



“FORMULATION AND EVALUATION OF LEVOFLOXACIN OCULAR EMULGEL”

Likitha B¹, F R Sheeba², Dr. Shivanand Mutta³, H S Keerthy⁴, Dr. Ashvini HM⁵

Research Student¹, Asso.prof.², HOD and Prof.³, Prof.⁴, Ast.prof.⁵

Dept. of Pharmaceutics¹, Dept. of Pharmaceutics², Dept. of Pharmaceutics³, Dept. of Pharmaceutics⁴, Dept. of Pharmaceutics⁵

Mallige College of Pharmacy¹, Mallige College of Pharmacy², Mallige College of Pharmacy³, Mallige College of Pharmacy⁴, Mallige College of Pharmacy⁵

#71 Silvepura, Chikkabanavara post,
Bangalore-560090. Karnataka, India.

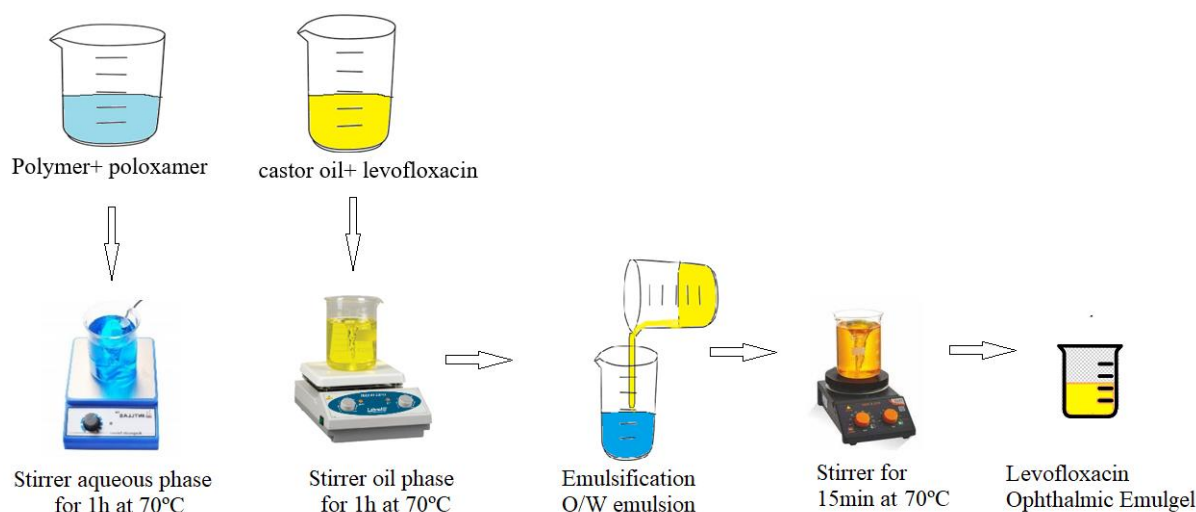
Abstract

The mixture of gels and emulsions leads to emulgels. Emulsions is an exact degree of elegance and is of course washed off whenever chosen, they take a high ability to penetrate the skin. Another necessary issue is to increase the drug release of even hydrophilic medicine by creating w/o emulgel. The project aims in preparing levofloxacin ocular emulgel to reduce instillation time, increase resident time in ocular tissues consequently improving patient compliance and thereby reducing bacterial infection. ⁽¹⁾

Emulgel is one among the new technologies in NDDS used locally having characteristics of double control release i.e., emulsion as well as a gel. Emulgels are convenient delivery systems because it incorporates a double release system i.e., gel and emulsion. Once gel and emulsion are employed in a combined type, it is stated as emulgels.

Index Terms: - Levofloxacin, Emulgel, emulsion, gel, Anti-bacterial, Xantham gum, methyl cellulose, sodium alginate

Graphical Abstract



Introduction

Emulgel is one among the new technologies in NDDS used locally having characteristics of double control release i.e., emulsion as well as a gel. Emulgels are convenient delivery systems because it incorporates a double release system i.e., gel and emulsion. Once gel and emulsion are employed in a combined type, it is stated as emulgel.

Emulgel is employed to treat aches and pains caused by colds, headaches, muscle aches, backaches, arthritis, and different conditions and injuries. The patient's adherence to topical formulations is critical concerning chronic skin diseases, like plant infections, acne, and psoriasis.^[1]

Topical drug administration could be a localized drug delivery system anyplace within the body through ophthalmic, rectal, vaginal, and skin as topical routes. These are applying a good spectrum of preparations for cosmetic and dermatologic, to their healthy or pathologic skin. These formulations place chemistry nature from solid through semisolid to liquid. Drug substances are hardly administered alone, however somewhat as a part of a formulation, together with one or a lot of non-medicated agents that serve a varied and specific pharmaceutical operation. medicine is administered local action at the situation of application or general effects^[2]. Drug absorption through the skin is increased if the drug substance is in solution, if it's a good lipid/water partition coefficient and if it's a nonelectrolyte. Drugs applied to the skin for local action include antiseptics, antifungal agents, skin emollients, and protectants. The most advantage of a topical delivery system is to bypass first-pass metabolism, avoidance of the risks and inconveniences of therapy and the numerous conditions of absorption like pH changes, presence of enzymes, and gastric emptying time are different benefits of topical preparations.^[3]

The rationale of emulgels as a new formulation:

Topical preparations like cream, and ointment have several limitations like less spreading constant, less penetration through stratum corneum, less patient compliance because of its viscosity or to apply with rubbing, etc. Similarly, gels have the limitation of carrying hydrophobic medication. Here emulgel is selected based on the term of solubility study of antimicrobial agent in them and emulsifier, therefore the solubility of the drug may be solubilized in emulgel, which might penetrate through stratum corneum for drug action at the viable soft tissue of the skin. As globules of the drug might penetrate the stratum corneum relatively larger extent may well be accessible for drug action, thus less dose of the drug might offer a lot of pharmacologic action. Moreover, choosing alternative excipients might assist pharmacologic action in one or in our way. Emulgel might offer edges of each emulsion and gel. Emulgel will increase drug deposition over to the skin. However, the emulsion has a lot of bioavailability than emulgel however there's the matter of stability and it is less patient compliance, as well. Hence Emulgel has numerous benefits over ointment and gels.^[4]

MATERIALS AND METHODS

Materials used

Drug and chemicals

Levofloxacin was obtained as a gift sample from Aarti drugs LTD, Mumbai. Sodium alginate, Methyl cellulose and Xanthan gum were procured from Yarrow chemicals, Karnataka. Other excipients and chemicals were procured from verified suppliers. All the solvents and reagents used were of analytical grade. Distilled water was used in throughout the experiments.

Pre formulation studies

Standard curve of Levofloxacin

Preparation of standard stock solution

The levofloxacin reference standard solution was prepared by accurately weighing 50mg of levofloxacin reference in a 50 ml of volumetric flask. Again, 10 ml of this solution was transferred to 100 ml volumetric flask. The standard stock solution was then serially diluted with pH7.4 saline phosphate buffer to get a concentration of 2, 4, 6, 8, 10 µg/ml of Levofloxacin at 298nm.

Drug excipient compatibility studies

Fourier transforms infrared (FT-IR) spectroscopy

The infrared spectra of levofloxacin and other excipients was recorded using FT-IR spectrophotometer. The IR spectra of physical matrix were compared with that of levofloxacin to check for any possible drug – excipients interaction.

FORMULATION OF LEVOFLOXACIN OCULAR EMULGEL

Procedure:

Emulgel is generally formulated in three steps which are:

- preparation of the emulsion phase,
- preparation of the gel phase, and
- mixing the two phases for the formation of the emulgel.

Preparation of O/W emulsion: Levofloxacin was dissolved in castor oil to form the oil phase and the aqueous phase was prepared by dissolving poloxamer 188 (as emulsifying agent), and benzalkonium chloride (as preservative) in distilled water. Both oil and aqueous phases were heated using hot plate magnetic stirrer to 70°C. After heating, the oil phase was dispersed in the aqueous phase with constant stirring at 1500 rpm until a homogenous emulsion was formed. Then, the emulsion was left to cool down at the room temperature.

Preparation of the gel phase: The gel phase was prepared by dissolving the gelling agent in iso-osmotic containing 3% glycerin solution. Different gelling agents were used at various concentrations for the preparation of the gel phase.

Preparation of emulgels: The final emulgel was prepared by mixing the emulsion and gel phase at 1:1 ratio with a high-speed mixer for 15 min at 1500 rpm until a smooth homogenous emulgel was formed.

Table 1: Formulation of Levofloxacin Ocular Emulgel

Sl.no.	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
01.	Levofloxacin (mg)	500	500	500	500	500	500	500	500	500
02.	Sodium alginate (mg)	500	-----	-----	750	-----	-----	1000	-----	-----
03.	Methyl cellulose (mg)	-----	500	-----	-----	750	-----	-----	1000	-----
04.	Xanthan gum (mg)	-----	-----	500	-----	-----	750	-----	-----	1000
05.	Castor oil (gm)	3	3	3	3	3	3	3	3	3
06.	Poloxamer (mg)	660	660	660	660	660	660	660	660	660
07.	Benzalkonium chloride(ml)	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
08.	Iso osmotic 3% glycerin (ml)	49	49	49	49	49	49	49	49	49
09.	Distilled Water up to	100ml	100ml	100ml	100ml	100ml	100ml	100ml	100ml	100ml

EVALUATION OF LEVOFLOXACIN OCULAR EMULGEL**Physical properties**

The physical properties of the prepared emulgel formulations such as color, homogeneity, consistency and phase separation were examined.

pH determination

The pH was determined using pH-meter by positioning the tip of the electrode into the emulgel and after (2 min) the result was recorded.

Rheological study

The viscosity of the prepared emulgels was determined using Brookfield viscometer (Brookfield LV, spindle no. 64). A glass container was filled with emulgel sample, and the spindle of the viscometer was allowed to rotate at predetermined speeds (5, 10, 20, 30, 50, 60, and 100 rpm) and recorded the viscosity.

Drug content determination

One gram of emulgel sample was dispersed in 100 ml phosphate saline pH 7.4 and sonicated for 2 h. The sonicated mixture was filtrated using 0.45 µm Millipore filter and analyzed using UV at 298nm.

Swelling Index:

For determination of swelling index of formulated emulgel following procedure adopted, 1 gm of the gel is taken on porous aluminum foil and then placed separately in a beaker of 50 ml containing 10 ml of 0.1 N NaOH. Then samples were taken from beakers at different time points and put it on a dry place for some time after it reweighed. Swelling index is calculated as follows:

$$\% \text{Swelling Index (SW)} = [(W_t - W_o) / W_o] \times 100.$$

Where,

W_o = Original weight of emulgel at zero time after time t,

W_t = Weight of swollen emulgel

Spreadability:

Spreadability is determined by apparatus suggested by Multimer et al (1956) which is suitably modified in the laboratory and used for the study. It consists of a wooden block, which is provided by a pulley at one end. By this method, spreadability is measured on the basis of 'Slip' and 'Drag' characteristics of emulgels. A ground glass slide is fixed on this block. An excess of emulgel (about 2 gm) under study is placed on this ground slide. The emulgel is then sandwiched between this slide and another glass slide having the dimension of fixed ground slide and provided with the hook. A 1 Kg weight is placed on the top of the two slides for 5 minutes to expel air and to provide a uniform film of the emulgel between the slides. Excess of the emulgel is scrapped off from the edges. The top plate is then subjected to pull of 80 grams. With the help of string attached to the hook and the time (in seconds) required by the top slide to cover a distance of 7.5 cm be noted. A shorter interval indicates better

$$S = M.L/T$$

Where,

S = spreadability,

M = Weight tied to upper slide,

L = Length of glass slides

T = Time taken to separate the slides completely from each other.

Centrifugation study:

This method is used to determine the stability of emulgel. It is done only after one week of preparation. This study was done by using minicentrifuge at 3000 rpm for 30 minutes.

Antibacterial activity

In -vitro antibacterial activity of the optimum formula was carried out by using Muller Hinton agar plate, which was prepared by dispersing 28 g of powder in 1 l of deionized water, swirl to mix and sterilized by autoclaving at 15 lbs. pressure (121°C) for 15 min

then cool it to 47°C, then the medium was poured in sterile plates under a septic condition and was allowed to solidify at the room temperature. Two different types of bacteria were tested; *Escherichia coli* and *Staphylococcus aureus*. Accurately 0.1 mL bacterial suspension having a uniform turbidity (106 CFU/mL) was distributed gently over the surface of the medium with a sterile glass spreader. The wells were made aseptically with cork borer having 6 mm diameter. In each of these plates, sufficient quantity of the optimum formula and levofloxacin ocular emulgel were placed in the pore with the help of syringe, and then the plates were incubated at 37°C for 24 h. The diameters of the inhibition zones were measured in millimeters.

In Vitro Release Study:

Franz diffusion cell (with effective diffusion area 3.14 cm² and 15.5 ml cell volume) was used for the drug release studies. Emulgel (200 mg) was applied onto the surface of egg membrane evenly. The egg membrane was clamped between the donor and the receptor chamber of diffusion cell. The receptor chamber was filled with freshly prepared PBS (pH 5.5) solution to solubilize the drug. The receptor chamber was stirred by magnetic stirrer. The samples (1.0 ml aliquots) were collected at suitable time interval. Samples were analysed for drug content by UV visible Spectrophotometer after appropriate dilutions. Cumulative corrections were made to obtain the total amount of drug release at each time interval. The cumulative amount of drug released across the egg membrane was determined as a function of time.

Stability Studies:

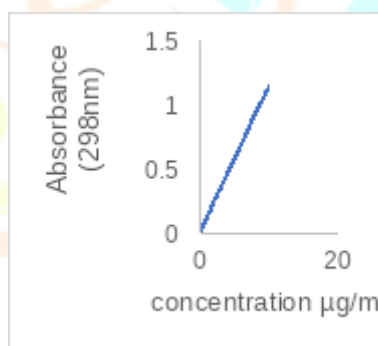
The formulation was kept for 3 months at room temperature and checked for its pH, spreadability, swelling index, drug content and *in-vitro* drug release for 2 hours. The results have showed negligible changes in the parameters of F3 after 3 months of storage

RESULTS AND DISCUSSION

The λ_{max} of Levofloxacin in 7.4pH phosphate buffer was found to be 298nm. The absorbance values are tabulated in the table. Levofloxacin obeyed Beer Lamberts law in the concentration range of 2-20 µg/ml.

Table 2: Absorbance of Levofloxacin

Concentration (µg/ml)	Absorbance (298nm)
0	0.00
2	0.24
4	0.46
6	0.68
8	0.92
10	1.12

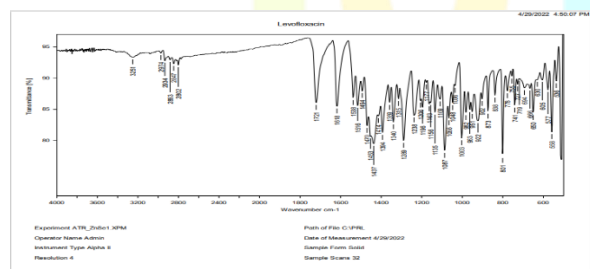


Graph 1: Standard curve of levofloxacin

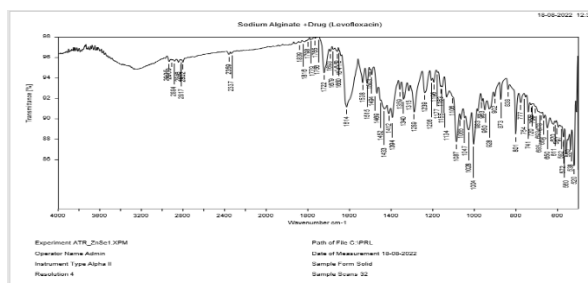
DRUG-EXCIPIENTS COMPATIBILITY STUDIES:

FT-IR Spectroscopy

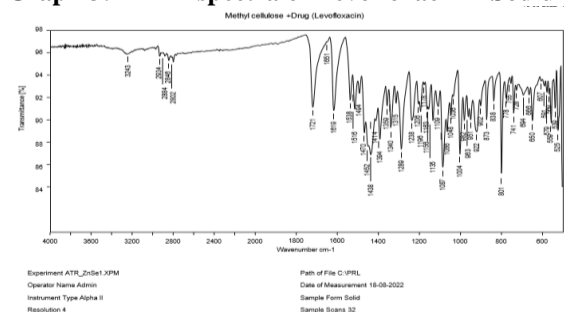
FTIR was performed to detect the possible interaction between levofloxacin and other components of emulgel formulation (Xanthan gum, methyl cellulose, sodium alginate), FTIR spectra for levofloxacin showed peak at 3251 cm which is assigned to C=C stretching in aromatic rings. The important absorption peak at 1538 cm is attributed to C-N stretching in tertiary amines. The corresponding peak at 1619cm is observed for C=O stretching in carboxylic acid. The peak at 873 was attributed to C-H stretching vibration in alkane. The peaks at 1725-1700cm are assigned to C=O stretching in primary alcohol. The FT-IR spectrum of film containing levofloxacin with optimized formulation. There are no peaks generated and no significant peaks shift are observed although there might be possible interaction between drug and polymer components.



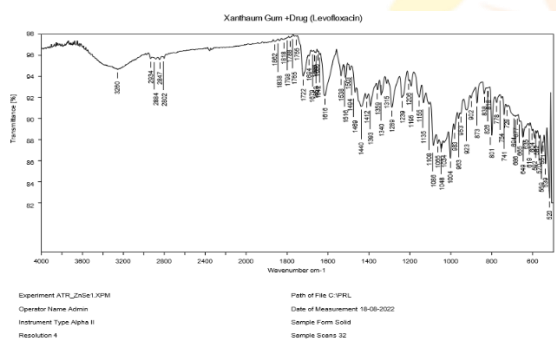
Graph 2: FTIR spectra of Levofloxacin



Graph 3: FT-IR spectra of Levofloxacin + Sodium alginate



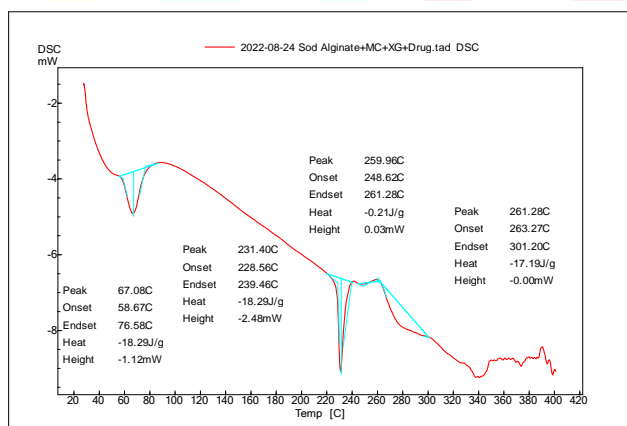
Graph 4: FT-IR spectra of Levofloxacin + Methyl Cellulose



Graph 5: FT-IR spectra of Levofloxacin + Xanthan Gum

DSC Analysis:

Thermal behavior of the drug, sodium alginate, methyl cellulose, Xanthan gum were studied with the help of DSC. The thermograms obtained are shown in graph 7. Drug has shown sharp endothermic peak at 259.96°C. Corresponding to its melting point. The methyl cellulose and Xanthan gum has shown sharp endothermic peak near 259.96°C-301.20°C. Therefore, Levofloxacin appeared in the physical mixture indicating that there was no possible interaction between the drug and the excipients in the ocular emulgel formulation.



Graph 6: DSC Thermogram of levofloxacin + sodium alginate + methyl cellulose + Xanthan gum

Table 3: Data for pH, Spreadability, Centrifugation and Viscosity

Formulation code	pH	Spreadability cm	Centrifugation	Viscosity CPS	Swelling index
F1	6.81±0.09	7.3±0.03	No separation	21,456±1.6	69.3±0.01%
F2	6.41±0.04	8.2±0.06	No separation	24,576±1.7	64.4±0.02%
F3	6.91±0.03	6.7±0.03	No separation	19,456±1.2	63.7±0.01%
F4	6.75±0.06	7.6±0.03	No separation	22,746±1.3	68.1±0.02%
F5	6.32±0.08	7.9±0.01	No separation	21,776±1.4	65.3±0.01%
F6	6.72±0.03	6.8±0.03	No separation	19,976±1.5	62.9±0.02%
F7	6.73±0.05	7.8±0.02	No separation	23,456±1.7	69.5±0.01%
F8	6.52±0.04	8.3±0.03	No separation	21,786±1.3	65.9±0.02%
F9	6.81±0.06	7.1±0.03	No separation	19,786±1.4	63.6±0.02%

- **pH**

The pH of all the formulated ocular emulgel exhibited uniformity in their values and were found to be between 6.32 ± 0.04 to 6.91 ± 0.01 . Hence no ocular irritation was expected and ultimately achieved patient compliance.

- **Spreadability:**

The spreadability of all the formulations of ocular emulgel exhibited uniformity and was found to be between 7.1 ± 0.1 to 8.3 ± 0.1 cm indicating its results in Table 03.

- **Centrifugation:**

The centrifugation was carried out for all the formulation and there was no separation for the duration of 10 minutes when it was kept in centrifuge. The centrifugation results are shown in Table 03.

- **Rheological studies:**

The viscosity of the formulated ocular emulgel was between $19,456 \pm 1.2$ to $24,576 \pm 1.7$ and the results was shown in Table 03

- **Swelling index:**

Swelling ratio of the levofloxacin ocular emulgel of all the formulation is shown in Table3, swelling ratio of each emulgel formulation was measured until emulgel was degraded. After determination the swell on the 0.1N NaOH at different time points. Swelling index of formulations ranges from 62.9% to 69.3%. Formulation F1 had highest swelling index (69.3%) and F6 had lowest value (62.9%)

- **Antibacterial activity:**

The antibacterial activity of all the formulation was carried out using E-coli bacteria and zone of inhibition was measured. Antimicrobial efficacy study was performed on formulations using Gram -ve E. coli organism. Clear zones showing inhibited zone of growth were observed and showed in Fig 1. The zones of inhibition of the formulations were shown in the Table 4. The study indicated levofloxacin retained its antimicrobial activity when formulated as gel against E. coli.

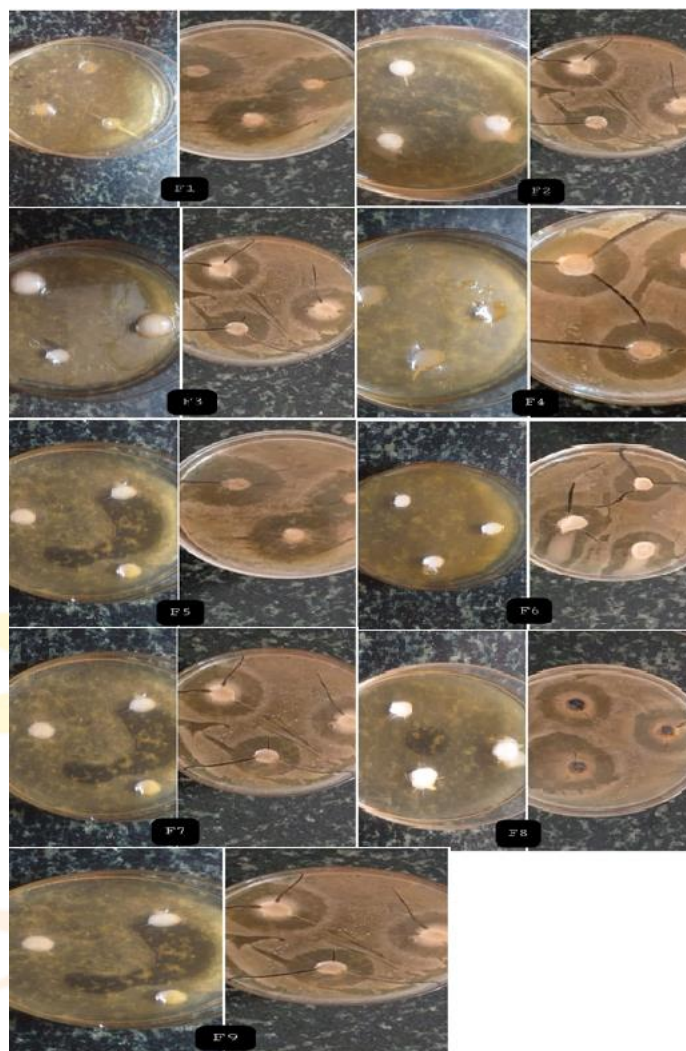


Fig. 1: Zone of inhibition against E-coli bacteria of formulation F1-F9

Table 4: Data for Antibacterial activity

Formulations	Zone of inhibition in diameter
F1	20mm
F2	19mm
F3	20mm
F4	16mm
F5	14mm
F6	14mm
F7	14mm
F8	18mm
F9	20mm

Drug content

Drug content uniformity study data is shown in Table12. The content uniformity for all the formulation prepared by using different concentration of Xanthan gum, methyl cellulose, sodium alginate was found to be 81.1% to 92.1% which showed that there was uniform distribution of the drug in emulgel.

Table 5: Data for drug content

FORMULATION	DRUG CONTENT
F1	81.1%
F2	91.8%
F3	90.3%
F4	89.3%

F5	83.8%
F6	82.8%
F7	91.3%
F8	92.1%
F9	91.7%

In-vivo permeation studies:

The drug diffusion profiles of all the formulation were fitted into various kinetic model such as zero order, first order, Higuchi model, korsmeyer- peppas model equation. From the results it was evident that all the formulations were more linear towards peppas models with R²value ranging from 0.7-0.9 indicating the drug release mechanism is by diffusion as given in the table 6.

Table 6: Data for Percentage cumulative drug release

Time in min	PERCENTAGE CUMULATIVE DRUG RELEASE								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
15	13%	9%	8.91%	12.70%	14%	13.10%	9.6%	14.71%	13%
30	22.25%	20.15%	13.39%	25.21%	25.65%	33.33%	31.69%	24.43%	26.39%
45	24.75%	29.30%	32.44%	39.97%	38.90%	43.90%	43.31%	38.53%	38.03%
60	35.39%	35.51%	45.84%	48.37%	60.85%	50.66%	53.64%	50.84%	46.65%
75	47.92%	44.55%	54.67%	63.65%	79.39%	62.07%	65.89%	62.36%	58.89%
90	67.57%	53.59%	65.31%	73.87%	86.99%	70.02%	79.09%	74.89%	74.34%
105	81.45%	68.82%	82.05%	87.02%	95.34%	78.71%	87.49%	78.39%	77.85%
120	93.75%	78.91%	94.01%	98.2%	98.92%	85.08%	94.13%	82.65%	81.17%

CONCLUSION

The ocular emulgel of levofloxacin were prepared using various polymers such as methyl cellulose, xanthan gum, sodium alginate. A total of nine different formulations were prepared. The following conclusions can be drawn from the results obtained.

The FT-IR studies revealed that there was no chemical interaction of pure drug (Levofloxacin) with the polymers and excipients. The Pre-formulation parameters like melting point, λ_{max} , standard curve of all the formulations were found to be within the standard limits. The Post-formulation parameters like pH, spreadability, centrifugation, swelling index, viscosity, drug content, anti-bacterial activity of all the formulations were within the standard limits of official books.

The formulation F3 selected for stability studies on the basis of their better and satisfactory evaluation studies parameter. Results showed there was no

t much variation in physical parameters even after the period of 90 days.

From the results obtained it was concluded that, formulations F3 containing Xanthan gum ratio 1:1 is found to be stable and retained their original properties during their study period.

Hence, this study demonstrates that levofloxacin emulgels has excellent potential for ocular bacterial infection and suitable for the reduce instillation time and increase resident time.

ACKNOWLEDGMENT

The authors thank Aarthi pharmaceuticals for a gift sample of levofloxacin. Authors also thank Mallige college of pharmacy, Bangalore for providing all other ingredients and the required infrastructure for conducting this research work.

BIBLIOGRAPHY

1. Sabry HS, Al-Shohani AD, Mahmood SZ. Formulation and evaluation of levofloxacin and betamethasone ophthalmic emulgel. Int J Pharm Biol Sci. 2021;13(2):205-09
2. Nair AB, Shah J, Jacob S, Al-Dhubiab BE, Sreeharsha N, Morsy MA, Gupta S, Attimarad M, Shinu P, Venugopala KN. Experimental design, formulation and in vivoss evaluation of a novel topical *in situ* gel system to treat ocular infections. PloS one. 2021 ;16(3): 1 - 18
3. Sreevidya V.S an Overview on Emulgel. Int. J. 2019;9(1):92-7
4. Prasanth VV, Ranjan S. Formulation and evaluation of *in-situ* ocular gel of levofloxacin. J Drug Deliv Sci Technol 2017;7(5):68-73.

5. Pujitha C, Jyothi JS, Sucharitha J, Lakshmi GN, Rao AL. Formulation and characterization of ofloxacin ophthalmic gel. Indian J. Pharm Pharm 2017;4(2):105-109
6. Kalpesh Ashara, Moninuddin M. Soniwala Ketan Shan Emulgel: A novel drug delivery system. J. Pakistan Assoc. Dermatologists 2016 Ashara K, Soniwala M, Shah K. Emulgel: A novel drug delivery system. J. Pakistan Asso. 2017 29;26(3):244-49.
7. Jul Makwana SB, Patel VA, Parmar SJ. Development and characterization of *in-situ* gel for ophthalmic formulation containing ciprofloxacin hydrochloride. Res pharm sci. 2016 1;(6):1-6.
8. Gadad AP, Wadkar PD, Dandghi P, Patil A. Thermosensitive *in-situ* gel for ocular delivery of lomefloxacin. Indian J Pharm Edu Res. 2016 1;50(2):96-105.
9. Shen Y, Ling X, Jiang W, Du S, Lu Y, Tu J. Formulation and evaluation of Cyclosporin A emulgel for ocular delivery. Drug delivery. 2015, 22(7):911-7.
10. Snehal P. Mulye, Kiran A. Wadka, Manish S. Kondawar Formulation development and evaluation of Indomethacin emulgel. Der Pharmacia Sinica 2013, 4(5):31-45
11. Nagesh C, Venkatesh JS, Raj SM, Rabadia J, Patil S, Shankraiah M. Intragastric floating drug delivery system of Levofloxacin Formulation and Evaluation. J Pharm Res. 2011,3(6):1265-72.
12. Bhavanam PR, Lekkala VK, Maddirala P, Reddy SN, Krishna AS, Rajesh CH. Formulation and evaluation of levofloxacin using different types and concentrations of superdisintegrants. Res. J Pharm Res. 2010,2(5):308-12
13. Kumar D, Singh J, Antil M, Kumar V. Emulgel-novel topical drug delivery system-a comprehensive review. Int J Pharm sci res. 2016;7(12):4733.
14. Panwar A, Upadhyay N, Bairagi M, Gujar S, Darwhekar G, Jain D. Emulgel: a review. Asian J Pharm Life Sci. 2011 (13); 2231:45.
15. Shehata TM, Nair AB, Al-Dhubiab BE, Shah J, Jacob S, Alhaider IA, Attimarad M, Elsewedy HS, Ibrahim MM. Vesicular emulgel based system for transdermal delivery of insulin: Factorial design and *in vivo* evaluation. Applied Sci. 2020 (15):5341-56.
16. Khan BA, Ullah S, Khan MK, Alshahrani SM, Braga VA. Formulation and evaluation of Ocimum basilicum-based emulgel for wound healing using an animal model. Saudi Pharm J. 2020 ;28(12):1842-50.
17. Burki IK, Khan MK, Khan BA, Uzair B, Braga VA, Jamil QA. Formulation development, characterization, and evaluation of a novel dexibuprofen-capsaicin skin emulgel with improved *in vivo* anti-inflammatory and analgesic effects. AAPS Pharm Sci Tech. 2020 21(6):1-4.
18. Nour El-Din HT, Elhosseiny NM, El-Gendy MA, Mahmoud AA, Hussein MM, Attia AS. A rapid lysostaphin production approach and a convenient novel lysostaphin loaded nano-emulgel; As a sustainable low-cost methicillin-resistant *Staphylococcus aureus* combating platform. Biomolecules. 2020 10(3):435-36.
19. Khan J, Norfarhani S, Sahu RK, Ruhi S, Kaleemullah M, Al-Dhali S, Yusuf E. Development and Evaluation of topical Emulgel of Aspirin using different Polymeric Bases. Res. J. Pharm. Tech. 2020 13(12):6300-4.
20. Siddiqui B, Rehman AU, Haq IU, Ahmad NM, Ahmed N. Development, optimization, and evaluation of nano encapsulated diacerein emulgel for potential use in osteoarthritis. J.microencapsul. 2020;37(8):595-608.