IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

FORMULATION AND EVALUATION OF LEVOFLOXACIN EYE OINTMENT

Nilofar N. Patwegar* , Shaila R. Borate[1] , Dr. K. M. Karande[2]

*, 1 M. Pharm Student, Department of Pharmaceutics, Satara College of Pharmacy, Satara 415004

2 Associate Professor, Department of Pharmaceutics, Satara College of Pharmacy, Satara 415004

Abstract: Levofloxacin belongs to class fluoroquinolone. The formulation was prepared with the polymer as a base that is white petroleum jelly. Levofloxacin is an anti-bacterial drug. The main goal including enhanced potency against gram-positive cocci, streptococcus pneumoniae and anaerobes, while maintaining the potency against gram positive bacteria. The preparation of anti-bacterial ophthalmic ointment by using levofloxacin drug is evaluated by physical parameters, pH, spreadability, extrudability, viscosity. The in-vitro study is evaluated by Franz diffusion cell apparatus. The main objective of this formulation is to increase the stability, and prolonged action of ointment during the anti-bacterial infection in the eye and increase the patient compliance. It can be reasonably concluded that the levofloxacin ophthalmic ointment is better suited for prolonged release of levofloxacin.

Keywords – Levofloxacin, Ointment, Eye, In-vitro drug study

INTRODUCTION

Amongst several physiological barriers in human body such as blood brain barrier, placental barrier etc. the 'Corneal Barrier' is equally important. It protects the inner structure of our eye from external object and infection. However it creates a problem by preventing many drugs from entering inside the eye beyond cornea. This is problematic because the major microorganism invading the structure of an eye includes 'bacteria' and when this occurs, the antibacterial drugs are unable to penetrate cornea leaving the infection untreated. (1)

Levofloxacin is used in the eye to treat bacterial infection, Levofloxacin is a broad spectrum antibiotic which belongs to the third generation of quinolones group. It prevents DNA replication in bacteria leading to bacterial cell death. This drug is considered as an important antibiotic in case of microorganism that is resistant to other class of antibacterial agents such as beta-lactam antibiotics; hence, its quality is critical in effective treatment.(2)

Levofloxacin has high bioavailability with rapid bactericidal activity. The possible risk factors suggested for the treatment failure of levofloxacin are poor quality medicines and drug resistance. (3)

Techniques for Preparation of Ointment:

Levigation method :

Adding coarse particles that are insoluble, this is also referred to as "wet grinding". A molten liquid base, a liquid base, or a semisolid base is used to rub coarse powder. The shearing force must be considered to avoid grittiness. (4)

Fusion method :

In the fusion technique, drugs and other solids are dissolved in an ointment base and then combined. By melting the ingredient into the base, the soluble constituents are dissolved. After speculation or trituration, the congeal mixture is smoothed out. Fusion uses special techniques to ensure that the base and other components will not be damaged by thermal degradation.(4)

Objectives:

The main objective of this formulation is to improve ocular bioavailability as levofloxacin has 99% of bioavailability. To overcome the ocular drug delivery barriers. It also increases the consistency of for the prolonged action. This formulation provides better patient complaince.

Materials and method :

Levofloxacin was purchased from Rajesh chemical Mumbai,India. White petroleum jelly was purchased from veda oils, Mumbai, India. White bees wax, Methyl paraben, Propyl paraben (Research-lab fine chem Mumbai, India) Propylene glycol (S.D lab chemical), and all chemical were of analytical grade.

Preformulation study:

UV analysis :

Determination of wave length- Standard stock solution is prepared from stock solution appropriate dilution are prepared and λmax was determined. Absorption maxima (λmax) was found to be 288 nm. Calibration curve of Levofloxacin – From stock solution, dilution having concentration 2, 4, 6, 8, 10 & 12 µg/ml were prepared and absorbance was taken. Then calibration curve was plotted. (5)

Formulation of ophthalmic preparation:

Emulsion base :

Emulsion base was prepared with the help of fusion method. Petroleum jelly was melted at 75°c in a porcelin dish. Propylene glycol and water were mixed together in a beaker. Later, propyl paraben and methyl paraben were added to the porcelin dish containing petrolleum jelly, and the propylene glycol was poured in it. It was heated to 75°c untill the preparation was found to be uniformly mixed.

Oleaginous base :

The weighed quantity of white petrolleum jelly was mixed together with the white bees wax in porcelin dish. It was heated to 75°c untill it got uniformly mixed. Finally, formed a Oleaginous base.

Formulation table of ophthalmic ointment :

Serial no.	Ingredients	F1 batch	F2 batch	F3 batch	F4 batch
1	Levofloxacin	0.3	0.3	0.3	0.3
2	Emulsion Base	12	14	12	14
3	Oleaginous base	18	18	16	16

Table no. 1

Evaluation of ophthalmic preparation

1. Spreadability:-

The spreadability of ophthalmic formulation were determined by taking two glass slides and placed 0.5 g of ointment in the middle of one glass slide. After this second glass slide over on which a first glass plate was placed. A 500 g weight was put on the upper glass slides. After 30 seconds calculated and noted the spreadability of ointment. (6)

2. Extrudability:-

The opthalmic formulations was filled in the collapsible tubes after, Then initial weight of tube is taken and applied weight on the tube. Finally, the gel is extruded within 10 seconds and calculated the final weight of the tube. (6)

3. pH :

About 2.5 g of all formulations were taken in dry beaker and 50 ml of water was added. Beaker containing ointments was heated on water bath at 60–70°C. The pH of ointments determined using a pH meter. The determinations were carried out in triplicate and the averages of three readings were noted. (7)

4. In-vitro studies :

Franz diffusion cell was used for the drug release studies. Ointment was evenly applied onto the surface of egg membrane. The egg membrane was clamped between the donor and the receptor chamber of diffusion cell. The receptor compartment was filled with phosphate buffer pH 7.4, and the assembly was maintained under constant magnetic stirring. With reference to Scale-up and Post-approval Changes guidelines laid by FDA, 300 mg of ointment was applied to the membrane on the donor compartment and then covered with aluminum foil to prevent drying out. Aliquots were withdrawn at predetermined time intervals over a period of 1 h and amount of levofloxacin released was analyzed at 288 nm using UV spectrophotometer. (8,9,10)

5. Viscosity :

The viscosity of the opthalmic formulations were measured by using Brookfield Viscometer. Rotations of ointment are done at 0.3, 0.6 and 1.5 rotations per minute and at each speed, the corresponding dial reading was noted. The viscosity of the ointment was obtained by multiplication of the dial reading with factor given in the Brookfield Viscometer catalogue. (6,11)

6. Drug content of levofloxacin :

Drug Content of Levofloxacin in the formulation was determined by diluting 1 g of ointment equivalent to 2 mg of drug in 10 ml of ethanol and volume was made up to 100 ml with pH 7.4 phosphate buffer. Absorbance was measured at 288 nm using ultraviolet (UV)-visible spectrophotometer and percentage drug content was calculated and average of three determinations was note. (8)

7. Sterility test :

Sterility test was performed as per the compendial method. The effectiveness of sterilization was determined by direct inoculation of ophthalmic ointment in agar medium. Sufficient quantity of formulation was spread aseptically on agar medium.The inoculated media was incubated for 2 days at 25°C in case of agar media.While a clear and uncontaminated agar media indicates efficient sterilization.Effect of sterilization on all the characterization parameters was ascertained. (12)

8. Stability study :

The developed ointment formulations were subjected to stability study as per the International Conference on Harmonization (ICH) guidelines. The formulated ointment was filled in the collapsible tubes and stored at different temperatures and humidity conditions, namely, 25°C±2°C /60%±5% RH, 30°C±2°C /65%±5% RH, and 40°C±2°C /75%±5% RH for a period of 3 months and studied for appearance, pH, viscosity, and spreadability. (13,14)

Results and discussion:

1. Melting point :

The Levofloxacin melting point found between 214-216°Cwhile the standard melting point is 213-218°C.

2. Calibration curve : The obtained data of concentration and absorbance at 288nm showing in table 2.

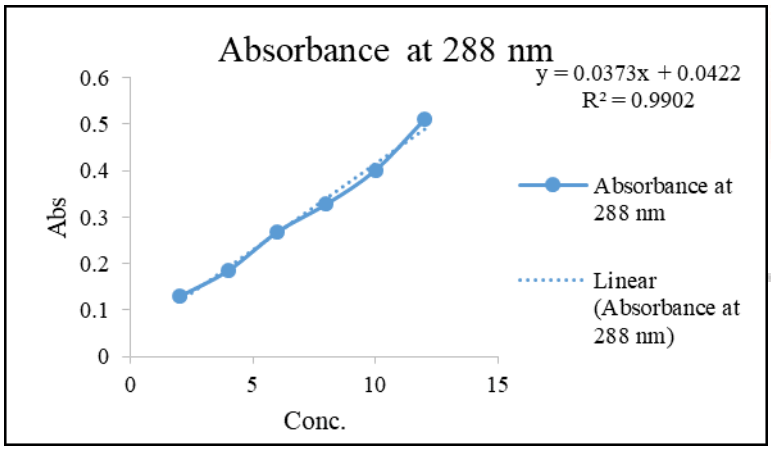

Figure no. 1

Sr. no	Concentration (µg/ml)	Absorbance (nm)
1	2	0.129
2	4	0.185
3	6	0.268
4	8	0.328
5	10	0.401
6	12	0.511

Table no.2

It was observed that the Levofloxacin obeyed the Beer-Lambert's law. The equation of calibration was obtained is : Y=0.0373x + 0.0422c

3. Spreadability, extrudabilty and pH :

Sr. No.	Batches	Spreadability (cm) ± SD	Extrudability (gm) ± SD	pH ± SD
1.	F-1	6.6 ± 0.21	3.24 ± 0.07	6.5 ± 0.08
2.	F-2	6.9 ± 0.26	3.58 ± 0.02	6.65 ± 0.09
3.	F-3	7.2 ± 0.35	4.31 ± 0.09	6.75 ± 0.2
4.	F-4	7.6 ± 0.15	4.60 ± 0.02	6.74 ± 0.08

Table no. 3

(A) The pH values of all prepared formulations F-1 to F-4 were found to be in the range of 6.5 to 6.75, which are considerable to be acceptable to avoid the risk of irritation or side effects if insert in the eye.

(B) The spreadability of F-1 to F-4 formulations found to be 6.6 to 7.6cm; indicating spreadability of formulations was good as compared to that of marketed brands spreadability value of ointments. F3 and F4 showed good spreadability.

(C) The values of extrudability of F-1 to F-4 batches found to be 3.24 to 4.60 gm ; in which F3 and F4 showed good extrudability.

4. Viscosity :

In the above table, the viscosity of F1 to F4 batches was found to be in the range of 4260 to 5490 Cp. The viscosity of F1 batch is 4260 which is minimum viscosity and F4 batch is 5490 which has highest viscosity. shown in table 4.

Sr. no.	Batches	Viscosity (cP)
1	F-1	4260
2	F-2	4362
3	F-3	5388
4	F-4	5490

Table no. 4

5. FTIR :

FTIR spectrum of levofloxacin :

The spectrum of Levofloxacin showed an intense, well defined peak, infrared band as shown in figure 2.

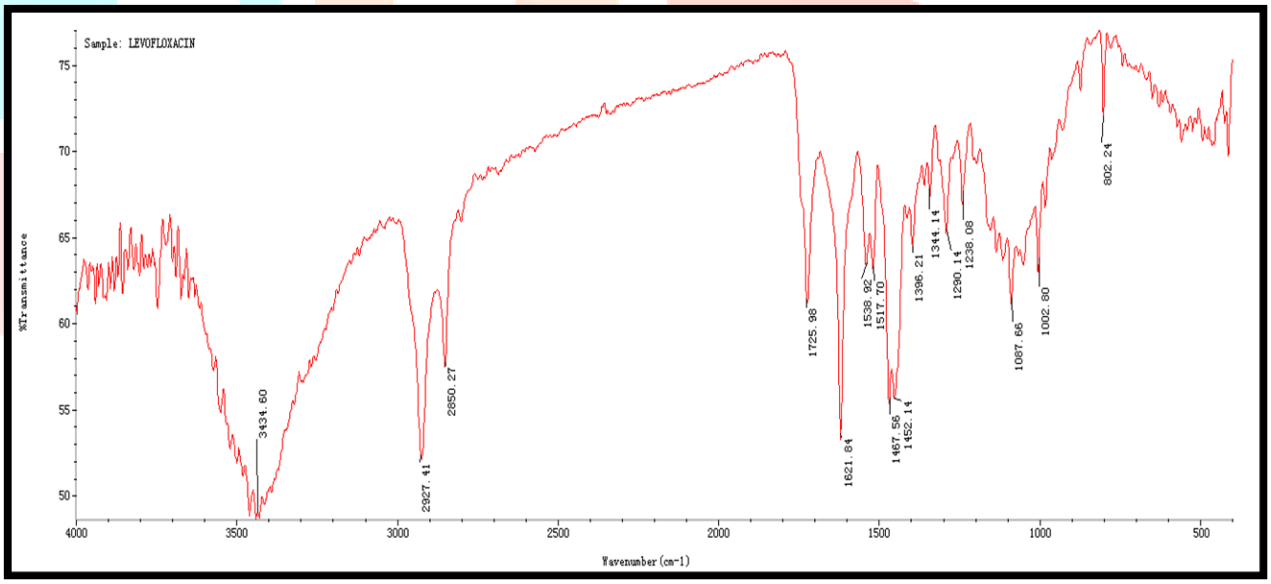

Figure no. 2

FTIR of petrolleum jelly :

The spectrum of White petroleum jelly showed an intense, well defined peak, infrared band as shown in figure 3.

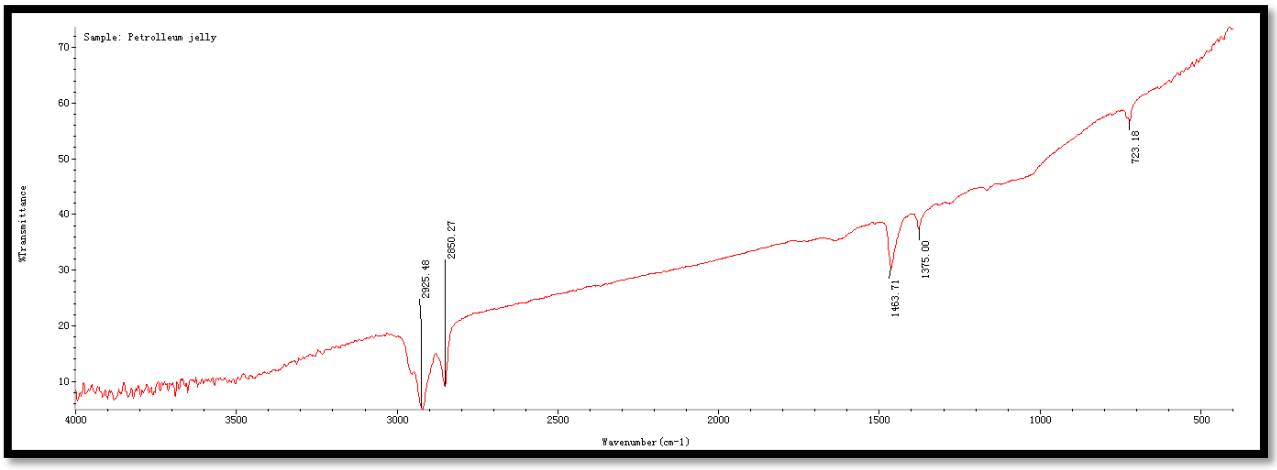

Figure no 3.

6. In-vitro Diffussion study :

In the in-vitro drug release study, the % drug release to be found by using Franz diffusion test apparatus. The formulations F2, F3 and F4 found to be maximum % drug release in the time intervals. The F4 batch found to be a maximum % drug release which releases the 81% of drug release as shown in figure 4.

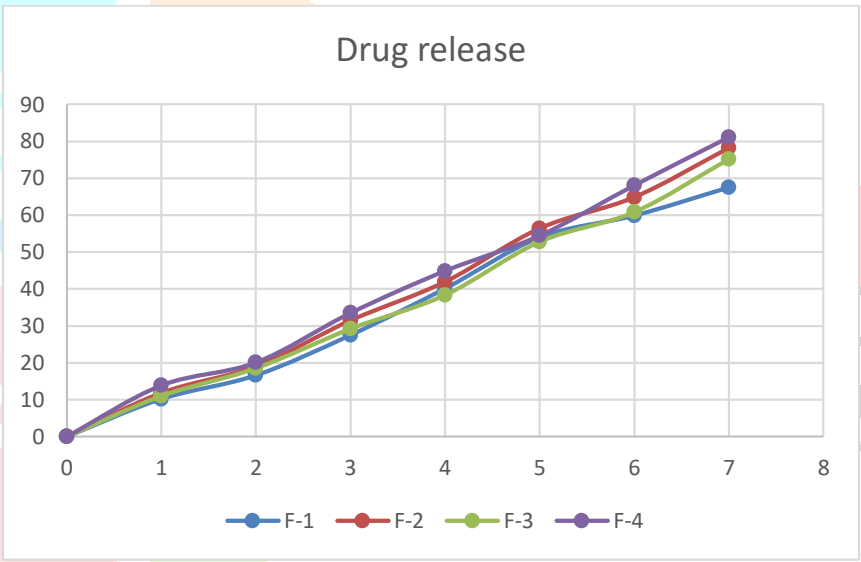

Figure no. 4

7. Drug content :

Ointment of levofloxacin was prepared by using different concentration of emulsion and oleaginous base out of which F4 batch shown good consistency, drug content in ointment was found to be 94.0%.

8. Sterility test :

A clear and uncontaminated agar media was found and it indicates efficient sterilization. Effect of sterilization on all the characterization parameters was ascertained and there was no significant changes, no turbidity was observed on the agar medium, implying absence of microbial growth, with consideration of observation from the sterility test, the developed formulation passed the test for sterility.

9. Stability :

The stability studie for optimized formulation were conducted at different temperatures and humidity conditions, namely, 25°C±2°C /60%±5% RH, 30°C±2°C /65%±5% RH, and 40°C±2°C /75%±5% RH for a period of 3 months and their was no remarkable difference in the physical properties which indicates that the optimized formulation displayed superior stability during evaluation.

10. Conclusion:

The levofloxacin ophthalmic ointment is formulated successfully by using emulsion base and oleaginous base. It can be concluded that the Levofloxacin ophthalmic ointment helps to increase the stability of drug. It also increases the consistency and prolonged period of action of the formulation. The F4 batch is optimized batch because it showed good spreadability and excrudability. It also release maximum % drug release that is 81%. The levofloxacin ophthalmic ointment has shown the good for ocular delivery, which helps for the better relief during the antibacterial infection for prolonged period of action and incresas the patient compliance.

Acknowledgements

The authors thank Satara college of pharmacy, satara for providing necessary facilities to carry out this research work.

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