer like carbopol and guargum.

MATERIALS AND METHODS

Naphazoline HCl was obtained from Panchsheel Organics Ltd, New Delhi. Carbopol was a gift sample from Parex Pharmaceuticals Pvt. Ltd., Mohali. Guar gum was purchased from Central Drug House (P) Ltd. New Delhi.

Formulation of Naphazoline HCl Films: The preparation of the ocular films was done by solvent casting method.

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Table 1: Composition of prepared ocular films of Naphazoline HCl

Ingredients	Formulationcode					
	F1	F2	F3	F4	F5	F6
Naphazoline HCl (mg)	150	150	150	150	150	150
Carbopol (mg)	16	18	20	22	24	26
Guar Gum (mg)	120	120	120	120	120	120
Glycerine (ml)	1	1	1	1	1	1
Distilled Water (ml)	40	40	40	40	40	40

6 batches (F1-F6) of the ocular film were prepared by varying the concentration of polymers. The batches were prepared by dispersing the carbopol in the warm water by continuous stirring, then theguar gum was added to the mixture and stirring was continued for half an hour. To the above solution known amount of drug was added and stirring was continued until the drug gets properly dispersed in the solution. Glycerol was added to the solution which acts as a plasticizer. The same procedure was repeated to prepare 6 batches of the film as per the composition shown in Table 1 [7].

Evaluation of Physicochemical Parameters:
Surface pH: The surface pH was determined by swelling the film in distilled water for 1hr. The pH of the film was determined by pH meter. The electrode of the instrument was dipped in the beaker containing the film till the reading flashed on the instrument. The reading was noted down. The same procedure was repeated thrice for the calculation of the mean [6].

Swelling Index: Ocular films (1 cm^2) were cut from each batch. The film was weighed accurately and placed in the Petridish containing 10ml of distilled water. Weight of the dried film for different batches of formulation was taken at different interval of 15, 30, 45, 60, 120, 180, 240, 300 minutes. The swelling index was calculated by the formula[6].

$$\text{Swelling index} = \frac{\text{Final weight-initial weight}}{\text{Initial weight}} \times 100$$

Drug Content Estimation: The film wascut in three pieces having the size of 1 cm^2 and was kept in different beakers which consist of 10ml of simulated tear fluid. The film along with fluid was stirred upto6hrs and the solution was left as such for 24hrs without any disturbance. The solution was then filtered and analyzed by UV spectrophotometer at 280nm and diluted further for the estimation of the drug content using the formula. Same procedure was repeated for other batches [6].

$$\text{Drug Content} = \frac{\text{Concentration} \times \text{DF} \times \text{Bulk Volume}}{1000}$$

where, DF is Dilution factor

Thickness Uniformity: The film of all of the prepared batches was taken and the film thickness was estimated by screw gauge by placing it at different place. The procedure was repeated thrice and standard deviation was calculated.

Tensile Strength: It determines the flexibility of the film. The instrument used for the strength determination was tensile tester. Hook was inserted in the paper holder which was connected to one end of the film while the other end of the film strip of dimension 1 cm^2 was fixed between the two iron screens to give support to the film. To this hook a thread was tied which was passed over the pulley and to hold the weight a small pan was attached to the other end. A small pointer, attached to the thread, which travels over the scale, was affixed on the base plate. Pulley system pulled the patch to determine tensile strength. To increase the pulling force, weights were progressively added to the pan till the patch was broken. The weights which were necessary to break the film were considered as its tensile strength. The tensile strength was calculated in kg/cm^2 using the formula [6].

$$\text{Tensile Strength} = \frac{\text{Force at break}}{\text{Cross sectional area of film}} \times 100$$

Folding Endurance: 1cm^2 film was taken from each formulation. Folding endurance was determined by repeat folding of film at the same place till it breaks. The number of time is counted down for the film upto which it is folded without breaking determines the folding endurance of the film. Three reading was taken for all the batches and the average was calculated.

Weight Uniformity: Four films from all the batches (1cm^2) were taken andthe weight of the film was determined by the single pan balance. The standard deviation was calculated from the average reading [7].

Disintegration: The disintegration of the film was done by Petridish method. In this method 1cm^{2}area of all the films was cut and kept in the Petridish containing 10ml of simulated tear fluid, slight movement was provided to maintain the condition as per ocular delivery. Film disintegration time will be noted.

Dissolution: *In vitro* study was conducted in simulated tear fluid. The insert was placed on dialysis cell and was in contact with isotonic buffer solution using cellophane membrane. Temperature was kept at 37± 1°C. 1 ml sample was withdrawn at 1, 2, 5, 10,15, 20, 25, 30, 45, 60, 90, 120 and 240 minutes. The drug content of the film was estimated spectrophotometrically at 280 nm [8].

RESULTS AND DISCUSSION

Surface pH: The change in the concentration of polymer has slightly effected the change in the pH of the formulation. The pH of the formulation was found to be from 6.8±0.01 to 7.1±0.03. The pH of the film was found to be almost neutral hence there are no chances of irritation.The concentration of the drug, guar gum, glycerine and water was kept constant were as that of carbopol the concentration was changed. The results are shown in Figure 1.

Swelling Index: The measured swelling index shows maximum swelling in F5 f ormulation and least in F2. The results forswelling index of different film are shown in Figures 2 and 3.

Drug Content Estimation: Estimation of drug content was done to check the uniform distribution of drug. The triplicate reading for all the formulation was taken to estimate the drug content. The reading showed that drug was uniformly distributed in all films. The percentage drug content was in the range of 65.36±0.11 to 90.3±0.05 [9].

Thickness Uniformity: The thickness of the films ranges from 0.196 to 0.212. The prepared film shows uniform thickness. It can be concluded that the drug was uniformly distributed and the dose in each strip administered was accurate.

Tensile Strength: The results data of the tensile strength shows that film possessed good strength. The range of the tensile strength varies from 5.32±0.04 to 3.82±0.05. The tensile strength was found to be highest for F5 and least for F2.

Folding Endurance: This parameter depicts the flexibility of the film in the way that flexible film has high value of folding endurance and brittle film show lower endurance value.As the data obtained no film had shown any crack even after 350 times folding, hence film shows satisfactory flexibility.
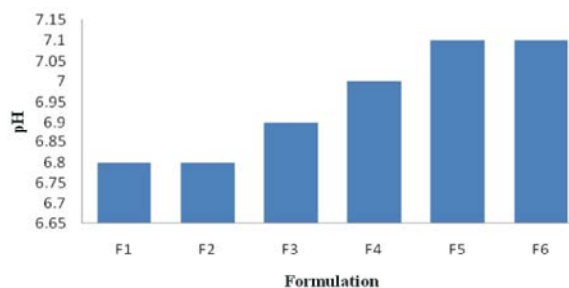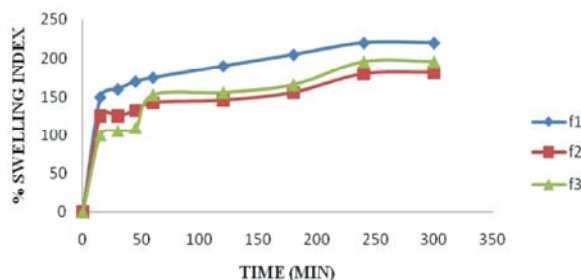

Fig. 1: pH for various formulations

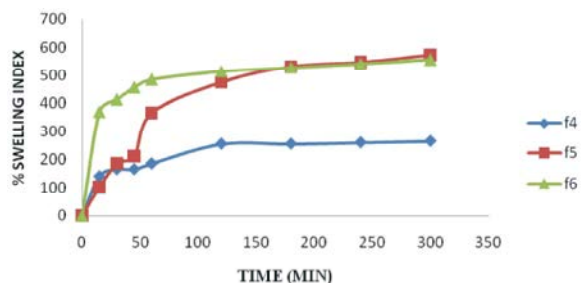Fig. 2: Swelling index of different films (F1-F3)

Fig. 3: Swelling index of different films(F4-F6)

Weight Uniformity: All the formulation shows uniform weight and it ranges from 0.039 to 0.049gms. By increasing the weight of the polymer the weight of the film also increases.

Disintegration: The results of the disintegration time of the ocular film are shown in Table 2. The disintegration time of formulation F5 was minimum i.e. 18 min and for F2 was maximum of 31 min.

The different evaluation parameters of the prepared films are summarized in Table 2.

Dissolution: It helps to evaluate the ability of the formulation to release the dose in expected time.

The release study showed that all the formulation has released the drug in all formulation. Maximum *in vitro* release was found to be 99.12% with batch F5 and least was 89% with batch F2.The graph was plotted between percentage cumulative drug release and time which is shown in Figures 4 and 5.

Table 2: Evaluation parameters of the films

| Parameters | Formulation Code | | | | | |
	F1	F2	F3	F4	F5	F6
Surface pH	6.8	6.8	6.9	7.0	7.1	7.1
Thickness (mm)	0.198±0.02	0.196±0.05	0.204±0.04	0.209±0.05	0.212±0.03	0.21±0.04
Tensile Strength (kg/mm^2)	3.94±0.04	3.82±0.05	4.93±0.04	5.13±0.05	5.32±0.04	5.25±0.07
Drug Content	65.36%	64.51%	74.8%	81.8%	90.5%	83.01%
Folding Endurance	□350	□350	□350	□350	□350	□350
Weight Uniformity (gm)	0.039	0.041	0.042	0.045	0.046	0.049
Disintegration Time (mins)	24	31	23	20	18	21
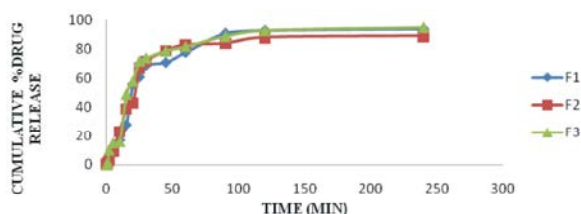
Fig. 4: *In vitro* drug release for different film(F1-F3)
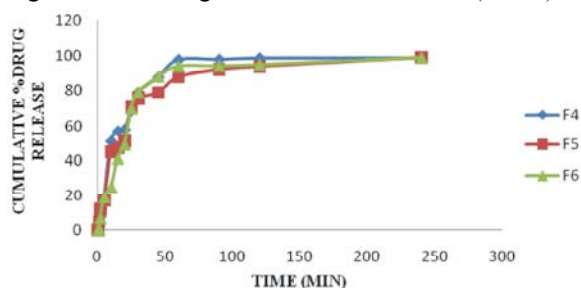
Fig. 5: *In vitro* drug release of different films (F4-F6)

Our results are in agreement with those reported by Venkateshwar Rao [10].

CONCLUSION

Six batches of the ocular films were prepared by solvent casting method. Naphazoline HCl was the drug used for the preparation of films along with carbopol, guar gum and glycerine. All the evaluation parameters for the film wereperformed on each batch and they were correlated. All the films were almost neutral in terms of pH. The thickness was in range of0.196-0.21 mm and the tensile strength in range of 3.82-5.32 kg/mm^2. Drug content of F5 batch (90.5%) was found to be maximum amongst all the other batches. Folding endurance of all the batches was found to be more than 350 which suggest that all the films possessed good mechanical characteristics. Weights of films were in range from 0.039-0.049gms. Results of *in vitro* release suggest that maximum release was found to be 99.12% with F5 batch and minimum with batch F2 of 89%. Therefore it was concluded from the research work that F5 batch was best

from the other batches prepared in terms of tensile strength, drug content and drug release.

Conflict of Interest: Author has no conflict of interest.

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