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Review Article

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FORMULATION AND EVALUATION OF AN IN SITU GEL-FORMING OPHTHALMIC FORMULATION OF FLUROQUINOLONE DRUG

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ABSTRACT

Most commonly available ophthalmic preparations are eye drops and ointments. The eye as a portal for drug delivery is generally used for local therapy to avoid the risk of eye damage. In eye the target tissue absorbs a very less fraction of drug. Due to this reason, concentrated solutions and frequent dosing are required for the instillation to achieve an adequate level of therapeutic effect. The in situ gel forming ophthalmic formulations are directly inserted in to the cul-de-sac that space is between the sclera and eyelid. Compared with the conventional dosage forms these gel provide comfort to the patient. The objective of planning a supportive system is to give and accomplish the right centralization of a drug at the fitting term and dynamic area.

KEYWORDS: cul-de-sac, in situ gel.

BACKGROUND/AIM

The aim of the present investigation is to prepare and evaluate in situ gel-forming ophthalmic drug delivery system ofloxacin.

2. INTRODUCTION

One of the body's most significant and fundamental organs is the eye. In the eye, prescription is directed in numerous areas, including the cornea, conjunctiva, and scleral, to get the best bioaccessibility. The ophthalmic quiet transport structures can be separated into two classes: customary and more present day. Eye drops and balms are the ophthalmic items that are most often utilized. The objective tissue in the eye retains an incredibly less piece of the prescription. For the instilled to accomplish a satisfactory measure of recuperating influence, centered arranging and visit dose are fundamental. When contrasted with liquid subtleties, visual implants, which are strong gadgets put in the eye's parkway, have various benefits. The convincing calm fixation inside the eye might be guaranteed throughout a drawn out time span thanks to the extensive upkeep of the gadgets and a controlled release.

The eye is an exceptional organ from a physical and physiological viewpoint since it has various unquestionably unmistakable designs, each with a particular physiological reason. The choroid and ciliary cycles are profoundly vascularized and show very high blood streams, though the cornea and the translucent focal point are the main tissues in the body, beside ligament, that don't have a blood supply. An expansion of the diencephalon in the focal sensory system, the retina and optic nerve assume an exceptionally remarkable part in the cycles of visual discernment and transduction.

Qualities of a Modified-Release Ophthalmic Drug Delivery System: A well-designed modified release ophthalmic drug delivery system must deliver the active ingredient to the right place.

- Improve the ratio of local activity to the systemic effects.
- Reduce the number of installations per day, once-a-day being considered the optimal goal.
- Should easy to self-administer.
- Not induce a foreign-body sensation, long-lasting blurring, or a very bad after taste.

In situ gel ofloxacin is a manufactured antibacterial anti-infection that is somewhat less compelling against Gram-positive microbes than it is against various Gram-negative microorganisms. This medication's essential technique for activity includes hindering the bacterial DNA gyrase protein, which is liable for keeping up with the state of DNA.

3. MATERIALS AND METHODS

MATERIALS

General chemicals and reagents

Unless otherwise stated general chemicals and reagents were purchased from

Drug

Drug used for the studies and the corrsponding suppliers are summarized**.**

Drug	Supplier
Ofloxacin	Yarrowchem Products, Mumbai,India

Excipients

The excipients used for the study are following. They were purchased from Yarrowchem Products, Mumbai, India. All the chemicals and reagents used are analytical grades.

Excipients	Supplier
HPMC E 15	Yarrowchem Products, Mumbai, India
Eudragit R L 100	Yarrowchem Products, Mumbai, India
PEG 400	Yarrowchem Products, Mumbai, India
Dichloromethane	Yarrowchem Products, Mumbai, India
Ethanol	Ezhuthachan College of Pharmaceutical Science

Chemicals used in the study

Instrumentation

The instruments used for the present research are summarized as follwing

Table: Instruments used for the study.

Name of instruments	Supplier
FTIR Spectrophotometer	Genuine Scientific Instruments
UV-Visiblespectrophotometer	Genuine Scientific Instruments
Analytical balance	Genuine Scientific Instruments
Verniercaliper	Laboratory Suppliers

General laboratory consumables and plastic wares

The general laboratory consumables and plastic wares used for the present research study are summarized in the following table

PREPARATION OF STANDARD CALIBERATION CURVE OF OFLOXACIN

Preparation of standard solution

Exactly 100 milligrams of unadulterated ofloxacin were gauged. Once, it was moved to a volumetric flagon of 100 ml. Then it was moved toward a volume of 100 ml and broke up in phosphate cradle with a PH of 7.4. The 1 mg/ml (1000 g/ml) result that was initially alluded to as "stock arrangement" stood out.

MAKING OF THE OFLOXACIN ALL INCLUSIVE ADJUSTMENT BEND

Aliquots of 4, 6, 8, 10, and 12 ml from the previously mentioned stock arrangement have been moved to a 100 ml volumetric cup and weakened with phosphate cushion with a PH of 7.4. The UV Spectrophotometer was once used to quantify the arrangement's retention at 254 nm. Through cautious thought of the X hub and absorbance on the Y pivot, an adjustment bend was once plotted.

METHOD

Ofloxacin was exposed to various solvents fully intent on testing its dissolvability. Methanol and water were used as solvents.

FTIR

METHOD FOR FTIR

An IR range of the chose parts alongside the medication and other excipients was used to evaluate the uprightness of the medication in the equation. The spectra were caught with a Shimadzu IR Renown 21. As opposed to normal spectra, there was the spectrometer. The palletization of potassium bromide (KBr) was utilized in this review. Potassium bromide was entirely mixed with the example in the proportion of one part of example to 100 parts of KBr prior to being totally dried at 1000C for one hour to make the pellet. Using kicks the bucket, the blend was compacted to make a plate. This circle was placed in the example chamber, and the product program programming, which is likewise not entirely clear, used to get a range.

FORMULATION DEVELOPMENT

4.2.4.1 Composition of in-situ gel.

Ingredients	F 1	F 2	F 3	F 4
Ofloxacin(mg)	3	3	3	3
HPMC E15(mg)	150	500	550	90
Eudragit RL 100(mg)	230	50	150	330
Ethanol (ml)	5	5	5	5
Dichloromethane (ml)	5	5	5	5
PEG400 (ml)	0.5	0.5	0.5	0.5

Table: Preparation of Ocusert

Key ingredients and their roles in formulation

INGREDINTS	ROLE
HPMC E15, Eudragit RL-100	Modifiers of drug release pattern
Dichloromethane, PEG 400	Plasticizer

Table Ingredients

Formulation of in situ gel

Method of preparation of Ocusert

Solvent casting method

By utilizing the dissolvable projecting technique and a copolymer called Eudragit RL100 with Stake 400 as a plasticizer, HPMC E-15 was utilized to make the visual solid movies of ofloxacin. Dichloromethane and ethanol were used as projecting solvents. Utilizing an attractive

stirrer to accomplish a uniform scattering, the necessary polymers (2% w/v) and plasticizer (30% w/w) were disintegrated in the fitting solvents to make the projecting arrangements. The substrate utilized was mercury, which was poured onto a petri dish. The form was hung on the mercury's level, smooth surface while 10 cc of the arrangement was added to it. Following 24 hours, the dry film was taken out and put on melded calcium chloride in a desiccator to be utilized later.

Surface; Simply by contacting the film's surface, the surface was evaluated.

Mass consistency; Three movies from every definition were chosen and weighed independently on an electronic scale for the mass consistency test. Table 5 has the typical weight computations.

Thickness; Three movies from every definition in different groups were picked aimlessly, and the thickness of each film was estimated utilizing a screw check at different areas.

Drug Content Consistency; Every detailing's three film units were set in individual 100 ml volumetric cups with 100 ml of reenacted tear liquid at pH 7.4 and whirled consistently for 24 hours. The arrangements were separated, fittingly weakened, and exposed to UV spectrophotometer examination. The last not entirely set in stone by averaging the medication content of three motion pictures.

Assessment of the extent of dampness consumed; Visual inserts were gauged and put away in aluminum chloride-filled desiccators. Visual inserts were eliminated and rechecked three days after the fact. The condition was utilized to register the level of dampness consumed.

Dampness Ingestion Rate = Mf - Mi/Mi 100..
Dampness Retention Rate = Mi - Mf/Mi 100

In Vitro Medication Delivery; Using a dialysis layer in STF pH 7.4 arrangements, an in vitro dispersion investigation of ofloxacin visual supplements was led. The in vitro send off examinations were directed utilizing a bichambered contributor recipient compartment model made utilizing a business semi-porous film of clear and recovered cellulose type (Sigma Dialysis Layer).

4.1 PREFORMULATION STUDY (Pure Drug)
4.1.1 Organoleptic evaluation
Organoleptic evaluation
Colour-Off-white ,Odour-Odourless
Taste- Bitter

λmax for pure Ofloxacin
In accordance with the procedure outlined in 4.2.2.1, the absorbance maximum of pure ofloxacin was calculated. At 295.5 nm, the absorption maximum was measured.

Table 4.2: Calibration Curve.

Sl.No.	Test	Specifications of IP	Results
1	Character	Off-white, Odourless, hygroscopic crystalline powder.	Off-white, Odourless, hygroscopic crystalline powder.
2	Solubility	Slightly soluble in water and in methyl alcohol, slightly soluble to soluble in dichloromethane, soluble in glacial acetic acid.	Slightly soluble in water and in methyl alcohol. Soluble in dichloromethane.
3	IR spectra	The potassium bromide disc contain drug was prepared to record the spectrum by using FTIR Spectrometer	The spectrum showed the prominent peak of ofloxacin.
4	Melting point	250-257^{0}C	254^{o}C

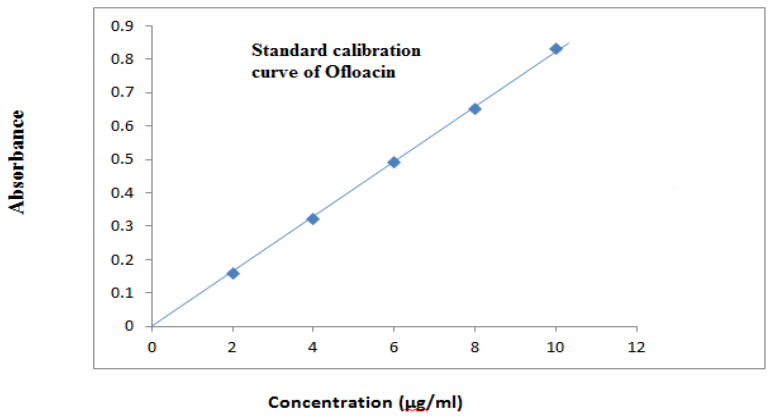

Fig. 4.1: Standard calibration curve of Ofloxacin.

4.3 Drug – Excipient Compatability Studies
The FTIR studies were done based on strategy determined in 4.2.3

FTIR For unadulterated medications, drug polymer blends, and medication excipient combinations, FTIR examination was finished. The FTIR studies were led as per the methodology. The medication's FTIR range shows the significant tops according to utilitarian gatherings. There is no way to see a collaboration between the medication, polymer, and excipients, as per the FTIR range of the actual combination of the medication with the polymer and the medication with the excipient. The trademark drug top was not changed in that frame of mind of the medication polymer blend.

4.4 Formulation Development
The Ofloxacin ocuserts were prepared by method described in above sec ***In vitro*** **Evaluation**s

4.5.1 General appearance
Colour - white off white
Taste – Tasteless
Odour – odourless
Shape – Round

4.5.2 Physical Evaluation
The physical evaluation of prepared Ofloxacin ocusewrs were carried out as per the methods described in sections above

Table 4.4: Physical Evaluation of Ocusert.

Sl. No	Formulation	Surface texture	Mass uniformity	Thickness (mm)	Folding Endurance	Surface pH
1	F1	Smooth	32.2	0.210	82	6.7
2	F2	Smooth	34.3	0.281	86	6.7
3	F3	Smooth	36.0	0.242	98	6.8
4	F4	Smooth	35.4	0.226	110	6.7

4.5.3 Estimation of Drug content of Formulations
Ofloxacinocuserts were produced, and their drug content was tested using the procedure outlined in section 4.2.4.3.6.

Table 4.5: Estimation of drug content of ocuserts.

Sl.No	Formulation	Amount of drug present (mg)	Percent drug present (%)
1	F1	2.7171	90.57
2	F2	2.7549	91.83
3	F3	2.7732	92.44
4	F4	2.8077	93.59

All of the batches' uniform drug content was examined using the procedure outlined in 3.2.3.3.6. All batches' homogeneous medication content fell within the range of 86 to 93%.

4.5.4 Percentage Moisture Content
According to the procedure outlined in 3.2.3.3.7, the prepared Ofloxacin Ocuserts' moisture content was measured as a percentage.

Formulation F1
The dissolution profile of formulation F1 has been obtained as in table 4.8.

Table 4.7: Dissolution Profile of Formulation F1.

Sl. No	Time (hrs)	Cumulative Percentage of drug release(%)
1	0	0
2	1	6.25
3	2	10.01
4	3	13.45
5	4	17.94
6	5	23.54
7	6	29.43
8	7	33.93
9	8	39.11
10	9	44.54
11	10	49.31

12	11	52.43
13	12	59.75
14	13	63.11
15	14	66.74
16	15	78.13
17	16	83.48
18	17	85.41
19	18	88.74

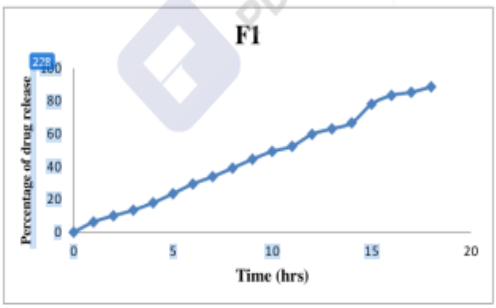

Fig. 4.8: Dissolution data of F1.

Table 4.9: In vitro dissolution of Formulation F2.

The dissolution profile of formulation F2 has been obtained as in table 4.9.

Table 4.8: Dissolution Profile of formulation F2.

Sl. No	Time (hrs)	Cumulative Percentage of drug release(%)
1	0	0.00
2	1	9.62
3	2	12.43
4	3	16.13
5	4	20.42
6	5	25.55
7	6	29.51
8	7	34.11
9	8	40.41
10	9	48.32
11	10	54.33
12	11	57.41
13	12	62.44
14	13	64.92
15	14	73.71
16	15	76.42
17	16	79.52
18	17	83.84
19	18	86.58

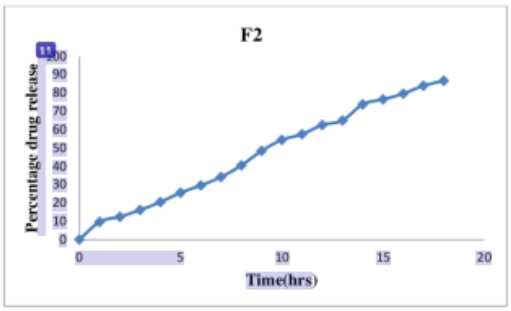

Fig. 4.8: Dissolution data of F2.

Formulation F3

Table 4.10 In vitro dissolution of Formulation F3

The dissolution profile of formulation F3 has been obtained as in table 4.10

Table 4.9: Dissolution Profile of Formulation F3.

Sl. No	Time (hrs)	Cumulative Percentage of drug release(%)
1	0	0
2	1	7.22
3	2	9.19
4	3	13.23
5	4	18.14
6	5	22.29
7	6	24.44
8	7	30.11
9	8	33.65
10	9	38.44
11	10	40.43
12	11	43.11
13	12	51.13
14	13	55.43
15	14	60.75
16	15	68.32
17	16	76.45
18	17	84.11
19	18	90.58

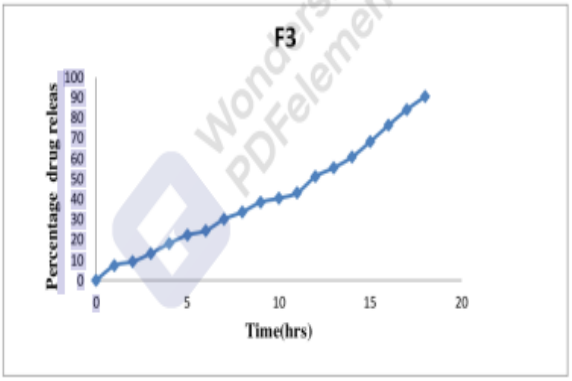

Fig. 4.10: Dissolution data of F3.

Formulation F4

The dissolution profile of formulation F4 has been obtained as in table

Table 4.10: Dissolution profile of formulation F4.

Sl. No	Time (hrs)	Cumulative Percentage of drug release(%)
1	0	0
2	1	7.66
3	2	9.21
4	3	13.99
5	4	18.74
6	5	24.29
7	6	30.21
8	7	32.31
9	8	38.81
10	9	44.82
11	10	53.65
12	11	59.69
13	12	63.78
14	13	69.78
15	14	73.43
16	15	78.21
17	16	83.41
18	17	85.21
19	18	88.74

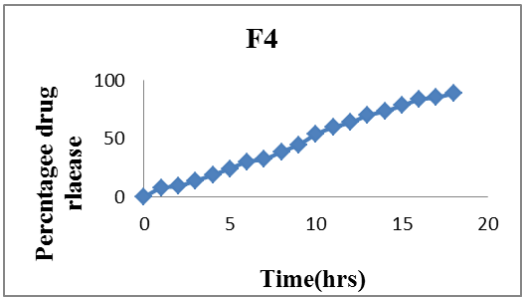

Fig4.11: Dissolution data of f4.

SUMMARY AND CONCLUSION

1. Various physicochemical appraisals have been performed on four definitions. Visual supplements that have been coordinated have been clean and have passed all assessment strategies. As indicated by Plan F2, a most extreme total extent medicine send off ought to end following 18 hours. The occuserts that were made likewise breezed through the sterility assessment. In vitro and in vivo send off tests were utilized to lay out zeroorder send off of the drug. Microbial viability studies showed that the medication portrayed in the motion pictures was solid against explicit microorganisms. The review's methodology was clear and repeatable. The polymers used were reasonable and generally open. To make the ofloxacin in situ gel wer, water solvent polymers like HPMC and Eudragit RL 100 were utilized. Concentrates on utilizing FTIR innovation uncovered that there is no undeniable contrariness among polymers and ofloxacin. The medication discharge from the superior definition F5 was 92.64% following 18 hours, and every one of the actual measurements were great.

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