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Formulation and Development of Controlled Released Ocular Insert

Dr. Amol U.Gayke[1] ,Ms. Sakshi A Tribhuvan[2], Prof. Vikas S.Shinde[3], Prof. Preetam L.Nikam[4], Dr. Pradyumna Ige[5]

Department of Pharmaceutics

SND College of Pharmacy, Babhulgaon, Yeola, Dist.- Nashik 423201.

Corresponding Author:Dr.Amol U.Gayke

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KEYWORDS

Ocular Insert**,** HPMC, Ethyl Cellulose, solvent casting

ABSTRACT:

The primary goal of this study is to create flurbiprofen ocular inserts that are successful in preventing ocular infections. By increasing the medication's bioavailability through prolonged drug-eye contact times and regulating trans-corneal drug penetration, these inserts can improve ocular therapy. Our goal is to optimize the formulation to demonstrate a continuous release of the medicine, allowing for the maintenance of the dose for an extended duration. In order to do this, we created formulations of flurbiprofen ocular inserts using a variety of polymers, varying quantities of HPMC, ethyl cellulose, and a plasticizer called dibutyl phthalate. The produced formulations were assessed for stability, appearance, durability, v homogeneity of drug contents, in vitro and in vivo release of the drug, and other physical and analytical parameters. Flurbiprofen ocular implants were made using solvent casting.

Introduction

Pharmaceutical scientists find that among the different drug delivery methods, the area of ocular drug delivery is one of the most fascinating and difficult to work in. This method of medication administration circumvents the hepatic first pass effect and enters the systemic circulation, making it easily palatable. Extending an eye drug's contact with the corneal surface can significantly increase its therapeutic efficacy. To accomplish this, the medication is manufactured in a water-insoluble ointment formulation or viscosity-enhancing chemicals are added to eye drop preparations to prolong the period of intimate drug-eye contact. **[1]**.

Unfortunately, these dose forms do not produce a constant drug bioavailability and only provide a little more sustained drug-eye contact than eye drop solutions. Medication must still be taken often throughout the day. Therefore, applying the idea of controlled release as exemplified by ocular inserts presents a compelling alternative strategy to address the challenging issue of extending the pre-corneal drug residence period. **[2]**.

Ocular insert:

A sterile preparation having a solid consistency, specifically sized and shaped for eye application is known as an ocular insert. They are basically made of a drug-containing polymeric support.

The properties of the polymer, the casting solve

3nt, and the plasticizers employed determine how permeable the pharmaceuticals are through the ocular films. [3,8]

Material And Methdology

Flurbiprofen was received as gift sample from Sun Pharmaceutical Industries LTD. Andheri (E), Mumbai. HPMC E15, Ethyl Cellulose, Dichloromethane, Ethanol, Divutyl phthalate, sodium chloride, Calcium Chloride, Sodium Bicarbonate, Sodium Hydroxide pellets, Sulphuric acid were procured from S.D Fine Chemicals, Loba Chemie, etc. All the chemicals and reagents were of analytical grade.

Journal of Chemical Health Risks

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Shimadzu's Ultraviolet spectroscopy (UV-1601), Shimadzu FTIR spectrophotometer (8400S), Diffuse Cell Apparatus, Differential Scanning Calorimeter (DSC 60), Sonicator were used for spectroscopic analysis.

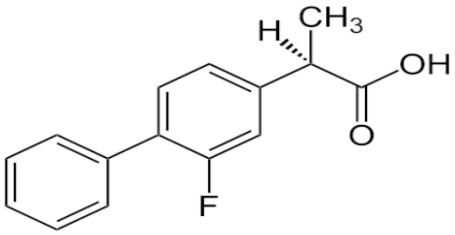

Fig 1. Chemical Structure of Flurbiprofen

Flurbiprofen is indicated for the management of vernal kerato conjunctivitis, post-operative ocular inflammation, herpetic stromal keratitis, excimer laser photorefractive keratectomy and ocular gingivitis. Recent reports suggest potential topical and systemic use of flurbiprofen in radio-protection, inhibition of colon tumor, protection of post-irradiation myelosuppression, pain management [6,9].

Solvent casting method:

One method of prep9aring ocular inserts is through solvent casting. 30% w/w of the polymer is the concentration at which plasticizer is introduced. Casting solvents include ethanol, dichloromethane, and distilled water. Using a magnetic stirrer to achieve a uniform dispersion, the proper polymers (2% w/v) and plasticizer (30% w/w) are dissolved in the right solvents to create the casting solutions. The substrate, mercury, is poured into a petri dish. Ten milliliters of the solution are poured into the mold, which is resting on the horizontal, smooth surface of the mercury. The dried film was obtained after 24 hours, and it was removed and kept at room temperature in a desiccator over fused calcium chloride for further use. [5,7].

3. Experimental work and Results

In present study, ocular inserts were prepared using solvent casting technique. This technique has been used extensively for the preparation of ocular inserts using variety of polymers starting from cellulose derivatives to acrylic polymers and biodegradable lactide and glycolide polymers.

- **Method of preparation of Ocular inserts**

All the required ingredients were accurately weighed. Dibutyl phthalate (DBP) was incorporated as a plasticizer at a concentration of 30% w/w of the polymer. Dichloromethane and ethanol (5:5) was used as casting solvent. The casting solution was prepared by dissolving the appropriate polymers (2% w/v), plasticizer (30%w/w) and Flurbiprofen (36 µg) in casting solvents using a magnetic stirrer to get a uniform dispersion. Mercury was use as the substrate and poured in to petridish. The mould was kept on the smooth horizontal surface of the mercury and 10 ml of the solution was poured into mould. After 24 h the dried film was obtained. The dried film thus obtained was taken out and stored over fused calcium chloride in a desiccator at room temperature for further use[10,11].

Table 1 : Formulation of batches of ocular insert:

Ocular inserts were prepared by using various polymer ratios (*i.e.*)

Ingredients	**Formulation code**								
	FO1	**FO2**	**FO3**	**FO4**	**FO5**	**FO6**	**FO7**	**FO8**	**FO9**
Flurbiprofen (µg)	36	36	36	36	36	36	36	36	36
HPMC E15 (mg)	200	160	120	80	40	500	525	550	575
EC(mg)	200	240	280	320	360	100	75	50	25

Journal of Chemical Health Risks
www.jchr.org
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Ethanol (ml)	5	5	5	5	5	5	5	5	5
Dichloromethane (ml)	5	5	5	5	5	5	5	5	5
DBP (ml)	1.2	1.2	1.2	1.2	1.2	1.8	1.8	1.8	1.8

Validation Of Optimized Formulation

All above primary 9 batches studies, Batch FO3 containing polymer ratio 7:3 was found to release the drug 99.70 % in 36 h and content uniformity was found to be highest 98.43% and hence was considered optimum for validation studies.

Optimized formula:

TABLE 2: OPTIMIZED FORMULA FOR FORMULATION OF OCULAR INSERT

Ingredients	FO3
Flurbiprofen (µg)	36
HPMC E15 (mg)	120
EC (mg)	280
DBP (ml)	1.2
0Ethanol (ml)	5
Dichloromethane (ml)	5

Five different batches of formulation FO3 were prepared and studied for evaluation of it's *in vitro* drug release and drug release kinetics. To the means of results of evaluation of different batches, one-way ANOVA test was applied to check the variance between the batches.

Result Of Optimized Formulation

Sr. No.	Evalution Parameter	F0A	F0B	F0C	F0D	F0E
A	Weight Variation	38.06333	37.09333	37.41	37.28333	37.64667
B	Thickness	0.366	0.363	0.368	0.366	0.364
C	Folding Endurence	225.3333	222.3333	225	226.3333	227
D	%Moisture loss	2.676667	3.623333	2.7	2.626667	3.53
E	%moisture Absorbance	6.25	6.51	6.35	6.18	6.28

F. Swelling Studies

Sr. No.	Time	Weight of Increase in mg				
		F0A	F0B	F0C	F0D	F0E
1	0	0.00	0.00	0.00	0.00	0.00

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(3), 3274-3284 | ISSN:2251-6727

2	10	4.33	4.33	3.67	2.67	3.34
3	20	6.33	6.00	5.67	6.00	5.67
4	30	9.00	8.66	9.00	9.56	8.34
5	40	10.67	10.66	10.00	11.34	10.34
6	50	11.67	11.66	11.00	12.00	11.34
7	60	12.00	11.66	11.67	12.67	12.00

G. I*n vitro* drug release studies :

Table 3: In Vitro Drug Release Data From Various Ocular Insert Formulations Of Fo3

Time (h)	**Batch code**				
	FO3 A	FO3 B	FO3 C	FO3 D	FO3 E
0.	0±0.00	0±0.00	0±0.00	0±0.00	0±0.00
1.	9.67±0.04	9.24±0.07	9.39±0.05	8.78±0.04	9.33±0.06
2.	13.74±0.04	13.48±0.06	13.23±0.04	12.87±0.10	13.67±0.09
3.	15.81±0.05	15.29±0.07	14.53±0.06	16.26±0.08	15.75±0.23
4.	17.36±0.05	17.85±0.04	17.35±0.06	18.81±0.07	17.82±0.08
5.	19.29±0.05	19.46±0.04	20.18±0.08	19.97±0.04	19.93±0.06
6.	23.76±0.04	23.46±0.05	22.97±0.04	22.19±0.05	23.19±0.06
7.	24.42±0.04	24.89±0.05	25.23±0.04	24.93±0.08	24.24±0.07
8..	26.83±0.08	26.45±0.07	27.82±0.06	27.68±0.05	26.31±0.06
9.	28.58±0.52	28.04±0.34	29.44±0.40	28.42±0.33	28.41±0.45
10.	29.47±0.52	29.35±0.58	30.67±0.60	30.03±0.51	29.94±0.70
11.	31.35±00.70	31.29±0.46	32.36±0.39	32.79±0.63	31.34±0.58
12.	34.28±0.35	34.84±0.17	34.46±0.26	35.14±0.45	34.38±0.30
13.	36.12±0.37	36.34±0.35	36.28±0.42	37.07±0.51	36.29±0.43
14.	39.35±0.60	39.56±0.56	40.59±0.63	38.97±0.71	39.75±0.47
15.	43.68±0.45	43.87±0.53	43.28±0.55	42.83±0.61	43.88±0.59
16.	45.28±0.51	45.59±0.48	46.05±0.39	46.64±0.50	45.98±0.62
17.	49.46±0.04	49.78±0.06	49.26±0.04	48.97±0.05	49.86±0.07
18.	53.39±0.04	53.45±0.04	52.39±0.05	51.42±0.06	53.28±0.08
19.	57.62±0.05	57.93±0.09	56.3±0.07	56.39±0.05	57.46±0.04
20.	61.47±0.05	62.32±0.07	62.19±0.05	63.25±0.07	61.24±0.06

Journal of Chemical Health Risks
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21.	64.39±0.05	65.96±0.08	65.37±0.09	65.72±0.05	64.04±0.07
22.	67.24±0.05	68.34±0.06	67.85±0.04	66.98±0.06	67.45±0.08
23.	71.46±0.04	71.68±0.04	72.12±0.05	72.73±0.06	71.4±0.05
24.	73.21±0.04	74.32±0.05	74.29±0.04	74.21±0.07	73.26±0.06
25.	75.47±0.08	75.2±0.07	76.32±0.06	75.61±0.06	75.04±0.09
26.	78.28±0.04	77.39±0.05	79.83±0.06	77.18±0.04	78.58±0.07
27.	81.46±1.05	81.35±1.12	82.39±0.93	80.85±1.03	81.68±0.96
28.	83.35±0.05	83.23±0.03	85.45±0.04	83.65±0.05	83.26±0.07
29.	85.29±0.56	85.88±0.09	86.83±0.06	86.05±0.07	85.58±0.05
30.	87.83±0.94	87.56±0.67	88.23±0.73	88.26±1.03	87.66±0.84
31.	90.16±0.58	92.01±0.61	91.84±0.53	91.81±0.74	90.41±0.64
32.	92.36±0.32	93.06±0.46	93.26±0.58	92.98±0.39	92.63±0.43
33.	94.95±0.88	94.93±0.11	95.15±0.31	93.69±0.28	94.26±0.16
34.	96.34±0.07	95.85±0.08	97.69±0.10	95.87±0.09	96.31±0.07
35.	97.46±0.05	96.31±0.06	98.54±0.06	98.03±0.07	98.28±0.08
36.	98.99±0.09	98.71±0.10	98.96±0.23	98.98±0.08	98.95±0.07

*All values are expressed as mean ± SD (n=5).

➢ **Drug Release Kinetics:**

➢ In order to study the drug release kinetics of the most promising batch, the dissolution profile of five batches of FO3 were analyzed according to zero order, first order, Higuchi,s plot and Korsemeyer Peppa's plot respectively.

➢ **TABLE 5:** KINETIC TREATMENT OF DRUG RELEASE DATA OF VALIDATION BATCHES OF FO3

Formulation Code	**Zero order equation**	**First order equation**	**Higuchi's equation**	**Korsmeyer Peppas equation**	**Diffusion coefficient (n)**
	R^2				
FO1 A	0.820	0.993	0.939	0.884	0.635
FO2 B	0.845	0.991	0.941	0.888	0.629
FO3 C	0.813	0.992	0.940	0.891	0.627
FO4 D	0.819	0.992	0.941	0.891	0.628
FO5 E	0.813	0.993	0.940	0.886	0.633

Journal of Chemical Health Risks
www.jchr.org
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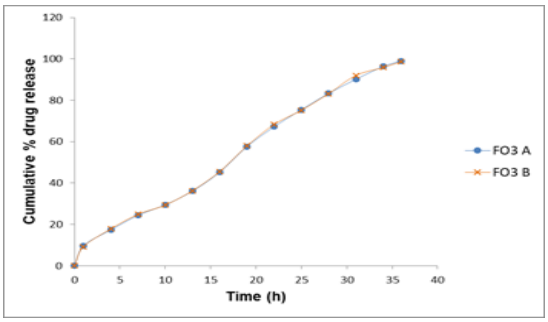


Figure 2: Zero order plot of drug release of validation batches of FO3 A & FO3 B

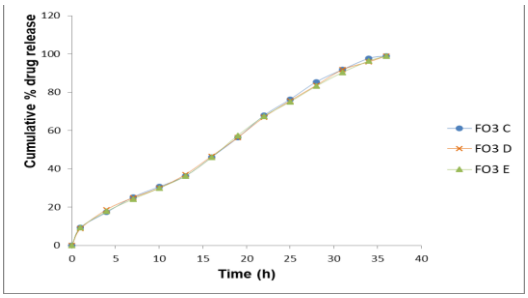


Figure 3: Zero order plot of drug release of validation batches of FO3 C to FO3

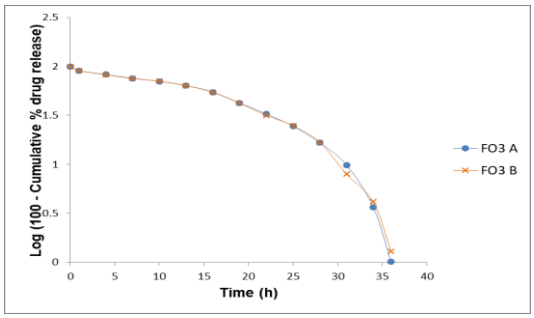


Figure 4: First order plot of drug release of validation batches of FO3 A & FO3 B

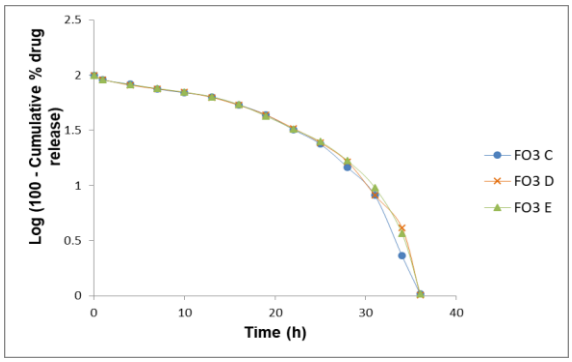


Figure 31: First order plot of drug release of validation batches of FO3 C to FO3 E

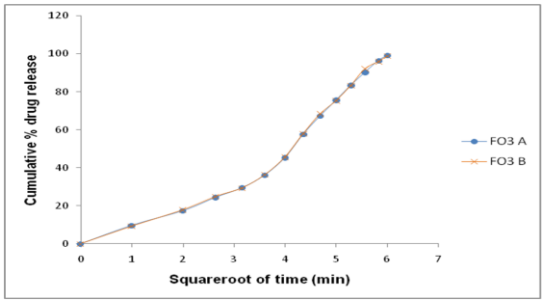


Figure5: Higuchi plot of drug release of validation batches of FO3 A & FO3 B

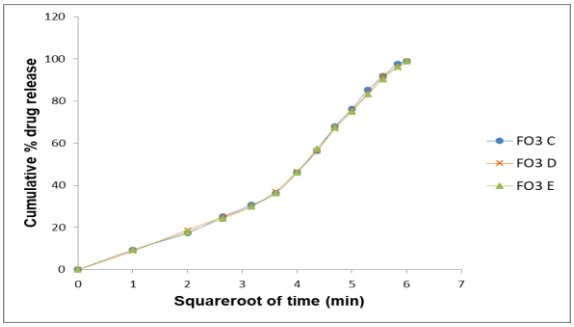


Figure 6: Higuchi plot of drug release of validation batches of FO3 C to FO3 E

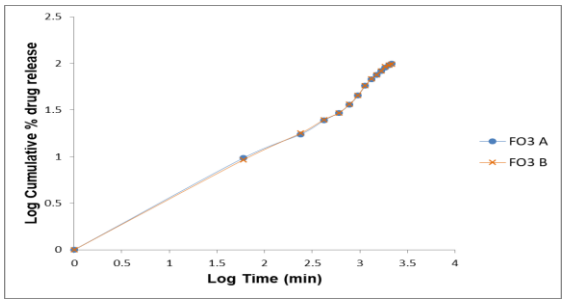


Figure 7: Korsmeyer Peppas Peppas plot of drug release of validation batches of FO3 A & FO3 B

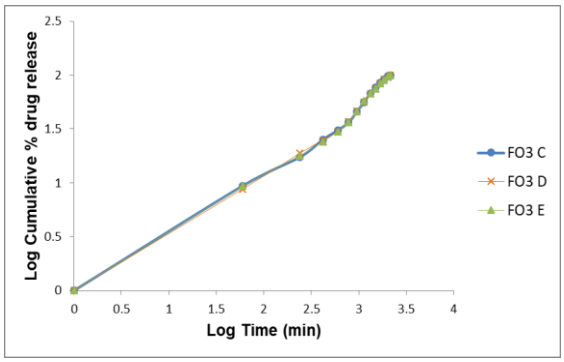


Figure 8: Korsmeyer Peppas plot of drug release of validation batches of FO3 C to FO3 E

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(3), 3274-3284 | ISSN:2251-6727

Table 4: Standard Calibration Curve Of Flurbiprofen In Ph 6.4 Sodium Phosphate Buffer

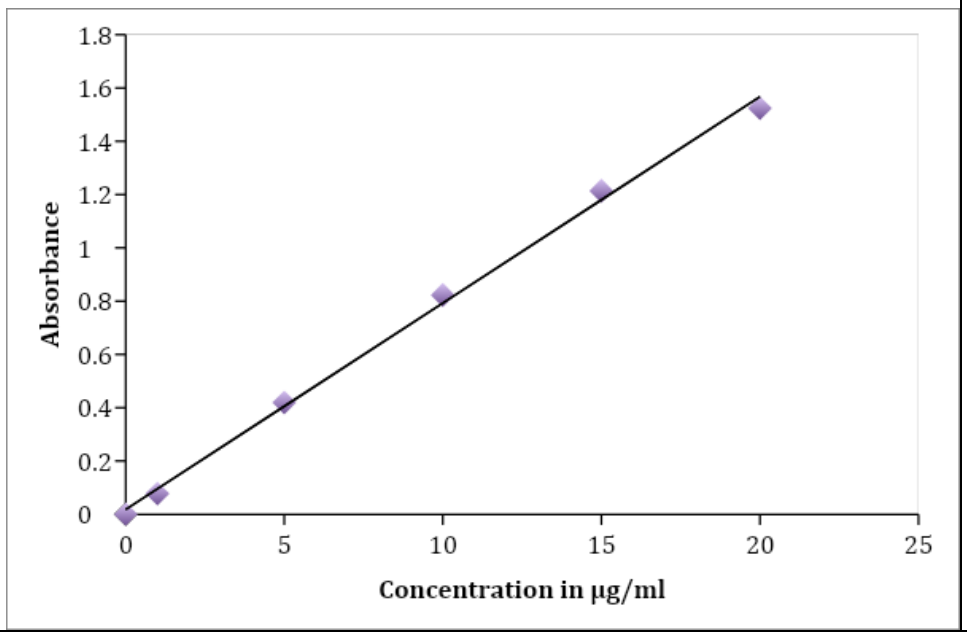
Sr. No.	Concentration in µg/ml	Absorbance at 247nm
01.	0	0
2.	1	0.0781
3.	5	0.4193
4.	10	0.8231
5.	15	1.2143
6. 	20	1.5239

Figure 2: Standard calibration curve of Flurbiprofen in pH 6.4 sodium phosphate buffer

Discussion:

The study efforts were to prepare Ocular insert of flurbiprofen to improve its residence time by preparing its controlled release formulation using different polymer in different concentration.

4.1 Identification Tests:

The procured sample of Flurbiprofen and polymers HPMC E15, EC were tested for their identification. The samples showed compliance with the data given in Indian Pharmacopoeia and tests official in USP respectively.

To assess any interaction between the drug and the polymer UV studies were performed. The data obtained suggested that there was no interaction between the drug and the polymer. The UV analysis of polymer and drug shows no absorbance of the polymer at 247 nm.

4.2 Interaction studies:

The characteristic IR absorption peaks of Flurbiprofen at 2966 cm^{-1} (aliphatic C–H stretch), 2837 cm^{-1} (O–CH3

Journal of Chemical Health Risks

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JCHR (2024) 14(3), 3274-3284 | ISSN:2251-6727

stretch), 2393 cm^{-1} (amine HCl), 1679 cm^{-1} (lactam C=O stretch), 839 cm^{-1} (o-substituted aromatic C–H out of plane deformation) and 781 cm^{-1} (p-substituted aromatic C–H out of plane deformation) were obtained.

The characteristic IR absorption peaks of HPMC K4M at 3583 cm^{-1} and 3423 cm^{-1} (O-R streching),2837 cm^{-1} (aliphatic C-H streching) and 1650 cm^{-1} (C=Ostreching) were obtained. The characteristic IR absorption peaks of HPMC K15M at 3496 cm^{-1} and 3420 cm^{-1} (O-R streching), 2837 cm^{-1} (aliphatic C-H streching) and 1645 cm^{-1} (C=Ostreching) were obtained. The characteristic IR absorption peaks of HPMC K100M at 3585 cm^{-1} and 3420 cm^{-1} (O-R streching), 2837 cm^{-1} (aliphatic C-H streching) and 1650 cm^{-1} (C=Ostreching) were obtained.

4.3 Preparation of ocular insert:

In the present study, ocular inserts were prepared by using different polymers Hydroxy propyl methyl cellulose (HPMC E15) and Ethyl cellulose at different polymer ratio with plasticizer Dib3utyl phthalate(DBP). The weighed quantity of drug were mixed thoroughly in different ratios of polymers and ocular insert were prepared by solvent casting method using ethanol and dichloromethane in 1:1 ratio. The prepared ocular inserts were evaluated for its physical appearance, thickness of film, weight variation, folding endurance, surface pH, swelling studies, estimation of drug content, hydrolytic test, estimation of percentage moisture absorption, estimation of percentage moisture loss, *In vitro* diffusion studies, sterility testing, stability studies, validation of optimized batch.

4.4 Evaluation of ocular insert:

A) Physical appearance:

The fabricated ocular insert were thin, transparent and visually smooth surfaced.

B) Uniformity of thickness:

The thickness of the films varied from 0.262 ± 0.001 to 0.397 ± 0.0012. Formulation F1 having the least thickness i.e. 0.262 ± 0.001 while FO5 having the highest 0.397 ± 0.0012.

C) Weight variation:

The average weight of ocular insert from each group of formulation was reported in (table 8) by using six ocular insert for standard deviation. The weight of ocular insert ranges from 32.2 ± 0.836 to 42.0 ± 1.000. Results indicated that formulation FO6 having highest mass while formulation FO9 having the least among the different formulations.

D) Folding endurance:

The recorded folding endurance of the formulation shows 183-255 times , which reflects the flexibility of the films. This test ensures that the ocular inserts were prepared without breaking or tearing. Result indicated that all the formulation of ocular insert shows good folding endurance, among all ocular insert FO1 shows least folding endurance which having equal concentration of HPMC E15 and ethyl cellulose(1:1). As the concentration of HPMC E15 decreases and concentration of ethyl cellulose increases the folding endurance was increases.

E) Surface pH:

The surface pH of all the films exhibited almost uniformity in their values and they were found in between 6.00 to 7.00 indicating its compatibility with eye pH.

F) Swelling studies:

A one-hour swelling study was conducted on all batches of ocular inserts FO1 to FO9. Based on the results, it was determined that swelling increases over time as a result of the polymer's hydrophilicity, which causes it to gradually absorb water. The swelling index of the film also increases as the concentration of EC increases..

In the present study, the higher swelling index was found for ocular insert of batch FO5 containing EC and HPMC E15. Thus, the viscosity of the polymer had major influence on swelling process, matrix integrity.

G) Estimation of drug content:

The percentage of drug content for FO1 to FO9 was found to be between 89.69 - 98.43 % of Flurbiprofen , the results indicated that the drug was uniformly dispersed and it complies with official specifications.

H) Hydrolytic test:

To establish whether ocular insert can withstand hydrolytic degradation, hydrolytic test was performed of unloaded ocular inserts. For the consecutive three days both unirradiated and irradiated with UV radiation were taken to compare the extent of hydrolytic degradation.

Journal of Chemical Health Risks

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JCHR (2024) 14(3), 3274-3284 | ISSN:2251-6727

The hydrolytic degradation of ocular insert from each group of formulation was reported in table 20 by using six ocular insert for standard deviation. From the investigations, polymer matrices were found to be quite stable in an aqueous environment.

I) Estimation of percentage moisture absorption:

The percentage moisture absorption of the ocular inserts was determined. It was observed that as the concentration of Ethyl cellulose increases percentage moisture absorption decreases.

J) Estimation of percentage moisture loss:

The percentage moisture loss of the ocular inserts was determined. It was observed that as the concentration of Ethyl cellulose increases percentage moisture loss.

K) *In vitro* diffusion studies:

The *in-vitro* release study was carried out on all the batches using diffusion cell apparatus at 80 rpm, 8ml of STF pH 7.4 used as diffusion media and temperature was maintained $37^0C \pm 0.5^0C$. The *in vitro* drug diffusion data was given in table 22, 23 and drug diffusion profiles are shown in figure 11 to 14.

From the result it was observed that, formulations FO1 to FO5 containing polymer concentration(HPMC E15, EC) ratio 1:1, 2:3, 3:7, 1:4 and 1:9 exhibited 94.36, 93.66, 99.70, 96.78 and 92.16 % of drug diffusion in 36 h.

Formulations FO6 to FO9 containing polymer ratio 5:1, 7:1, 11:1 and 23:1 prepared with EC:HPMC E15 exhibited 94.59, 93.54, 93.26 and 89.45 % of drug diffusion in 36 h.

From the above results, it was observed that formulation FO3 shows highest drug diffusion, while FO9 shows the lowest drug diffusion. Much difference was not observed in the drug diffusion rates of formulations. Only highest concentration of HPMC E15 in FO9 shows low drug diffusion.

L) Drug Release Kinetics:

The *in vitro* drug diffusion data was subjected to goodness of fit test by linear regression analysis according to zero order, first order kinetic equations, Higuchi and Korsmeyer models to ascertain the mechanism of drug diffusion.

Drug release from all formulations was found to follow zero order kinetics when the regression coefficient "r" values of the zero order and first order plots were compared. The zero order plot's "r" values were found to be in the range of 0.96 to 0.99, while the first order plot's "r" values were found to be in the range of 0.67 to 0.97.

Since the "r" values of the Higuchi plots were closer to unity, the Higuchi model's good fit to the diffusion profiles of all the formulations indicated that this is the main mechanism limiting drug release.

The in vitro diffusion data as log cumulative percent drug release versus log time were fitted to Korsmeyer equation, values of the exponent 'n' was found to be in the range of 0.56 to 0.63 indicating that the drug release is by Non-Fickian diffusion mechanism. Among the various formulations studied, formulation Fo3 was considered as an ideal formulation which exhibited 99.70 % of drug release in 36 h. Hence it is selected for further short term stability studies.

M) Optimization of ocular inserts:

Nine formulations were tested, and the one with EC and HPMC E15 (7:3) (FO3) demonstrates complete and regulated release with 99.70% at the conclusion of the 36-hour period and satisfactory physical properties. It uses a diffusion rate-controlled mechanism with first-order kinetics; more research on the same formulation was conducted.

N) Sterility testing:

A microbiological investigation was conducted on the chosen ocular implant (FO3). To determine the biological activity of the chosen formulation against the test microorganism, microbiological investigations were conducted. In the Petri dish, a layer of nutrient agar containing the test organism (S. aureus) was left to solidify. After being taken out of the pack, an ocular insert was carefully put over the agar layer at an appropriate distance. After that, the plates were incubated for 24 hours at 37±0.5˚C. Following incubation, the ocular insert's zone of inhibition was evaluated.

O) Stability studies:

The improved formulation FO3 was chosen for stability investigations in the current investigation. To determine if a medicine degrades over its shelf life, stability tests of

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JCHR (2024) 14(3), 3274-3284 | ISSN:2251-6727

the drug formulations are carried out. The medication is stable in the optimized formulation for the duration of the trial, according to the findings from the stability research.

P) Drug-excipients compatibility study:

a] Using FTIR spectroscopy:

The IR spectra of Flurbiprofen, polymers and their physical mixture was found to be identical . IR spectrum of Flurbiprofen exhibits characteristic broad peak at 2500-3500 cm^{-1} (-H bonding) and sharp peak at 1698 cm^{-1} and 2912 cm^{-1}(-carbonyl and hydroxyl stretching). While IR spectrum of HPMC shows characteristic peaks at 3583 and 3423 cm^{-1} (O-R stretching),2837 cm^{-1} (aliphatic C-H stretching) and 1650 cm^{-1} (C=O stretching). IR spectrum of EC exhibits characteristic broad peak at 3357 cm^{-1} (-OH stretching) and 2930 cm^{-1}(-CH stretching). IR spectrum of formulation FO3 shows characteristic broad peak at 2500-3500 cm^{-1} (-H bonding) and sharp peak at 1699 cm^{-1} and 2953 cm^{-1}(-carbonyl and hydroxyl stretching). The peak at 3582 and 3501 cm^{-1} (O-R stretching), 2837 cm^{-1} (aliphatic C-H stretching), 1653 cm^{-1} (C=O stretching), 3380 cm^{-1} (-OH stretching) and 2953 cm^{-1}(-CH stretching) [82].

The FTIR spectra obtained indicated that no chemical interaction occurred between the drug Flurbiprofen and the polymers used in formulating the Ocular insert. But, a slight shift in absorption peaks position was noticed which indicated that physical interaction might have occurred between drug and the polymer.

b] Using DSC:

DSC thermograms of the pure drug and its optimized formulation after stability studies were recorded to evaluate whether the drug has undergone any degradation during the study period. From the DSC data obtained , it was evident that the melting point of Flurbiprofen is not changed after keeping the ocular insert for stability studies. Hence, it may be inferred that there is no interaction between Flurbiprofen and polymers used. From DSC results it can be concluded that the drug maintained its chemical identity throughout the process.

Q) Validation of optimized batch:

Five batches of formulation FO3 were prepared and showed maximum drug content uniformity and in vitro drug release was observed up to 36 hours. The cumulative percentage release was found to be between 98.71% and 98.99%, and release kinetics indicated that the mechanism of drug release was Non-Fickian or anomalous transport. Batch FO3 was chosen for the validation study because it demonstrated maximum in vitro drug release (99.70%) in 36 hours and content uniformity (98.43).

These batches were analyzed statistically by using ANOVA (analysis of variance) for different parameters. The F-values were calculated for uniformity of thickness, weight variation, folding endurance, swelling study, estimation of drug content and percentage moisture absorbed and moisture loss. These calculated F-values were then compared with tabulated F-values from the table for critical values of the F distribution. All five batches showed close similarity factor indicative of similarity in the evaluation parameter

Conclusion:

The approach of the present study was to develop ocular insert of Flurbiprofen and henceforth evaluate the release profiles of these formulations. It can be concluded from the above studies that Flurbiprofen possesses all requisite qualities required for controlled drug delivery system in the form of ocular insert. The ocular insert of Flurbiprofen were formulated using the solvent casting method using ethanol and dichloromethane as a casting solvent. The evaluation data for properties such as Physical appearance, Thickness of film, Weight variation, Folding endurance, Surface pH, Swelling studies, Estimation of drug content, Hydrolytic test, Estimation of percentage moisture absorption, Estimation of percentage moisture loss, In-vitro diffusion studies, Sterility testing, Stability studies and Validation of optimized batch indicated that the prepared ocular inserts were well within the specified standards. Drug polymer compatibility studies were carried out using FT-IR and UV Visible spectroscopy. It shows there is no significant interaction between polymers and drug. The results proved that prepared ocular inserts exhibited excellent *in vitro* drug release as well as controlled the drug release over 36 h. The polymer mass ratio can affect the *in vitro* drug diffusion. From the stability studies, it is clear that the formulation was stable for thirty days and the DSC thermograms and FTIR spectra obtained indicated no change in chemical identity of the drug.

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Among the various formulation, the formulation FO3 was found to be optimum formulation. The formulation FO3 containing polymer ratio (3:7), EC and HPMC E15 fulfilled all desirable requirements for formulation of ocular insert. Formulation FO3 was found to release the drug for 36 h (99.70%) and follow Korsmeyer-Peppas model in dissolution studies.

Method of preparation of ocular inserts was found to be simple and reproducible. The polymers used were non-toxic, relatively less expensive and easily available. Polymers were found to be effective at different concentration in providing a constant release of drug from the formulation for a longer period of time.

Reference:

1. Rajasekaran A, Kumaran KSGA, Preetha JP, Karthika K. A comparative review on conventional and advanced ocular drug delivery formulations. International Journal of Pharm Tech Research 2010;2(1):668-674.
2. Rathore KS, Nema RK. Review on Ocular Inserts. International Journal of PharmTech Research 2009;1(2):164-169.
3. Avis.KE, Liberman L, Krishna M, Bapatla, Lorenzetti OJ. Editors. Pharmaceutical Dosage Forms: Parentral Medications. NewYork : Marcel Dekker;2005,Vol II. p. 541--578.
4. Robinson JR, Lee VH, editors. Controlled Drug Delivery: Fundamentals and Applications. 2nd ed. New York: Marcel Dekker,Inc;2009. p. 10-11
5. Patel DH, Patel MP, Patel MM. Formulation and Evaluation of Drug-free Ophthalmic Films Prepared by Using Various Synthetic Polymers. J Young Pharm 2009; 1(2):116-120.
6. Jain D,Carvalho E, Banerjee R. Biodegradable hybrid polymeric membranes for ocular drug delivery. Acta Biomat 2010;6:1370:1379.
7. Indian Pharmacopoeia 2007. Vol. 2. The Indian Pharmacopoeia Commission. Ghaziabad; p. 492,591
8. Brandup J, Immergut EH, Grulke EA. Polymer handbook. 4th ed. New York: A Willey Interscience Publication; 1999:529-30.
9. Jain NK, Menqi SA, Deshpande SG. editors. Controlled and novel drug delivery. Delhi: CBS Publishers; 1997. p. 82-111.
10. Devu.Satya Sireesha.B.Lakshmi Prasanna, M.Harini, V.Shirisha4, T.Rama Rao, formulation and evaluation of ocular inserts of diclofenac sodium for controlled release drug delivery,International journal and novel research development,p 262-272
11. Lee VHL, Robinson JF. Review : Topical ocular drug delivery; recent developments and future challenges. J Ocul Pharmacol 1976;2:67.
12. Keister JC. et al. Limited on optimizing ocular drug delivery. J Pharm Sci 1991; 80(1): 50.
13. Gevariya HB , Patel JK, Girhepunje K, Pal RS. Sustained ophthalmic delivery of Levofloxacin from once a day ocular inserts. Indian journal of pharmacy and Indian J Pharm Sci 2009;1:24-32 39
14. Colo GD, Burgalassi, Chetoni P, Fiaschi MP, Zambito Y, Saettone MF. Gel-forming erodible inserts for ocular controlled delivery of ofloxacin. Int J Pharm 2001;215: 101-111
15. Dumortier G, Zuber M, Chast F, Sandouk P, Chaumeil JC. Systemic absorption of morphine after ocular administration:evaluation of morphine salt insert in vitro and in vivo. Int J Pharm Sci 1990;59:1-7.