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Bioadhesive Inserts of Prednisolone Acetate for Postoperative Management of Cataract – Development and Evaluation

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Abstract:-

➢ ***Objective***

To Formulate and evaluate the bioadhesive sustain release inserts of prednisolone acetate for postoperative management and treatment of cataract. The bioadhesive local delivery system decreases dose and administration frequency of the drug and helps in fast healing and patient compliance.

➢ ***Methods***

Teflon coated glass moulds were used to formulate matrix bioadhesive inserts using solvent evaporation technique and evaluated for invitro drug release studies. Different formulations of hydroxyl propyl methyl cellulose (HPMC), sodium carboxy methyl cellulose (SCMC) in ratios 80:20,70:30,60:40 and 50:50, along with varying concentration of glycerine as plasticiser were prepared and evaluated. The Prepared formulations were evaluated for the parameters such as weight variation, thickness, folding endurance, flexibility, stretching strength, drug content, in vitro drug release, bioadhesion strength, surface pH, swelling index, % moisture loss, moisture adsorption, sterility studies and stability studies and optimized.

➢ ***Results***

The formulation 'PEF-06, 08, 11, & 13' was optimised through the Evaluation parameters obtained. The optimized batches were then studied for invitro, drug Release, invitro permeation, and sterility and stability studies. During the studies the duration of drug release and the retention time of the PEF -06 in ocular cavity were found excellent.

➢ ***Conclusion***

The formulated bioadhesive insert showed extended drug release and increased retention time due to bioadhesive polymers which will help to overcome the disadvantages of conventional preparations.

Keywords:- *Ophthalmic Inserts, Eye Inserts, Bioadhesive Inserts, Cataract, Prednisolone.*

I. INTRODUCTION

Cataract surgery or lens replacement surgery, in which the natural eye lens is removed due to development of opacification / cataract. During the surgery the lens is replaced with an artificially made intraocular lens. The opacification of the naturals lens occurs due to metabolic changes, which results in impairment or complete loss of vision.

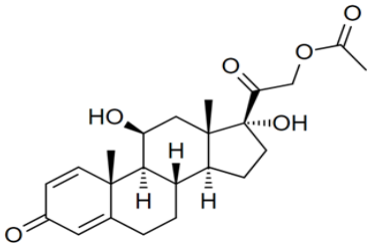
Following cataract surgery, the main concerns is preventing infection and reducing inflammation. Hence the prednisolone is the popular choice for treating inflammation in post-operative cataract management. Being an important and sensitive organ and due to its drug disposition characteristics many parts of the eye are relatively inaccessible to systemically administered drugs. Generally, topical drug delivery is preferred under most circumstances because of convenience and safety. To provide intraocular treatment bioadhesive local drug delivery systems are developed. The regular application of eye drops is essential to maintain required level of drug. Suitable polymers are added to enhance the bioavailability and contact time by prolonging retention on the site of action.

Bioadhesive local drug delivery system are single, sterile and thin drug formulations, the size and shape specifically designed for application in eye. The formulation offer several benefits such as prolonged retention on the site of action, slow and constant drug release pattern, less systemic absorption of drug, patient compliance, improved shelf life, low risk of sensitivity reactions and extended drug release activity.

Prednisolone is a man-made form of a natural substance (corticosteroid hormone) made by the adrenal gland. It is used to treat various diseases to reduce symptoms such as pain, swelling and allergic-type reactions. The dosage and length of treatment with prednisolone is based on the patient's medical condition and response to treatment. The usual dose in postoperative cataract management is one to two drops into the conjunctival sac two to four times daily for 4 - 5 weeks. Prednisolone is safe during pregnancy and lactation. The elimination half-life of prednisone is around 3 to 4 hours, its molecular formula is $C_{23}H_{30}O_6$ and its IUPAC name is [2-[(8*S*,9*S*,10*R*,11*S*,13*S*,14*S*,17*R*)-11,17-dihydroxy-10,13-dimethyl-3-oxo-7,8,9,11,12,14,15,16-

octahydro-6*H*-cyclopenta[a]phenanthren-17-yl]-2-oxoethyl] acetate.

Prednisolone Acetate



In this research work, an effort was made to prepare a bioadhesive local drug delivery system of prednisolone acetate by adding polymers to overcome the disadvantages of conventional dosage form like dose, frequency of administration, poor bioavailability, drug wastage due to spilling as well as naso-lachrymal drainage.

II. MATERIALS AND METHODS

❖ *Materials:*

Prednisolone acetate was obtained from Wyeth pharmaceutical, Goa, India, as a gift sample. Hydroxy Propyl Methyl Cellulose (HPMC) and Sodium Carboxy Methyl Cellulose (SCMC), Glycerine were obtained from S.D Fine Chemicals Ltd., Mumbai. Other chemicals used were of analytical grade.

❖ *Method:*

➢ *Drug and excipient compatibility:*

As a part of pre formulation study, it is essential that the drug and the additives used in formulation should be evaluated for any chemically and physical incompatibility. The compatibility studies provide information on the framework the drug and pharmaceutical excipients in the fabrication of a dosage form. The selection of suitable excipients for pharmaceutical formulation and its compatibility with the drug is a most important factor.

Hence in the present study, IR spectra of drug and excipients were carried out using Shimadzu FTIR spectrometer. The IR Spectra was recorded to find out any possible chemical interaction between the drug and excipients. The IR spectrum of drug and other excipients individually and as mixture drug and excipients was recorded in range of (4000-400 cm^{-1}) . The IR spectrum of drug was compare with that of the physical mixture of the drug and excipients used to check for any possible drug-excipients interaction.

➢ *Formulation of bioadhesive insert for local drug delivery system of gatifloxacin:*

Prednisolone acetate bioadhesive inserts was optimised through 2^4 factorial design process parameters. The bioadhesive inserts with prednisolone acetate was formulated by solvent evaporation method in different compositions. Required quantity of HPMC and SCMC was weighed accurately and dissolved in 10 ml of distilled water (milipore) and the solution was kept aside for 5 min for swelling of the polymers. The above polymer solution was stirred using magnetic stirrer (Remi Equipments, India). Concurrently prednisolone acetate was accurately weighed in quantity such that 5 mm^2 of bioadhesive insert contained 5 mg of drug and was added to the polymer solution and mixed thoroughly with the help of a magnetic stirrer. Glycerine in different concentration such 10 %, 15 %, 20% and 25% of the polymer was added and volume was made up to 20ml with distilled water of the polymer solution and mixed thoroughly with the help of magnetic stirrer. The drug and polymer solution was transferred into the Teflon coated glass moulds of 5cm X 5cm size (Fabricated) and place on a flat surface to ensure equal distribution of the solution in the mould. The entrapped air from the drug and polymer solution was removed using vacuum desiccator (Biocraft Scientific, Agra, India). The above solution was kept in hot air oven (Inlab Equipment) at 50˚c for 5 hr. for drying. The dried preparation was cut into 5mm X 5mm size and individual inserts was packed and sealed in polythene sheets using heat sealing. The inserts were sterilized separately by exposing them to UV radiation for 30 min. Similarly, 16 batches was prepared and coded from PEF-01 to PEG-16[8]. Composition of buccal films formulated was recorded in Table 1 and 2.

Composition	PEF-01	PEF-02	PEF-03	PEF-04	PEF-05	PEF-06	PEF-07	PEF-08
Drug (mg)	250	250	250	250	250	250	250	250
HPMC (%w/v)	4	3.5	3	2	4	3.5	3	2
SCMC (%w/v)	1	1.5	2	2	1	1.5	2	2
Glycerine (%w/w)	0.5	0.5	0.5	0.5	0.75	0.75	0.75	0.75
Distilled Water (ml – QS)	20	20	20	20	20	20	20	20

Table 1:- Composition of All the BUCCAL Film Formulation Coded from PEF 1 to PEF 8.

Composition	PEF-09	PEF-10	PEF-11	PEF-12	PEF-13	PEF-14	PEF-15	PEF-16
Drug (mg)	250	250	250	250	250	250	250	250
HPMC (%w/v)	4	3.5	3	2	4	3.5	3	2
SCMC (%w/v)	1	1.5	2	2	1	1.5	2	2
Glycerine (%w/v)	1	1	1	1	1.25	1.25	1.25	1.25
Distilled Water (ml – QS)	20	20	20	20	20	20	20	20

Table 2:- Composition of All the BUCCAL Film Formulation Coded from PEF 9 to PEF 16.

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➢ *Evaluation of Bioadhesive inserts [9]:*

Bioadhesive inserts are in the form of small films and was evaluated for their physical properties, bioadhesion, release properties, microbiological studies, sterility studies and stability studies. The following important parameters were evaluated with regard to bioadhesive inserts.

➢ *Physical Appearance*

The formulated inserts were checked visually for physical parameters such as appearance and colour. The physical appearance of all the formulation was reported in Table-3.

➢ *Thickness Uniformity:*

The thickness of the dosage form determines the uniformity of content and also its aesthetic value to an extent. Digital screw gauge (Mitutoyo MMO-25DS) was used to measure the thickness of the prepared bioadhesive inserts. The average thickness of all the batches was reported in Table- 3.

➢ *Weight Uniformity:*

Digital balance (Fisher Brand PS-200) was used to weigh all the formulated batches. The weight variation was evaluated to determine drug content; deviation in weight represents the difference in the amount of drug or the polymer in an individual bioadhesive insert. The average weight s was reported in Table -3.

➢ *Size Uniformity:*

Size is an important parameter in the preparation of bioadhesive inserts as it quantify the amount of drug content of the insert. Vernier calliper was used to measure the size of all the prepared batches of bioadhesive inserts and was reported in Table -3.

➢ *Folding endurance:*

The strength and handling stress of the prepared bioadhesive inserts was determined through the folding endurance. The folding capacity was studied by subjecting the inserts to extreme conditions of folding at the centre several times until it was broken. The average Folding Endurance of all the batches was reported in Table -3.

Batch Code	Appearance	Thickness Uniformity * (mm)	Weight Uniformity * (mg)	Size Uniformity* (mm)	Folding Endurance*
PEF-01	Transparent	0.143 ± 0.02	0.752 ± 0.81	5 X 5 ± 0.5	197
PEF-02	Transparent	0.143 ± 0.03	0.752 ± 0.62	5 X 5 ± 0.5	186
PEF-03	Transparent	0.143 ± 0.02	0.752 ± 0.45	5 X 5 ± 0.5	230
PEF-04	Transparent	0.143 ± 0.01	0.752 ± 0.73	5 X 5 ± 0.5	199
PEF-05	Transparent	0.143 ± 0.04	0.752 ± 0.89	5 X 5 ± 0.5	256
PEF-06	Transparent	0.143 ± 0.03	0.752 ± 0.78	5 X 5 ± 0.5	287
PEF-07	Transparent	0.143 ± 0.02	0.752 ± 0.62	5 X 5 ± 0.5	266
PEF-08	Transparent	0.143 ± 0.01	0.752 ± 0.59	5 X 5 ± 0.5	285
PEF-09	Transparent	0.143 ± 0.03	0.752 ± 0.83	5 X 5 ± 0.5	249
PEF-10	Transparent	0.143 ± 0.04	0.752 ± 0.95	5 X 5 ± 0.5	277
PEF-11	Transparent	0.143 ± 0.02	0.752 ± 0.46	5 X 5 ± 0.5	286
PEF-12	Transparent	0.143 ± 0.01	0.752 ± 0.68	5 X 5 ± 0.5	264
PEF-13	Transparent	0.143 ± 0.02	0.752 ± 0.61	5 X 5 ± 0.5	288
PEF-14	Transparent	0.143 ± 0.01	0.752 ± 0.76	5 X 5 ± 0.5	282
PEF-15	Transparent	0.143 ± 0.04	0.752 ± 0.69	5 X 5 ± 0.5	259
PEF-16	Transparent	0.143 ± 0.03	0.752 ± 0.58	5 X 5 ± 0.5	264
*Average of six readings was recorded.					

Table 3:- Thickness, Weight, Size Uniformity and Folding Endurance of Inserts

➢ *Swelling index:*

Simulated tear fluid (STF) pH 7.2 was used as medium to evaluate the swelling index. The bioadhesive insert from each formulated batch was weighed individually and kept over a pre-weighed stainless steel wire mesh. The bioadhesive insert along with wire mesh was immersed into 4ml STF medium. To determine the swelling index of the inserts the weight was checked at pre-set time intervals until a constant weight is seen. Swelling index was calculated using equation 1. Swelling Index of all the batches was reported in Table -4.

$$\text{Swelling index} = \frac{\text{Weight after swelling} - \text{Initial weight}}{\text{Initial weight}} \quad \ldots\ldots(1)$$

➢ *Moisture Content:*

The mechanical strength and drug release pattern of the bioadhesive inserts was determined through moisture content evaluation. The bioadhesive inserts was weighed individually and were kept under vacuum desiccation until constant weight was obtained. The below mentioned equation was used to calculate the moisture content and was reported in Table -4.

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$$\% \text{ Moisture content} = \frac{\text{Initial Weight} - \text{Final Weight}}{\text{Initial Weight}} \times 100 \quad \ldots\ldots (2)$$

➢ *Moisture absorption:*

The bioadhesive inserts from all theformulated batches were weighed for three days. After three days, the inserts were reweighed. The below mentioned formula was used to calcutae the % moisture absorbed and was reported in table -4.

$$\% \text{ Moisture content} = \frac{\text{Final weight - Initial Weight}}{\text{Initial Weight}} \times 100 \quad \ldots\ldots (3)$$

➢ *Flexibility and Streching strength*

To evaluate the flexibility and streching strength of the bioadhesive inserts at an apparatus was constructed in the laboratory. The constructed apparatus consisted of a fixed end tied to a burette stand and a moving end with a paper clip on each end. The formulated bioadhesive inserts from each batch was used for the study. One end of the insert under study was clipped with the fixed end and another end was clipped with the paper clip on the moving end which was tied with a thread, tied with a pan on other end to hold weights. A small pointer was attached to the thread that travels over the stainless steel scale fixed to the shaft of the burette stand. Gradually weight was added to the pan untill the film break. The weight required too break the insert was noted as breaking force and instantaneously the distance travelled by the pointer on the scale represents the streching strength of the inserts. The below mentioned formula was used to calculate the flexibility and streching strength of the inserts and reported in table - 4.

$$\text{Flexibility (g/mm2)} = \frac{\text{Breaking force (g)}}{\text{Cross-sectional area of the sample (mm2)}} \quad \ldots\ldots (4)$$

$$\text{Stretching strength (\%)} = \frac{\text{Increase in length at break point (mm)}}{\text{Original length (mm)}} \times 100 \quad \ldots\ldots (5)$$

➢ *Surface pH:*

The bioadhesive inserts of all the formulated batches were kept in a agar plate, prepared by dissolving 2% agar with Simulated tear fluid (STF) pH 7.2 to evaluate surface pH. The inserts were left on the agar plate for 1 hr. to swell. The pH paper was used to check the surface pH of the bioadhesive insert and was reported in Table -04.

➢ *Ex-vivo bioadhesive studies [10, 11]:*

Construction of the test assembly:

A students dispensing balance was used to construct the basic structure of the assembly to evaluate the bioadhesive strength of the formulated bioadhesive inserts. The right side pan of the dispensing balance was replaced with stainless steel block attached with string and required weight to equate with the left side pan.

Determination of adhesion force: The goat conjunctival membrane was washed and was tightly tied over a Stainless steel block, this assembly was attached to the right side pan using a string and another conjunctival membrane is tied to another stainless steel block with the conjunctival mucosa side facing upwards. The stainless steel block with the conjunctival membrane was placed inside a glass beaker with sufficient quantity of STF 7.2 pH, such that the STF reaches the surface of the conjunctival membrane and keeps it moist. This beaker was placed under the right side pan of the balance. A bioadhesive insert was stuck onto conjunctival membrane with a drop of water and the assembly with conjunctival membrane attached to the right side pan is pressed over the insert placed over the conjunctival membrane stainless steel block placed inside the beaker. The assembly was kept in this position for 3mins and then weights were added gradually on the left pan till the patch gets separated from the mucosal surface completely. The excess weights of the pan i.e., the total, gives the measure of force of detachment of the film in grams. From this the bioadhesion strength can be calculated by Force of adhesion (N) = F X 9.81. Where F is the excess weight added to the pan. A fresh portion of tissue was used for each measurement. The average bioadhesive strength all the batches was reported in Table -4.

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Batch Code	Swelling Index * (2hr)	% Moisture absorption	Flexibility (g/mm2)	% Stretching strength	Surface pH*	Bioadhesive Strength *
PEF-01	19.45 ± 1.21	23.09 ± 0.5	0.265 ±0.0032	31.01	6.23 ± 0.05	3216.23 ± 0.58
PEF-02	16.24 ± 1.41	22.03 ± 0.5	0.324 ±0.0014	32.02	6.45 ± 0.05	4203.54 ± 0.87
PEF-03	18.62 ± 1.34	23.06 ± 0.5	0.314 ±0.0024	32.45	6.24 ± 0.05	4123.04 ± 0.56
PEF-04	17.85 ± 1.10	23.03 ± 0.5	0.324 ±0.0045	32.72	6.51 ± 0.05	4823.06 ± 0.23
PEF-05	24.25 ± 0.98	24.03 ± 0.5	0.421 ±0.0032	34.56	6.48 ± 0.05	5121.32 ± 0.45
PEF-06	**36.16 ± 1.16**	**24.06 ± 0.5**	0.521 ±0.0014	39.01	**6.89 ± 0.05**	**6132.45 ± 0.64**
PEF-07	32.05 ± 1.12	24.05 ± 0.5	0.427 ±0.0021	34.12	6.45 ± 0.05	5732.56 ± 0.41
PEF-08	**35.89 ± 1.46**	**24.07 ± 0.5**	0.536 ±0.0028	39.25	**6.78 ± 0.05**	**6235.32 ± 0.21**
PEF-09	30.25 ± 1.22	24.02 ± 0.5	0.410 ±0.0015	34.81	6.23 ± 0.05	4932.75 ± 0.61
PEF-10	29.89 ± 0.95	23.97 ± 0.5	0.425 ±0.0014	33.56	6.34 ± 0.05	6123.52 ± 0.84
PEF-11	**35.78 ± 0.81**	**24.03 ± 0.5**	0.535 ±0.0019	38.86	**6.76 ± 0.05**	**6223.43 ± 0.67**
PEF-12	30.56 ± 0.93	24.01 ± 0.5	0.314 ±0.0024	33.20	6.22 ± 0.05	5208.86 ± 0.68
PEF-13	**36.20 ± 0.67**	**23.96 ± 0.5**	0.537 ±0.0021	39.24	**6.72 ± 0.05**	**6230.21 ± 0.71**
PEF-14	35.06 ± 0.78	23.99 ± 0.5	0.430 ±0.0024	36.18	6.51 ± 0.05	5823.52 ± 0.82
PEF-15	30.82 ± 0.86	24.02 ± 0.5	0.345 ±0.0026	35.81	6.29 ± 0.05	5831.96 ± 0.45
PEF-16	31.69 ± 0.84	23.93 ± 0.5	0.348 ±0.0017	35.62	6.45 ± 0.05	6036.18± 0.78

Table 4:- Swelling Index, Moisture Content, Flexibility, Streching Strength, Surface PH And Bioadhesive Strength of Formulated Inserts

➢ *In vitro Release Study* *[12, 13, 14]:*

USP XXIV six station dissolution apparatus type 1 (slisca -6 JDR, Slisca Ltd., India) with 900 ml STF 7.2 pH (dissolution medium) was used to evaluate *in vitro* drug release study of the optimized batches. Bioadhesive inserts of optimised batch was fixed with the central shaft using a cyanoacrylate adhesive. The temperature and rotation speed of the apparatus was maintained at 37±0.5° and 50 rpm, respectively. The sample was collected for 12hrs; the first sample was withdrawn at 30 min. followed by sample collection every hour for 12 hrs. Samples were withdrawn from each station and the fresh medium was replaced equivalent to sample collected after every sample withdrawal. The collected samples were filtered, diluted suitably and then analysed spectrophotometrically at 247 nm in a UV visible spectrophotometer. The results were recorded in Table -05 and FIG- 01

➢ *In vitro permeation Study:* *[15, 16]*

The modified Franz diffusion cell was used to study the *ex vivo* permeation studies of formulated bioadhesive inserts through an excised layer of goat conjunctival membrane (washed in isotonic phosphate buffer (pH 6.6) after excising and trimming from the sides) were carried. An insert of each formulation under study was placed in intimate contact with the excised conjunctival membrane and the topside was covered with aluminium foil as a backing membrane. The contents of receptor compartment filled with 100 ml of STF pH 7.2 (with Teflon magnetic bead placed inside) were stirred with a magnetic stirrer and temperature of 37±1° was maintained throughout. The samples were withdrawn at every hour, filtered, diluted suitably and then analysed using UV spectrophotometer at 247 nm in a UV visible spectrophotometer, the weavelength was selected based on absorbance maxima of drugs as per UV spectrum 247 nm was optimum for the active ingredients. The drug permeation was reported in Table-6 and represented in FIG-2

Time (hr.)	PEF-06	PEF-08	PEF-11	PEF -13
0.5	16.23	13.36	14.02	13.23
1	30.89	25.42	26.18	24.56
2	43.08	27.15	29.12	26.95
3	51.06	36.06	35.02	34.23
4	60.98	47.56	46.85	47.12
5	68.46	55.62	51.65	54.19
6	75.62	62.31	59.23	61.45
7	83.68	73.06	65.84	72.65
8	88.27	81.95	77.03	81.48
9	94.82	92.36	85.36	91.46
10	96.09	95.29	93.61	94.92
11	98.16	98.92	96.25	98.47
12	99.98	99.73	98.45	99.23
Cumulative % Drug Release Calculated				

Table 5:- In Vitro Drug Release in STF

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Time (hr.)	PEF-06	PEF-08	PEF-11	PEF -13
0.5	16.53	13.82	14.52	13.68
1	31.24	25.93	26.63	24.98
2	43.83	27.46	29.81	27.25
3	51.45	36.53	35.46	34.68
4	61.28	47.53	47.41	47.72
5	68.83	55.91	52.12	54.73
6	75.97	62.81	59.62	61.82
7	83.92	73.51	66.32	72.99
8	88.62	82.56	77.53	81.89
9	95.12	92.92	85.86	91.88
10	96.83	95.73	94.17	95.42
11	98.82	99.12	96.63	98.93
12	100.21	100.14	99.04	99.62
Cumulative % Drug Permeation Calculated				

Table 6:- In Vitro Drug Permeation Studies

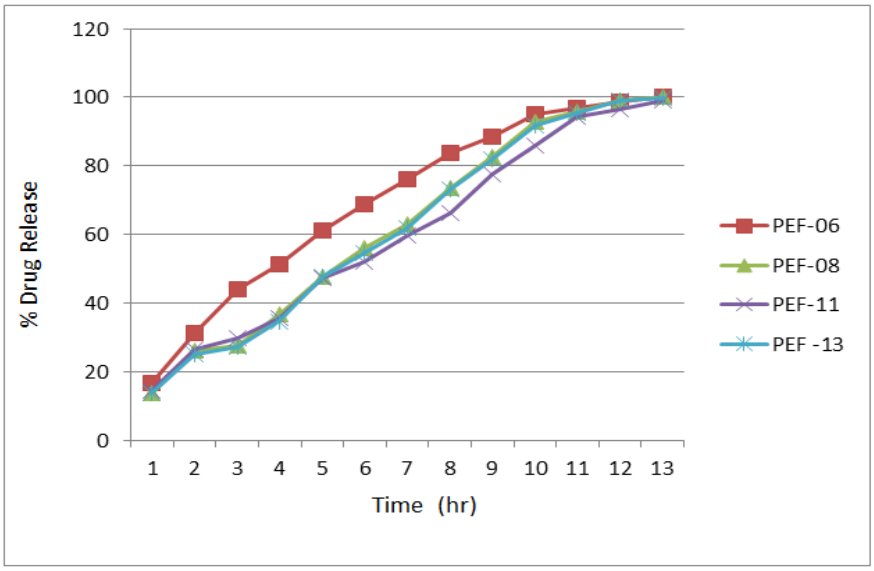

Fig 1:- Invitro Drug release studies

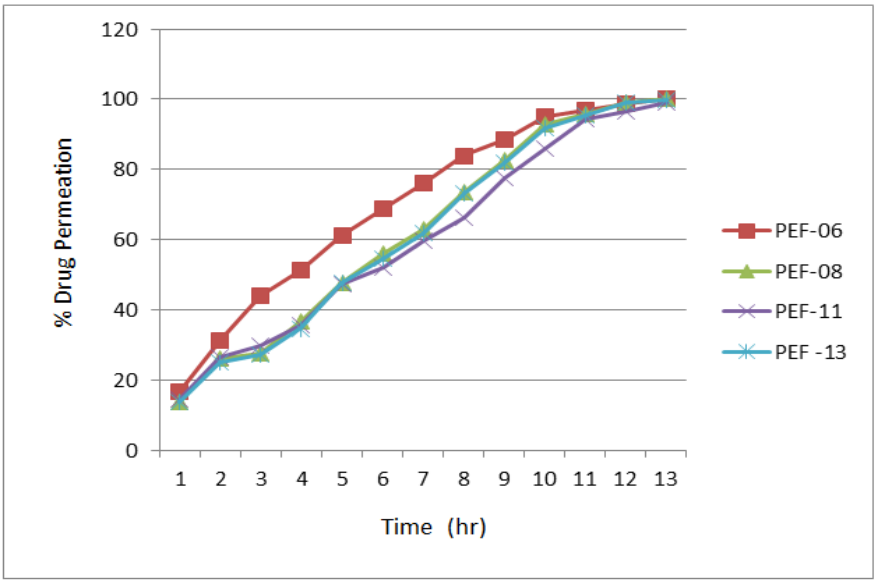

Fig 2:- Invitro Drug Permeation studies

➢ *Sterility testin [19.20]:*

The inserts from all the formulated batches were tested for sterility as per Indian Pharmacopoeia. The inserts were checked for the existence of any forms of contamination like bacteria, fungi and / or yeast. The direct inoculation method was carried out under aseptic conditions.

➢ *Stability Studies*

Stability an extent to which a product retains, throughout its storage period and use. Stability testing is conducted to guarantee that the formulation retain its aptness till its expiry date. The optimised batch of the formulate inserts was exposed to stability studies as per the ICH guidelines.[22] The stability studies were carried out at 40°C/75% RH for 6 months. The samples were tested for drug content and invitro drug release after 1, 3 and 6 month respectively and the results were recorded in table- 7 and 8.

Duration	PEF-06	PEF-08	PEF-11	PEF -13
1st Month	100.27	100.14	99.96	100.18
3rd Month	100.27	100.13	99.95	100.17
6th Month	100.26	100.11	99.95	100.16

Table 7:- Drug content during Stability Studies

Duration	PEF-06	PEF-08	PEF-11	PEF -13
1st Month	99.98	99.73	98.45	99.23
3rd Month	99.98	99.71	98.44	99.22
6th Month	99.97	99.70	98.43	99.21

Table 8:- Invitro Drug release during stability Studies

III. RESULTS AND DISCUSSION

FTIR spectra of Prednisolone Acetate in combination with excipients was recorded and no sign chemical interaction among the drug and the excipients used in the formulation exhibited. Glycerine was incorporated as plasticizer in different concentrations such as 10, 15, 20 and 25% w/w of polymer. From the study it was found that Glycerine gave good flexibility with 15 % w/w.

The Formulated bioadhesive inserts were found to be transparent, colourless, smooth, and uniform in appearance and no visible crack or imperfection was found. The tests for thickness, weight variation, folding endurance, surface pH, percentage moisture absorption, percentage moisture loss, swelling index, moisture content, flexibility and stretching strength, bioadhesive strength was passed by all the formulated batches. The drug content was found in range 95.36 % to 100.52% which is highly acceptable. The bioadhesive strength was found to bein a range of 3216.23 ± 0.58 to 6235.32 ± 0.21 and preferred for bioadhesive dosage forms. It was observed that the thickness of the inserts was in the range of 0.143 ± 0.01 to 0.143 ± 0.04 mm. The inserts was having a weight in the range of 0.752 ± 0.45 to 0.752 ± 0.95 mg. The thickness and weight of inserts were suitable enough and do not creat any irritation on application in ocular cavity. The folding endurance was recorded for all the formulated batches of bioadhesive inserts and found greater than186, therefore considered satisfactory and shows good handling properties. It was also observed that the surface pH of the inserts was within the range of 6.23 ± 0.05 to 6.89 ± 0.05. The flexibility and stretching strength was found in the range of 0.265 ±0.0032 to 0.536 ±0.0028 g/ mm2 and 31.01to 39.24% respectively. The swelling index was obtained in the range of 16.24 ± 1.41 to 36.20 ± 0.67. The % moisture absorption were evaluated and found to be 22.03 ± 0.5% to 24.07 ± 0.5 %.

On the basis of evaluation parameters the formulation PEF-06, 08, 11 and 13 was optimized and further studies were conducted only on optimised batches. The invitro drug release study showed extended drug release in all the optimised bioadhesive inserts. The release of drug from the formulations were found to be 98.45 to 99.98 % at the end of 12 h respectively, invitro drug release from PEF -06 was found to be 99.98% at the end of 12 hrs. The drug permeation studies were performed on optimised batches and found to be 99.62 % to 100.21 % , the drug permeation of PEF-06 was found to be 100.21% at the end of 12 hr.

The optimised batches were evaluated for sterility and stability. The sterility testing were performed as per IP and found to be free from any type of contamination which confirmed the insert's sterility and utility for further studies. Stability studies were carried out for six months and the drug content and invitro drug release studies were conducted. The stability study results indicated the stability of the formulation PEF-6.

IV. CONCLUSION

The formulated optimized ocular insert (PEF-06) containing Prednisolone acetate had a potential for sustained action of drug release. Thus, the ocular inserts were successfully formulated as an alternative to eye drops which showed bioadhesive effect and increased residence time along with the sustained drug release.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1]. Rathore KS, Nema RK. An insight into Ophthalmic Drug Delivery System. Int J Pharm Sci Drug Res. 2009;1(1):1-5.
[2]. Sikandar AV. Ocular drug delivery system: an overview. Int J Pharm Sci Res. 2011;2(5):1168-75.
[3]. Karatas A, Baykara T. Studies of indomethacin inserts prepared using water soluble polymers effect of the preparation method and polymers on drug release. J Fac Pharm. 2006;35(4):255-68.
[4]. Saettone MF, Salminen L. Ocular inserts for topical delivery. Adv Drug Deliv. 1995;16(1):95-106.
[5]. Gurtler F, Gurny R. Patent literature review of ophthalmic inserts. Drug Dev Ind Pharm.. 1995;21(1):1-18.
[6]. Khar RK, Vyas SP. Targeted and controlled drug delivery: novel carrier systems. 1st edn. New Delhi: CBS Publishers and Distributor. 2002;384.
[7]. Tadafumi T, Hitoshi S, Ichiro M, Kazuo S, Kenji O, Akira K. Effect of orally administered olopatadine hydrochloride on the ocular allergic reaction in rats. Allergol Int. 2003;52(2):77-83.
[8]. Lachman L, Lieberman HA, Kanig JL. The theory and practice of industrial pharmacy, 3rd edn. Bombay: Varghese publishing house. 1990;171.
[9]. British Pharmacopoeia. British Pharmacopoeia Commission Secretariat of the Medicines and Healthcare Products Regulatory Agency; UK. 2012;A493.
[10]. Suddhasattya D, Reddy V, Swetha B, Sandeep KD. Method development and validation for the estimation of olopatadine in bulk and pharmaceutical dosage forms and its stress degradation studies using uvvis spectrophotometric method. Int J Pharm Sci. 2010;2(4):212-8.
[11]. Gevariya H, Patel J, Girhepunje K, Pal R. Sustained ophthalmic delivery of levofloxacin from once a day ocuserts. Int J Pharm Pharm Sci. 2009;1(1):2432.
[12]. Safaa SE, Viviane FN, Ahmed NA. Formulation and evaluation of acyclovir ophthalmic inserts. Asian J Pharm Sci. 2008;3(2):58-67.
[13]. Patel UL, Chotai NP, Nagda CD. Design and evaluation of polymeric ocular drug delivery system for controlled delivery of moxifloxacin hydrochloride: in vitro and in vivo evaluation. Active Pharm Sci. 2010;52(4):523-35.
[14]. 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):116-20.
[15]. Kumar A, Malviya R, Sharma PK. Recent trends in ocular drug delivery a short review. Eur J Appl Sci. 2011;3(3):86-92.
[16]. Mishra DN, Gilhotra RM. Design and characterization of bioadhesive in-situ gelling ocular inserts of gatifloxacin sesquihydrate. Daru. 2008;16(1):1-8.
[17]. Wagh V, Wagh K, Inamdar B, Samanta M. The effect of forskolin ophthalmic inserts on intraocular pressure in rabbit eyes. Int J Pharm Pharm Sci. 2009;1(2):146-55.
[18]. Singhvi G, Singh M. Review: in-vitro drug release characterization models. Int J Pharm Sci Res. 2011;2(1):77-4.
[19]. Natu MV, Sardinha JP, Correia IJ, Gil MH. Controlled release gelatin hydrogels and lyophilisates with potential application as ocular inserts. Biomed Mater. 2007;2(4):241-49.
[20]. Indian Pharmacopoeia. Govt. of India, ministry of health and family welfare. India. 2007;53-9.
[21]. Basu S, Chakrabatorty S, Bandyopadhyay AK. Development and Evaluation of a Mucoadhesive Nasal Gel of Midazolam Prepared with Linum usitatissimum L. Seed Mucilage. Sci Pharm. 2009;77(4):899-10.
[22]. Dubey BK, Bhowmick M, Joshi A, Shahwal VK. Design and characterization of sustained release levofloxacin ocular inserts. Int J Biomed Adv Res. 2011;2(12):453-66.