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FORMULATION AND IN-VITRO CHARACTERIZATION OF MOXIFLOXACIN OCULAR FILM

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ABSTRACT

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. The objective of planning a supportive system is to give and accomplish the right centralization of a prescription at the fitting term and dynamic area. A supportive administrator's visual and end rely upon its physicochemical qualities as well as the basic visual life frameworks and physiology. The customary ophthalmic suspensions, portion structures, and visual game plans are as of now not adequate to treat these problems. Collagen safeguards, biodegradable polymeric structures, and implants are only a couple of the visual conveyance frameworks being created to build the visual bioavailability and save the movement of visual meds.

KEYWORDS: Ocular film, ocusert, biodegradable.

INTRODUCTION

The eye is one of the most vital organs in the body. In eye drug is administered at various site such as corneal, conjunctival and scleral for better achievement of bio availability. The ophthalmic drug delivery systems are classified as conventional and newer drug delivery systems. 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 ocuserts are directly inserted in to the cul-de-sac that space is between the sclera and eyelid. Compared with the conventional dosage forms ocuserts provide comfort to the patient.

Anatomy of human eye

After skin eye is the most easily accessible site for topical administration of drug. The accessory structures of eye are eyelids, eye lashes, eye brows, lachrymal apparatus and extrinsic eye muscle.

Orbital cavity: A thick layer of areolar tissue is interposed between the bone and eye. The adult eye ball measures about 24 mm in diameter.

Anatomically, the wall of the eye ball can be divided into three layers.

Outer fibrous layer – Tunica fibrosa,
Middle vascular layer – Tunica vasculosa
Inner nervous tissue layer – Tunica nervosa

Tunica externa

The fibrous tunic is the superficial coat of the eye ball which preserves shape of eye ball. It is avascular and consists of the anterior cornea and posterior sclera.

Cornea: Cornea is a transparent coat that covers the coloured iris and has diameter of 12 mm horizontally and 11 mm vertically which helps to focus on the retina which helps to focus light on the retina.

Sclera: The white of the eye which is a coat of dense connective tissue made up of collagen fibers and fibroblasts. At the junction of cornea and sclera is an opening known as the sclera venous sinus or canal Schlemm.

Tunica media

The vascular tunic or uvea is the middle layer of eye ball.it has three portions; choroid, ciliary body and iris.

Choroid: It lines the posterior five-sixth of inner surface of the sclera. This is composed of rich capillary plexus, small arteries and veins. It provides blood supply and absorbs scattered light.

Ciliary body: It consists of ciliary muscle and secretory epithelial cells.

Iris: It is placed between the cornea and lens.

Tunica interna
It lines the posterior three-quarters of the eye ball and which is the beginning of the visual pathway.
Retina: It is made up of ten layers and is receptor of vision. The retina consists of pigment epithelium.
Eye lid: Eye lids are 25 mm long and 11-12 mm wide. The margins of eyelids have sensitive hairs called cilia. Upper eyelids have 100-150 cilia and lower eyelids have 50-70 cilia and lower eyelids have 50-70 cilia. Meibomian glands and some sebaceous glands are situated in eyelids. These glands open into follicles of cilia. Eyelid protect eye from foreign particles.
Conjunctiva: It is the outer most layer of eye. It is thin mucous membrane. The surface of conjunctiva is lubricated by thin tear film secreted by lachrymal glands.
Lens: It is suspended from the ciliary body by the suspensory ligaments. It is crystalline in nature. It is biconvex, transparent and possesses elastic property. It is formed by long lens derived from anterior epithelium.

EYE CONDITIONS

Amblyopia: Often called lazy eye, this condition starts in childhood. One eye sees better than the other, so brain favors that eye. The weaker eye, which may or may not wander, is called the "lazy eye."

Astigmatism: A problem with the curve of your cornea. Eye can't focus light onto the retina the way it should. Glasses, contact lenses, or surgery can correct the blurry vision it causes.

Black eye: Swelling and discoloration around the eye caused by an injury to the face.
Cataract: A clouding of internal lens. It can cause blurred vision.

Conjunctivitis: Also known as pinkeye, it's an infection or inflammation of the conjunctiva.

Corneal abrasion: A scratch on the clear part of the front of the eye. Pain, light sensitivity, or a feeling of grit in the eye is the usual symptoms.

Diabetic retinopathy: High blood sugar damages blood vessels in the eye.

Diplopia (double vision): Seeing double can be caused by many serious conditions. It requires immediate medical attention.

Dry eye: Either the eyes don't produce enough tears, or the tears are of poor quality.

Glaucoma: This progressive loss of vision comes from increased pressure inside the eye. This disease is difficult to detect for years.
Keratitis: Inflammation or infection of the cornea.

Optic neuritis: The optic nerve becomes inflamed, usually due to an overactive immune system. Pain and vision loss are the result.

Retinitis: An inflammation or infection of the retina.
Scotoma: A blind or dark spot in the visual field.

Uveitis: The coloured part of the eye gets inflamed or infected.

CONVENTIONAL OCULAR DELIVERY SYSTEMS

Ointments
Ointments are semi solid preparations. The major problem ointment dosage form is blurring of vision, matting of eyelids.

Eye Drops
Eye drops are mainly used for the anterior segment diseases such as dry eye, infections, traumas, inflammatory reactions, cataract etc.

ADVANTAGE OF OCULAR DRUG DELIVERY SYSTEMS

Accurate dosing is possible
To provide sustained and controlled drug delivery
To increase the ocular bioavailability of drug by increasing the corneal contact time.
To provide targeting to prevent the loss to other ocular tissues.
To circumvent the protective barriers like drainage, lacrimation and conjunctival absorption.
To provide comfort, better compliance to the patient and to improve therapeutic performance of drug.
To provide better housing of delivery system.

CLASSIFICATION OF OPHTHALMIC INSERTS

Ophthalmic inserts are defined as sterile preparations, solid or semisolid consistency devices placed into cul-de-sac or conjunctival sac. There are two types of ocular inserts.
Non-erodible ocular insert: The Non-erodible ocular inserts include Ocusert, and Contact lens.

Erodible ophthalmic insert: The marketed devices of erodible drug inserts are Laciserts, SODI, and Minidisc.

- Lacisert: it is a sterile rod shaped device made up of hydroxy cellulose without any preservative is used for the treatment of dry eye syndromes.
- Sodi: Soluble Ocular Drug Insert is a small oval wafer.
- Minidisc: The minidisc consists of a contoured disc with a convex front and concave back surface in the contact lens with a diameter of 4-5mm.

Classification of Patented Ocular Inserts

- Insoluble inserts
- Soluble inserts
- Bio-erodible inserts

Insoluble ophthalmic inserts: classified in to three categories.
Diffusion systems
Osmotic systems
Hydrophilic contact lenses.

Diffusion inserts
The diffusion inserts are solid or semisolid consistency devices. Through the diffusion mechanism molecules penetrates across sclera and conjunctiva.

Osmotic inserts
In the case of osmotic inserts, drug molecules move from low concentration to high concentration through a semipermeable barrier. There are two parts central part and peripheral part.

Central part
- It is composed of a drug with or without an additional osmotic solute dispersed through a polymeric matrix, so that the drug is surrounded by the polymer as discrete small deposits.
- The drug and the osmotic solutes are placed in two separate compartments, the drug reservoir being surrounded by an elastic impermeable membrane and the osmotic solute reservoir by a semipermeable membrane.

Aim
In the present work an attempt was made to prepare the moxifloxacin Ocusert using different polymers by solvent casting method.

Objectives
Formulation of ocusert by solvent casting method
The study of incompatibility analysis of pharmaceutical ingredients
The study of In vitro evaluation of prepared formulations.

MATERIALS AND METHODS
Drug and the excipients are the materials.

METHODS
ORGANOLEPTIC EVALUATION
The organoleptic characters of drug can be recorded by using descriptive terminology. Following organoleptic properties have to be determined.
Colour
Odour
Taste

IDENTIFICATION OF DRUG
λmax For Pure drug.
Preparation of stock solution.
Determination of λ max
These are the main procedures.
Preparation of standard calibration of drug have to be carried out.

SOLUBILITY DETERMINATION
Procedure
Solubility test of drug can be performed by using various solvent. Water, ethanol can be used as solvent.

DRUG EXCIPIENT COMPATIBILITY STUDIES
FTIR
Integrity of the drug in the formulation is to be checked by talking an IR spectrum of he selected formulation along with the drug and other excipients.

FORMULATION OF OCUSERT
Method of preparation of Ocusert

Solvent casting method
The Ocular Monolithic films of moxifloxacin were prepared by solvent casting method with HPMC E-15 in combination with copolymer namely Eudragit RL100 with PEG-400 as plasticizer. Ethanol, dichloromethane were used as casting solvent. The casting solutions were prepared by dissolving the appropriate polymers (2% w/v) and plasticizer (30%w/w) insuitable solvents using a magnetic stirrer to get a uniform dispersion. Mercury was used as the substrate and is poured in to petri dish. 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 obtained were taken out and stored over fused calcium chloride in a desiccators at room temperature for further use.

Evaluation of ocusert
Physical appearance
The films observed visually for their physical appearance such as colour and transparency.

Surface texture
The surface texture of the film was evaluated by simply touching the surface of the film.

Mass uniformity
For the mass uniformity three films from every formulation were taken and weighed individually on electronic balance. The average weights were calculated in table5.

Thickness
Three films of each formulation of different batches were selected randomly and the thickness of the film was measured at different places using screw guage.

Folding endurance test
The folding endurance of the film was determined by repeatedly folding one film at same place till it broke.

Surface pH
Ocular inserts were left to swell for 5 h on agar plate which was prepared by dissolving 2 % (w/v) agar in warm STF (pH 7.4) under stirring and then pouring the solution into petri plate allow it till gelling at room

temperature. The surface pH was measured by means of a pH paper placed on the surface of swollen film.

Drug Content Uniformity
Three film units of each formulation were taken in separate 100 ml volumetric flasks, 100 ml of pH 7.4 simulated tear fluid was added and continuously stirred for 24 h. The solutions were filtered, diluted suitably and analyzed on a UV spectrophotometer. The average of drug contents of three films was taken as final reading.

Estimation of percentage moisture absorbed
Ocular inserts were weighed and kept in a desiccators containing aluminium chloride. After three days ocular inserts were taken out and reweighed. Percentage moisture absorbed was calculated using the equation.

% Moisture Absorbed = Mf – Mi / Mi × 100.

Estimation of percentage moisture loss
Ocular inserts were weighed and kept in a desiccators containing 22g of anhydrous calcium chloride. After three days insets were taken out and reweighed. Percentage moisture loss was calculated using the equation

% Moisture Absorbed = Mi – Mf / Mi × 100

Where, Mi is the initial weight and Mf is the final weight

In Vitro Drug Release
In vitro diffusion studies of moxifloxacin ocular inserts were carried out using dialysis membrane in STF pH 7.4 solutions. The in vitro release studies were carried out using a bichambered donor–receiver compartment model designed using commercial semi permeable membrane of transparent and regenerated cellulose type (Sigma Dialysis Membrane). The formulation prepared was subjected to diffusion tests for 18 h. At every 1 h interval, sample was withdrawn, and replaced by an equal volume of diffusion medium. Drug content in the diffusion sample was determined at 293.5 nm by UV spectrophotometer. Cumulative percent drug released was found out at each time interval and graph was plotted between cumulative % drug released and time in hour.

RESULT AND DISCUSSION

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

Identification of pure drug
The absorbance maximum of pure moxifloxacin was determined by standard calibration method. The absorbance maximum was measured at 294.5 nm.

Formulation Development
The moxifloxacin ocuserts were prepared by solvent casting method.
Drug – Excipient Compatibility Studies
The FTIR studies were carried out.

FTIR analysis was carried out for pure drug and drug polymer mixture and drug excipient mixtures. FTIR spectrum of drug shows the prominent peaks with respect to functional groups. The FTIR spectrum of physical mixture of drug with polymer and drug with excipient concluded that there is no significant interaction between the drug, polymer and excipients. In the spectrum of drugs polymer mixture, the characteristic peak of drug was not altered.

***In vitro* Evaluations**
General appearance
Colour - white off white
Taste – Tasteless
Odour – odourless
Shape – Round

Physical Evaluation
The physical evaluation of prepared moxifloxacin ocuserts were carried out.

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
5	F5	Smooth	33.0	0.251	92	7
6	F6	Smooth	30.2	0.151	79	6.7

Physical Evaluation of Ocusert
Post formulation studies of the formulated batches are shown in the above table from the physical evaluation of all the batches formulated, it was concluded that the ocuserts of all the batches had desirable physical properties. Thickness varies from 0.15– 0.25mm. Folding endurance varies from 75-110. Surface pH varies from 6.6 -6.7, which indicates the electrolytic balance. All the batches of formulations passes the wevariation test as per the limits prescribes in IP.

Estimation of drug content of prepared 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
5	F5	2.8002	93.34
6	F6	2.6082	86.94

Estimation of drug content of ocuserts

The drug content uniformity of all the batches were tested .The drug content uniformity of all the batches was in the limit of 86 – 93%.

Time (hr)	Cumulative %drug release	%drug remaining	Square root time	Log cumu %drug released	Log time	Log cumu %drug released	% drug released	Cube root of drug remaining (Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
1	8.75	91.25	1.000	1.960	0.000	0.942	8.75	4.502	0.140
2	11.75	88.26	1.414	1.946	0.301	1.070	2.99	4.452	0.190
3	14.5	85.5	1.732	1.932	0.477	1.161	2.76	4.405	0.237
4	18.75	81.25	2.000	1.910	0.602	1.273	4.25	4.331	0.311
5	22.5	77.5	2.236	1.889	0.699	1.352	3.75	4.264	0.378
6	25.25	74.75	2.449	1.874	0.778	1.402	2.75	4.212	0.430
7	27.25	72.75	2.646	1.862	0.845	1.435	2.26	4.175	0.467
8	32.75	67.25	2.828	1.828	0.903	1.515	3.76	4.067	0.575
9	35.99	64.01	3.000	1.806	0.954	1.556	4.67	4.000	0.642
10	42.82	57.18	3.162	1.757	1.000	1.632	3.42	3.853	0.789
11	47.83	52.17	3.317	1.717	1.041	1.680	5.32	3.737	0.905
12	54.55	45.45	3.464	1.658	1.079	1.737	7.44	3.569	1.073
13	61.53	38.47	3.606	1.585	1.114	1.789	8.25	3.376	1.266
14	67.54	32.46	3.742	1.511	1.146	1.830	4.31	3.190	1.452
15	74.92	25.08	3.873	1.399	1.176	1.875	4.45	2.927	1.715
16	85.71	14.29	4.000	1.155	1.204	1.933	2.43	2.427	2.215
17	89.84	10.16	4.123	1.007	1.230	1.953	2.43	2.166	2.476
18	92.64	10.63	4.243	1.054	1.255	1.945	2.65	2.075	2.354

The dissolution profile of optimized formulation F5 was fitted to various kinetic models like zero order, first order, higuchi model and korsmeyerpeppas models were used. The R^2 value shown in table shows the release kinetics followed by F5 and further explained in plots.

Formulation	Kinetic Models			
F5	Zero order	First order	Kosmeyer– peppas plot	Higuchi
R^2 Value	0.968	0.9796	0.9018	0.9762

Regression values of kinetic model

Kinetic model	R^2 value
Zero order	0.968
Firstorder	0.9796
Kors Peppas	0.9018
Higuchi	0.9762

Regression values of kinetic models

The dissolution profile of most satisfactory formulation F5 was fitted to zero order, first order, Higuchi model, Kosmeyerpeppas model to ascertain the kinetic modeling of the drug release. The kinetic treatment of the drug release data of F5 followed first order drug release with R^2 value 0.9796. It indicates that drug release was dissolution controlled and directly proportional to log cumulative percentage drug release.

CONCLUSION AND SUMMARY

The methodology adopted in present study was simple and reproducible. The polymers used were inexpensive and easily available. The moxifloxacin ocuserts were prepared by using water soluble polymers such as HPMC, Eudragit RL 100. FTIR studies showed that there were no marked incompatibility arises between moxifloxacin and polymers. Optimized formulation F5 showed a drug release of 92.64 % at the end of the 18h; all the physical parameters were satisfactory. The kinetic

treatment of the drug release data of F5 followed maximum drug release. From the present study it can be concluded that, ocular monolithic film for moxifloxacin with HPMC E-15 and Eudragit RL100 meet the ideal requirement for ocular inserts devices which can be good way to bypass other traditional drug delivery systems and increases bioavailability.

REFERENCES

1. Ashok H, Sachin M, Sachin S, Sameer N, Neela B,Prajakta B, Suryakant G, Kundan P. A Rational Approach To Ocular Drug Delivery Systems: A Overview. World Journal of Pharmaceutical Research, 2014; 3(2): 3324-3348.
2. Aswani D V, Kishore C, Ramya K V, Ashim KM. Aqueous Nano micellar Formulation for Topical Delivery of Biotinylated Lipid Prodrug of Acyclovir: Formulation Development and Ocular Biocompatibility. Journal Of Ocular Pharmacology And Therapeutics, 2014; 30(1): 49-58.
3. Bezza Benkaouha, I., LeBrun, C., Pisella, P.J., Chandenier, J. Lanotte P J. Fr.Ophtalmol, 2015; 38(2): 723-728.
4. Colo G D, Burgalassi, Chetoni P,Fiaschi M P, Zambito Y, Saettone MF. Gel-forming erodible inserts for ocular controlled delivery of ofloxacin. Int J Pharm., 2001; 215: 101-111.
5. Dinesh.S, Anil B. Design, Formulation, evaluation of Levobunol HCL ocular inserts. J Pharm Sci Res., 2011; 3(12): 1625-1631.
6. Gadhave M V, Pawar S D, Khilari s s, Gaikwad D D, Jadhav S J. Formulation and Evaluation of Moxifloxacin Ocusert. International Journal of Pharmaceutical and Clinical Research, 2016; 8(12): 1610-1615.
7. Geeta R, Shaweta S, Shalini C, Banshraj. Review on ophthalmic inserts. Int J Pharma Prof Res., 2013; 4(3): 912-920.
8. 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.
9. Ghelani T K, Seth A K, Saini V, Singhal S, Kumar S, Yadav Y C. Formulation and evaluation of Timolol maleate ocular insert. Assian J Bio chem Pharm Res., 2011; 1(1): 166-174.
10. Gratieri T, Gelfuso G M, Thomazini J A, Lopez R F. Excised porcine cornea integrity evaluation in an in vitro model of iontophoretic ocular research. Ophthalmic. Res., 2010; 4(3): 208–216.