



# Design And Evaluation Of Propranolol Loaded Bio Flexi Ocusert Using Cucumis Sativus Biopolymer

**DEEPIKA KUNWAR,\* DR N.V.SATEESH MADHAV**

ASSISTANT PROFESSOR, DIRECTOR

PHARMACEUTICS,

R.P.S COLLEGE OF PHARMACY, LUCKNOW, INDIA

## ABSTRACT-

Ocular drug delivery is one of the most challenging tasks faced by Pharmaceutical researchers. Major barriers in ocular medication are the ability to maintain a therapeutic level of the drug at the site of action for a prolonged duration. The ophthalmic preparations are available as sterile, buffered, isotonic solution. Several types of dosage forms are applied as the delivery system for the ocular delivery of drugs. The most prescribed dosage form is the eye drop solution as drops are easier to administer. Suspensions, gelled systems, ointment are also used for prolonged therapeutic action. Solvent casting technique was used to prepare the ocuserts. Ten formulation were prepared by using propranolol drug, cocos nucifera as biopolymer. The ocuserts were physically examined for colour and various other physical parameters were evaluated. Based on the physical parameters further studies were carried out like stability, invitro release studies. The therapeutic efficacy of an ocular drug can be greatly improved by prolonging its contact with the corneal surface. Newer ocular drug delivery systems are being explored to develop extended duration and controlled release strategy.

## INTRODUCTION:-

Topical application of ophthalmically active drugs is the most prescribed route of administration for treatment of various ocular disorders. It is generally agreed that the intraocular bioavailability of topically applied drug is extremely poor. This is mainly due to drainage of excess fluid by the nasolacrimal duct as well as dilution and elimination of the solution by tear turn over. Ocular bioavailability of drug is an important parameter influencing the efficacy of ophthalmic preparation. The commonly available ophthalmic ointments, although better retained than eye drops, do not efficiently release all types of drugs and they are poorly tolerated by many patients. Several approaches have been reported and numerous novel ophthalmic drug delivery systems were developed to achieve a higher bioavailability of drugs. Among these formulations are in-situ gel polymers, microspheres, nanoparticles, liposome and ocuserts. The advantages of ocuserts are solid devices placed in cul-de-sac of eye, in comparison with liquid formulation. Because of

the prolonged retention of the device and a controlled release, the effective drug concentration in the eye can be ensured over an extended time period.

Propranolol is a sympatholytic non-selective beta blocker. Sympatholytics are used to treat hypertension, anxiety and panic and glaucoma. It was the first successful beta blocker developed.

Propranolol is rapidly and completely absorbed, with peak plasma levels achieved approximately 1–3 hours after ingestion. The main metabolite 4-hydroxypropranolol, with a longer half-life (5.2–7.5 hours) than the parent compound (3–4 hours), is also pharmacologically active. Propranolol is a highly lipophilic drug achieving high concentrations in the brain. Propranolol is a non-selective beta blocker, that is, it blocks the action of epinephrine and norepinephrine on both  $\beta_1$ - and  $\beta_2$ -adrenergic receptors. It has little intrinsic sympathomimetic activity (ISA) but has strong membrane stabilizing activity.

Cucumber is a very edible fruit which comes from the cucumber plant *cucumis sativus*, which is part of the gourd family. It is being used for different purpose as it can be eaten raw or cooked. With so many health benefits it becomes one of the most important parts of food diet as well as skin diet. Coconut is a very versatile and indispensable food item for most people under the tropical belt. It is a complete food rich in calories, vitamins, and minerals. A medium-size nut carrying 400 g edible meat and some 30-150 ml of water may provide almost all the daily-required essential minerals, vitamins, and energy of an average-sized individual

## MATERIALS AND METHODS

- **Isolation of biopolymer from *cucumis sativus***

1kg of Cucumber taken and its outer portion was peeled off, inner portion removed & cut down into small pieces. It was then separately grinded with water in mixer. Both mixtures were filtered through muslin cloth. Both filtrates were centrifuged & divided into two parts. Aqueous extracts were shaken with chloroform to decolourize the extract. In one part Methanol and in another part acetone added and kept overnight in the refrigerator. The biomaterial was collected by centrifugation at 3000 RPM for 5-10 mins. The biomaterial was naturally dried for 20-30 hrs and finally screened through mesh size #120.

## Preparation of Ocuserts

The various formulations of bio flexi ocusert were prepared by solvent casting method. Different bio-flexi ocusert (1:1 to 1:10) were prepared with varying concentration of the biopolymer. Biopolymer was taken in mortar pestle and triturated properly for the fine powder. After that 50 mg of dextrose & 50mg of glucose was added along with 100 mg of nanosized drug (propranolol). Then 10 ml of distill water was added and triturated properly in uniform direction. After that magnetic stirring was done for 45 minutes and sonication was performed (3cycle). After that the mixture was uniformly spreaded on a petri-dish and dried at room temperature. Bio-flexi film was obtained.

## FORMULATION DETAIL

formulation	FB1(1:1)	FB2(1:2)	FB3(1:3)	FB4(1:4)	FB5(1:5)	FB6(1:6)	FB7(1:7)	FB8(1:8)	FB9(1:9)	FB9(1:10)
Propranolol mg)	10	10	10	10	10	10	10	10	10	10
Cucumis sativus biopolymer	1%	2%	3%	4%	5%	6%	7%	8%	9%	10%
dextrose	50	50	50	50	50	50	50	50	50	50
glucose	50	50	50	50	50	50	50	50	50	50
Distilled water	10	10	10	10	10	10	10	10	10	10

### Evaluation

The ocuserts were evaluated for thickness, folding endurance, drug content, surface pH, percentage moisture absorption, percentage moisture loss and in-vitro diffusion studies.

**Thickness** Insert thickness was measured by a Vernier caliper at five different points on the film. The mean thickness and standard deviation (SD) were calculated.

**Weight variation** Weight was calculated by digital balance. The inserts were subjected to weight variation by individual weighing of 5 randomly selected inserts and mean was calculated.

**Folding Endurance** Folding Endurance of the film was determined by repeatedly folding the inserts at the same place till it breaks. The ocuserts was folded in the center, between finger and thumb and then opened. This was one folding. The number of times, the film could be folded at the same place without breaking gave the value of folding endurance.

**Drug content** Uniformity of drug content was determined by assaying the individual inserts. Three inserts from each batch were powdered individually and each was dissolved in 100 ml of purified water by stirring on a magnetic stirrer for 2 hours. The absorbance of each of these solutions was then measured on UV-visible spectrophotometer at 290 nm.

**In-vitro diffusion studies** The in-vitro drug release studies were carried out using diffusion cell. 0.7 ml of isotonic phosphate buffer of pH 7.4 was placed in the donor chamber, which acted as tear fluid. Ocusert was placed in the donor compartment over a dialysis membrane. 25 ml of isotonic phosphate buffer was taken as the receptor medium and the apparatus was maintained at  $37^\circ \pm 2^\circ \text{ C}$  and was continuously stirred using magnetic stirrer. The samples were withdrawn at regular intervals and analyzed at 290 nm.

## RESULTS AND DISCUSSION

**Thickness-** The thickness of the ocuserts of all formulations was tabled.

s.no	formulation	Thickness
1	FC1	0.28
2	FC2	0.32
3	FC3	0.24
4	FC4	0.26
5	FC5	0.38
6	FC6	0.28
7	FC7	0.43
8	FC8	0.32
9	FC9	0.26
10	FC10	0.28

**Weight uniformity -** The weight uniformity of ocuserts of all formulations were tabled.

s.no	formulation	Weight uniformity
1	FC1	17.6
2	FC2	15.8
3	FC3	16.8
4	FC4	12.5
5	FC5	18.7
6	FC6	24.6
7	FC7	23.6
8	FC8	16.8
9	FC9	17.6
10	FC10	17.8

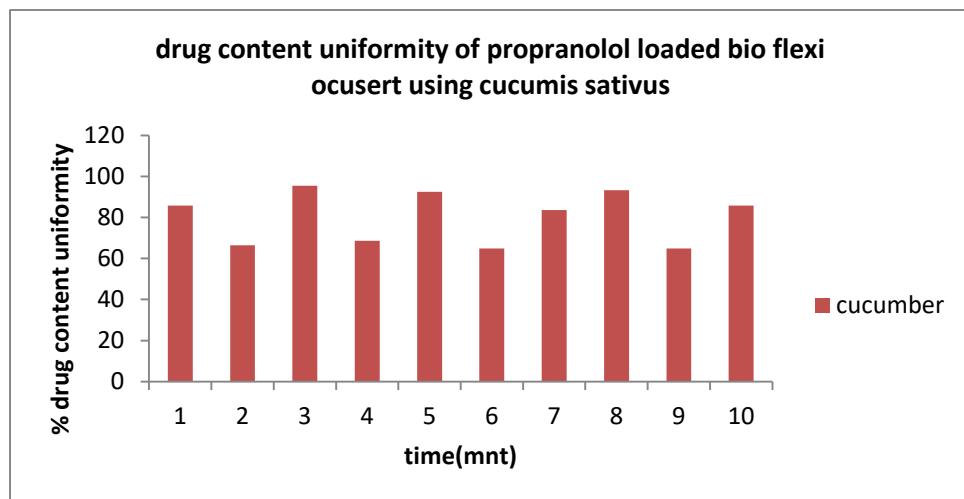
**Folding Endurance-** Use of less amount of plasticizer was observed to cause brittleness in the medicated discs, but use of greater amount of plasticizer (1ml plasticizer per 10 ml) displayed little opaqueness and good folding endurance

s.no	formulation	Folding indurance
1	FC1	112
2	FC2	143
3	FC3	106
4	FC4	132
5	FC5	108
6	FC6	165
7	FC7	121
8	FC8	128
9	FC9	162
10	FC10	158

**Drug content uniformity-** Results of the content uniformity test complied with the BP 2005 requirements.

These results showed that the method for the preparation of inserts gave reproducible results

s.no	formulation	%drug content uniformity
1	Fc1	33.58
2	Fc2	72.38
3	Fc3	85.07
4	Fc4	88.05
5	Fc5	27.61
6	Fc6	55.22
7	Fc7	91.04
8	Fc8	88.05
9	Fc9	89.56
10	Fc10	95.52



**In-vitro diffusion studies :-** in vitro diffusion studies of bio-flexi ocusert were tabled.

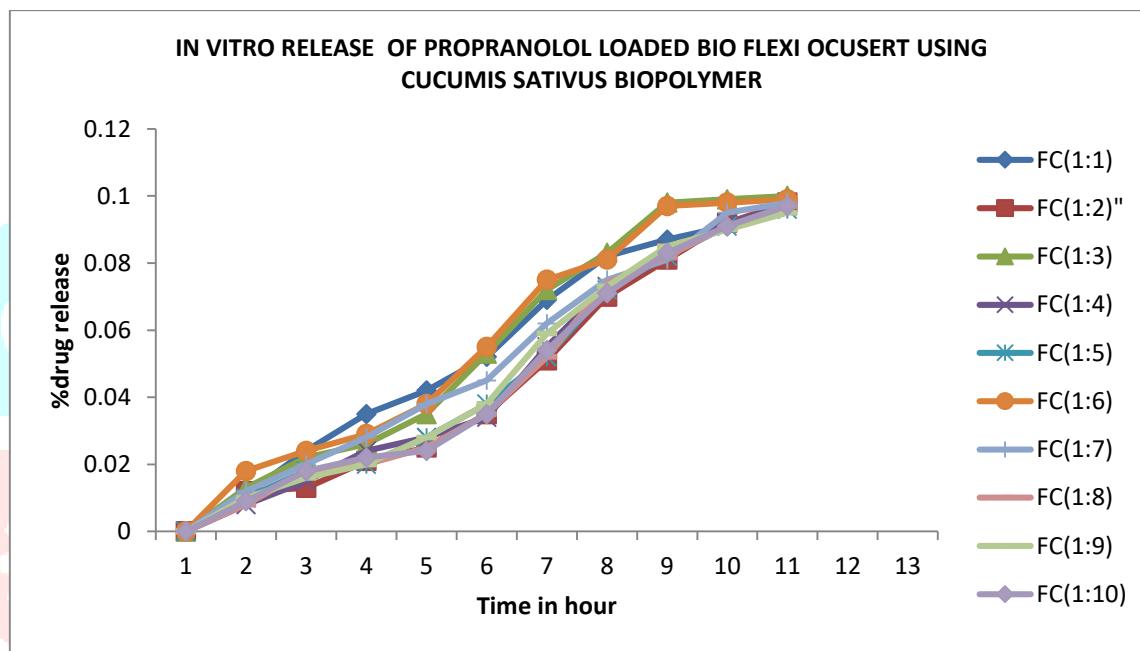


Figure- Invitro drug release of propranolol ocuser

## REFERENCE:-

- 1:- Deivasigamani Karthikeyan, Mithun Bhowmic, Vijay Prakesh Pandey, Jothivel Nandhakumar, singaravel sengottuvelu, sandeep sonkar, thangavel sivakumar,Asian Journal of pharmaceutics, the concept of ocular inserts as a drug delivery system,vol.2 issue 4, 192-200, year 2008.
- 2:- Deamin, R.D., In; Seymour, R.B. Eds., Additives of Plasticizers, Academic Press, New York, **1978**, 203
- 3:- G.P. Andrews et al., Mucoadhesive polymeric platforms for controlled drug delivery, *Eur. J. Pharm. Biopharm.*, 2009;71: 505-518
- 4:- Drug bank version 2.5 accesed on 01/12/2010.
- 5-Wikipedia the free encyclopedia ; propranolol; accessed on 23/11/2010
- 6:- [www.cucumberresearchcenter.org](http://www.cucumberresearchcenter.org)