ejpmr, 2019,6(10), 444-453

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

FORMULATION AND EVALUATION OF BIOADHESIVE OFLOXACIN HYDROCHLORIDE NIOSOMAL DISPERSION FOR EYE INFECTION

Sheik Rishan*[1], Dr. Krishnananda Kamath K.[2] and Dr. A. R. Shabaraya[3]

[1]Research Scholar, M. Pharm. (Pharmaceutics), Srinivas College of Pharmacy, Valachil, Mangalore, Karnataka, India.
[2]Professor, Department of (Pharmaceutics), Srinivas College of Pharmacy, Valachil, Mangalore, Karnataka, India.
[3]Principal, HOD, Department of (Pharmaceutics), Srinivas College of Pharmacy, Valachil, Mangalore, Karnataka, India.

***Corresponding Author: Sheik Rishan**

Research Scholar, M. Pharm. (Pharmaceutics), Srinivas College of Pharmacy, Valachil, Mangalore, Karnataka, India.

Article Received on 12/08/2019 **Article Revised on 31/08/2019** **Article Accepted on 21/09/2019**

ABSTRACT

Ocular drug delivery is a very challenging task faced by pharmaceutical scientists, inspite of the fact that eye is the most sensitive and accessible organ for the delivery of drugs. A major disadvantage associated with conventional dosage form is its low bioavailability, that is less than 10%. To improve the bioavailability, viscosity-enhancing agents or mucoadhesive polymers are used for treating severe ocular diseases. These polymers play an important role in increasing the precorneal residence of drug at ocular site. Ofloxacin eye drops were frequently used for the treatment of infectious eye. However, such formulations have a major drawback, that is short duration of action and usually require 4-6 times instillation daily. A bioadhesive polymer coated niosomal formulation of Ofloxacin was supposed to show a longer retention time on eyes and subsequent reduction in dosing frequency. The current study revealed that bioadhesive niosomal formulations enhances the ocular retention time and have sustained drug release into the eye.

INTRODUCTION

Eye is a complex organ with unique anatomy and physiology having various protective barriers that prevent the administered drugs from penetrating into the target tissues. Ocular drug delivery is a very challenging task faced by pharmaceutical scientists, inspite of the fact that eye is the most sensitive and accessible organ for the delivery of drugs. A major disadvantage associated with conventional dosage form is its low bioavailability, i.e. less than 10%. To improve the bioavailability, viscosity-enhancing agents or mucoadhesive polymers are used for treating severe ocular diseases. These polymers play an important role in increasing the precorneal residence of drug at ocular site.[1]

Niosomes (non-toxic surfactant vesicles) are microscopic lamellar structure. They are formed on addition of non toxic surfactant of the alkyl or dialkyl polyglycerol ether class and cholesterol followed by the subsequent hydration in aqueous media.[2]

Ofloxacin Hydrochloride is a second generation synthetic flouroquinolone derivative used for wide variety of ocular infections. Used either alone or combination. Mechanism of activity is interference with DNA gyrase, an enzyme essential for the replication of bacterial DNA. Ofloxacin niosomes and particularly niosomes coated with bioadhesive material can leads to a steady and sustained release of drug into ocular cavity without being washed away frequently and could overcome the retention problem of conventional eye drops. The increase in the retention time of the formulations leads to increase in transcorneal permeation of the drug and bioavailability.[3]

METHODOLOGY

Drug- Excipient Compatibility Studies by IR Spectrophotometric Analysis

The compatibility of drug with polymer was evaluated using FT-IR peak matching method. The sample was prepared by triturating 100 mg each of drug, Cholesterol, Span 60, HPMC 3CPS with approximately 300 mg of dry finely powdered potassium bromide. The resultant mixture was mounted on a suitable holder in the IR spectrophotometer. The spectrum was scanned in the wavelength range of 400-4000 cm-1. The spectrum obtained was analysed for drug-excipient compatibility.

Preparation of Ofloxacin Hydrochloride IP Niosomes Solvent Injection Method[4]

Weighed accurately the required quantity of Span 60 and Cholesterol as per table and dissolved in 5ml of chloroform. The required quantity of drug was then dissolved in the above lipid solution. The resultant solution was then taken in a 5 ml syringe and injected slowly into a beaker containing measured amount of ATF pH 7.4 maintained at 60-700 C with continuous stirring until the chloroform got evaporated. Stirring was

continued for 1hour at room temperature. The resultant solution was placed in a bath sonicator for 10min.

Table 1: Formulation Chart of Ofloxacin hydrochloride noisome.

Formulation code	Drug (mg)	Span 60 (mg)	Cholesterol (mg)	Chloroform (ml)	ATF pH 7.4 (ml)
F1	40	25	75	5	17.5
F2	40	35	65	5	17.5
F3	40	45	55	5	17.5
F4	40	50	50	5	17.5
F5	40	55	45	5	17.5
F6	40	65	35	5	17.5

Entrapment efficiency[5]

Determined by Centrifugation Method

The prepared niosomal suspension was taken in a centrifugation tube and centrifuged at 13000rpm for 30 minutes. The supernatant liquid was separated and the sediment was collected. Add 10 ml of isopropyl alcohol. Set aside for 30 minutes. Sufficient dilution was made with ATF, absorbance was measured using UV-Visible spectrophotometer. Niosomes prepared without drug was centrifuged in same manner and the same procedure was done and taken as blank. Entrapment efficiency was expressed as percentage of total drug entrapped.

$$Percentage\ entrapment = \frac{C}{T}100$$

T--------- Amount for drug added.

C--------- Amount of drug present in the supernatant.

Drug Content Estimation[6]

The prepared niosome was thoroughly mixed and pipette out 10ml of the niosomal dispersion. To that add 10ml of isopropyl alcohol and set aside for 30 minutes. Filter and sufficient dilutions were made with ATF, the absorbance were measured using UV visible spectrometer.

Coating of Niosome with Bioadhesive Polymer

The weighed quantity of polymer (HPMC 3CPS) as per table was dissolved in 2.5 ml of ATF. The resultant solution was slowly added to the prepared niosomal dispersion (formulation F4) and continued the stirring for 1 hour using a magnetic stirrer at room temperature.

Table 2: Composition of the coated niosomal formulations.

Formulation Code	Niosomal Dispersion (ml)	HPMC(3CPS) (mg)	ATF pH7.4 (ml)
FC 1	17.5	40	2.5
FC2	17.5	80	2.5
FC3	17.5	120	2.5

EVALUATION OF BIOADHESIVE NIOSOMAL FORMULATIONS

Drug Content Estimation of Coated Niosomes[6]

The prepared coated niosomes was thoroughly mixed and pipette out 10ml of the niosomal dispersion. To that add 10ml of isopropyl alcohol and set aside for 30 minutes. Filter and sufficient dilutions were made with ATF, the absorbance were measured using UV visible spectrometer.

***In vitro* drug release study[6]**

The *in vitro* drug release studies of Ofloxacin Hydrochloride from niosomes were carried out using membrane diffusion technique.

The cellophane membrane was hydrated with ATF for 12 hour before being fastened between the donor and the receptor compartment. The donor medium consisted of 1 ml of the bioadhesive niosomal formulation equivalent to 2000µg of Ofloxacin Hydrochloride and the receptor compartment was filled with 40 ml ATF. The receptor media was occasionally stirred. The temperature was maintained at 37±0.5^{0}C. 2.5ml of aliquot samples were withdrawn at different time intervals using a syringe filter and immediately replaced with an equal volume of fresh ATF maintained at 37±0.5^{0}C. The samples were analyzed for drug content by UV visible spectrophotometer after suitable dilutions. Similar procedure was done for marketed formulation of Ofloxacin Hydrochloride eye drop, Oflox 0.3% (B.No: AI00945, Cipla Ltd India). The cumulative amount of drug released across the cellophane membrane was determined as a function of time and compared the release kinetics.

***In vitro* Bioadhesion testing[7]**

The bioadhesive potential of the prepared bioadhesive niosomes was evaluated by method reported by Bachhav and Patravale, 2009. Test was done in an agar plate (1% w/w), prepared in ATF pH 7.4.

Preparation of Dye Entrapped Niosomes: Desired quantity of Span 60 and Cholesterol was dissolved in 5 ml of chloroform and add 50mg of Sudan III. This solution was then taken in a 5ml syringe and injected slowly into a beaker containing 17.5 ml of ATF pH 7.4

maintained at 60-70^0 C with continues stirring until the Chloroform got evaporated. Stirring was continued for 1 hour at room temperature. Coating is done with 2.5ml of HPMC 3CPS solution.

1ml of the prepared niosomal formulation with dye (Sudan III) was placed in the center of the agar plate. It was set aside for 5 minutes. Then the plate was attached to a disintegration test apparatus and moved up and down in ATF at 37±0.5^0 C. The residence time of the test samples on the plate was noted by visual appearance of the formulation over the plate.

Zetapotential[8]

The optimized niosomal dispersions were characterized for zeta potential and average size distribution by zeta sizer, dynamic light scattering technology.

Antimicrobial assay[9,10]

Antimicrobial assay was done in Gram negative bacteria. E.coli was selected as Gram negative bacteria. Test tubes and petridishes were sterilized in hot air oven at 170^0 C for 1 hour. Fresh nutrient agar media and nutrient broth media was prepared and sterilized in an autoclave at 121^0 C for 20 minutes. The Bacteria were sub cultured to the sterilized broth media and incubated for 24 hour at 37±0.5^{0}C. The sub cultured broth media was transferred to the nutrient agar media. 75 ml of the above agar media was poured into each petridish. Agar plate was placed in a refrigerator for solidify the plate. Small wells were made in each plate with an insulin syringe. Each plate contains 4 wells of 1cm diameter. 50 µL antibiotic formulations was introduced into each well using a micropipette and refrigerated for 1hour at 4-8^0 C. The plate was incubated for 24 hour at 37±0.5^0 C and zone of inhibition was measured.

Vesicle morphology[11,12]

The optimized niosome formulation was observed for its vesicle morphology using scanning electron microscope (Hitachi FESUM SU6600).

Drug release kinetics of the Bioadhesive Niosome[13,14,15]

To describe the kinetics of the drug release from the bioadhesive niosomal formulation, mathematical model such as zero order, first order, Higuchi, Korsmeyer-Peppas models were used. The criterion for selecting the most appropriate model was chosen on the basis of the goodness or fit test.

RESULTS AND DISCUSSION

Drug- Excipient Compatibility Studies

Table 4: FT–IR spectroscopic peaks obtained in pure drug (Ofloxacin Hydrochloride) and drug excipient mixture.

Pure drug (Cm^{-1})	Drug excipient mixture (Cm^{-1})	Characterization
1621.4	1621.4	aromatic C=C stretching
1513.3	1517.0	aromatic C=C stretching
874	834.9	C–H bending for substituted benzene
1703.4	1707.1	carboxylic acid C=O stretching
1185.3	1185.8	stretching of monofluorobenzene

The drug polymer compatibility study was carried out by FT-IR spectroscopy. The spectrum obtained from the physical mixture of Ofloxacin Hydrochloride, Cholesterol, Span 60 and HPMC 3CPS was compared with that of pure drug. All the major peaks present in the spectrum of pure drug was clearly observed in the spectrum of physical mixture of drug and polymer with negligible changes. This clearly suggested the absence of any drug polymer incompatibilities.

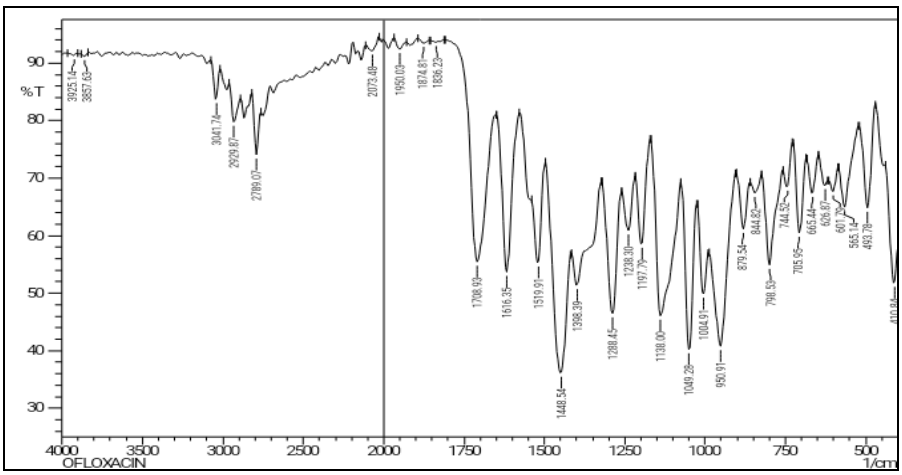

Figure 1: FT-IR Spectrum of Ofloxacin Hydrochloride.

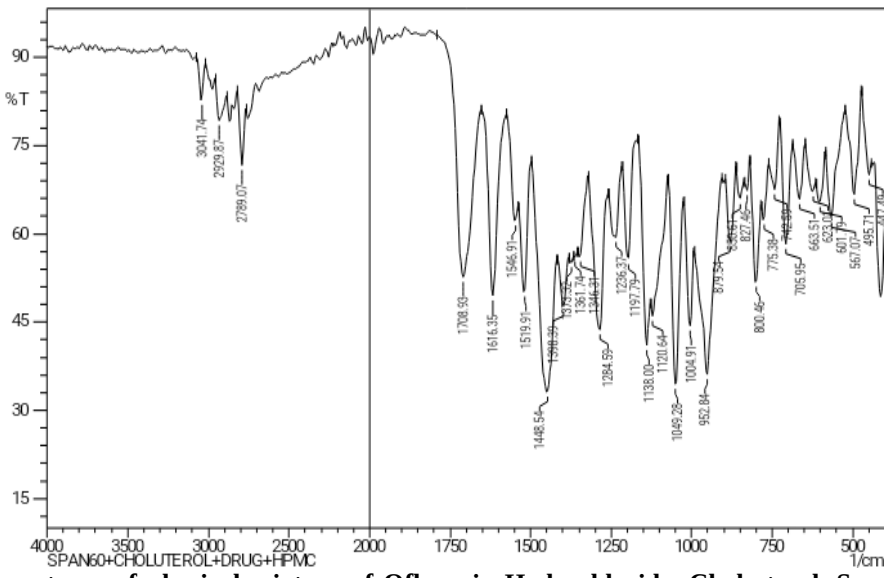

Figure 2: FT-IR spectrum of physical mixture of Ofloxacin Hydrochloride, Cholesterol, Span 60 and HPMC 3CPS.

Entrapment efficiency

Determined by centrifugation method

The percentage entrapment efficiency of various batches of Ofloxacin Hydrochloride niosomes were shown in table 5.

Table 5: Percentage Entrapment Efficiency of Niosomal Formulations.

Formulation Code	Percentage entrapment efficiency (Mean ±SD n=3)
F1	27.14±1.59
F2	35.81±0.66
F3	43.05±1.08
F4	**52.63±1.2**
F5	38.52±0.81
F6	31.25±1.1

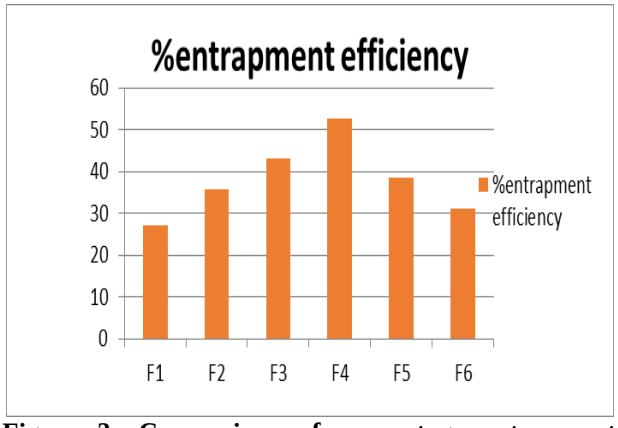

Figure 3: Comparison of percentage entrapment efficiency of different formulations of Ofloxacin Hydrochloride niosomes.

The Ofloxacin Hydrochloride niosomal formulation F1 was prepared in the surfactant: cholesterol ratio of 1:3. The percentage entrapment was found to be 27.14±1.59%. Hence further formulations F2 to F6 were prepared with increase in the concentration of surfactant. The entrapment efficiency was found to be increased up to formulation F4 (1:1 surfactant cholesterol ratio). It was found to be **52.63±1.2%**. Further increase in surfactant concentration resulted in the decrease in entrapment efficiency. This might be due to the leakage of drug from the vesicles with increase in span 60.

Drug Content Estimation

Table 6: Percentage Drug Content of Niosomal Formulations.

Formulation code	Drug content (mg) (Mean ±SD n=3)	Drug content (%)
F1	37.35±0.31	93.37±0.31
F2	37.88±0.90	94.71±0.90
F3	38.42±0.50	96.05±0.50
F4	39.38±0.66	98.37±0.66
F5	38.88±1.2	97.40±1.2
F6	38.42±0.95	96.05±0.95

All the formulations are prepared with 40mg of Ofloxacin Hydrochloride. The concentration is 2mg/ml. There is no marked loss of drug after the formulation. The amount of drug after formulation was all most 40mg.

Coating of Niosome with Bioadhesive Polymer

The coating of niosomes with bioadhesive polymers was done to increase the retention time of niosomes on eye and thereby to increase the bioavailability.

The entrapment efficiency analysis revealed formulation F4 (**52.63±1.2%**) has maximum entrapment of drug when compared to other formulations. Hence formulation F4 were considered for the coating with bioadhesive polymer. Formulations FC1 to FC3 were prepared with HPMC 3CPS as bioadhesive polymer.

EVALUATION OF BIOADHESIVE NIOSOMAL FORMULATIONS

Drug content estimation of coated niosomes

Table 7: Percentage Drug Content of Coated Niosomal Formulations.

Formulation code	Drug content (mg) (Mean ±SD n=3)	Drug content(%)
FC1	37.42±0.31	95.05±0.31
FC2	38.35±0.90	97.38±0.90
FC3	39.48±0.50	98.71±0.50

The drug content of all batches of prepared coated niosomal formulations was determined. It was revealed that there is no loss of drug during coating.

***In vitro* drug release study**

The ability of the bioadhesive niosomal dispersion to provide sustained drug release was assessed by conducting *in vitro* drug release studies in ATF for 12 hours.

***Table 8: In vitro* drug Release of Bioadhesive Of Loxacin Hydrochloride Niosomal FC3 Kinetic Parameters.**

Time (Hr)	Formulation code						
	FC1		FC2		FC3		Marketed
	CDR (mg)	%CDR (Mean±SD n=3)	CDR (mg)	%CDR (Mean ±SD n=3)	CDR (mg)	%CDR (Mean±SD n=3)	%CDR (Mean±SD n=3)
1	0.226	11.31±0.31	0.193	9.68±1.11	0.169	8.46±0.23	16.69±0.16
2	0.386	19.34±1.34	0.351	17.55±0.37	0.313	15.67±0.44	41.8±0.08
3	0.535	26.78±1.01	0.513	25.66±0.67	0.444	22.24±1.13	61.15±0.38
4	0.693	34.66±0.51	0.680	34.01±0.57	0.586	29.34±0.61	78.12±0.31
5	0.871	43.56±1.22	0.813	40.67±1.43	0.771	38.55±0.22	**96.86±0.53**
6	1.009	50.45±0.67	0.933	46.65±0.75	0.900	45.02±0.67	**96.86±0.53**
7	1.169	58.45±0.23	1.095	54.76±1.31	1.004	50.23±1.46	**96.86±0.53**
8	1.315	65.78±1.56	1.251	62.55±1.11	1.147	57.37±1.31	**96.86±0.53**
9	1.429	71.46±0.56	1.364	68.23±0.73	1.308	65.43±0.78	**96.86±0.53**
10	1.589	79.45±0.82	1.548	77.42±1.09	1.480	74.02±0.98	**96.86±0.53**
11	1.747	87.35±0.98	1.703	85.17±0.65	1.624	81.23±1.12	**96.86±0.53**
12	1.893	**94.68±0.76**	1.856	**92.81±0.65**	1.766	**88.32±0.56**	**96.86±0.53**

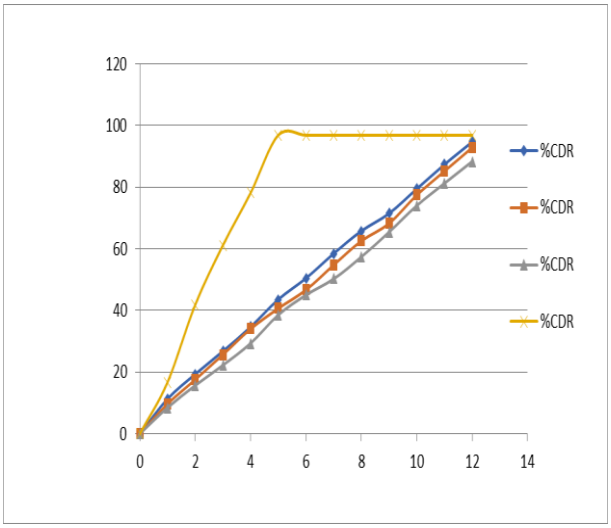

Figure 4: *In vitro* drug release of bioadhesive Ofloxacin Hydrochloride niosomal formulations (FC1 to FC3) in ATF.

All the three formulations (FC1-FC3) showed more sustained release of drug when compared with marked formulation of Ofloxacin Hydrochloride eye drop.

The formulations FC1, FC2 and FC3 were coated with 0.2%, 0.4% and 0.6% w/v of HPMC 3CPS respectively. The formulation FC1 has **94.68±0.76**% drug release after 12 hours. The formulation FC2 has **92.81±0.65**% drug release after 12 hours. The formulation FC3 has **88.32±0.56**% drug release after 12 hours. A slight decrease in drug release was observed when there was increase in HPMC 3CPS concentration.

The drug release of marketed formulation, Oflox 0.3% (B. No: HKS0151, Cipla Ltd, India) was found to be **96.86±0.53**% at the end of 5 hours and the product showed a release only up to 5 hours.

As compared with the marketed formulation, the bioadhesive niosomal formulations showed a sustained drug release. It was revealed that the coating of the niosomes with bioadhesive polymer doesn't alter the release pattern of the drug.

***In vitro* Bioadhesion testing**

The bioadhesive potential of HPMC 3CPS coated niosomal formulations were compared by using agar plate bioadhesion assembly and result was shown in the table.

Figure 5: *In vitro* bioadhesion test assembly.

Table 9: *In vitro* bioadhesion time of coated niosomal formulations.

SL No	Formulation code	Bioadhesion time (min)
1	FC1	45
2	FC2	90
3	FC3	185

The result clearly indicated that the HPMC 3CPS coated niosomes have bioadhesive property and the bioadhesion time increased with increase in concentration of the polymer.

Formulations FC1 to FC3 coated with HPMC 3CPS showed increased bioadhesiveness with increasing concentrations (0.2, 0.4 and 0.6% w/v of HPMC 3CPS). The bioadhesion time was elevated along with increase in concentration of polymer. Formulation FC3 has maximum bioadhesion time of 185 minutes and FC1 has minimum (45minutes) among HPMC 3CPS coated niosomal formulations.

Zeta potential

The optimized niosomal dispersions were characterized for zeta potential by zeta sizer, dynamic light scattering technology.

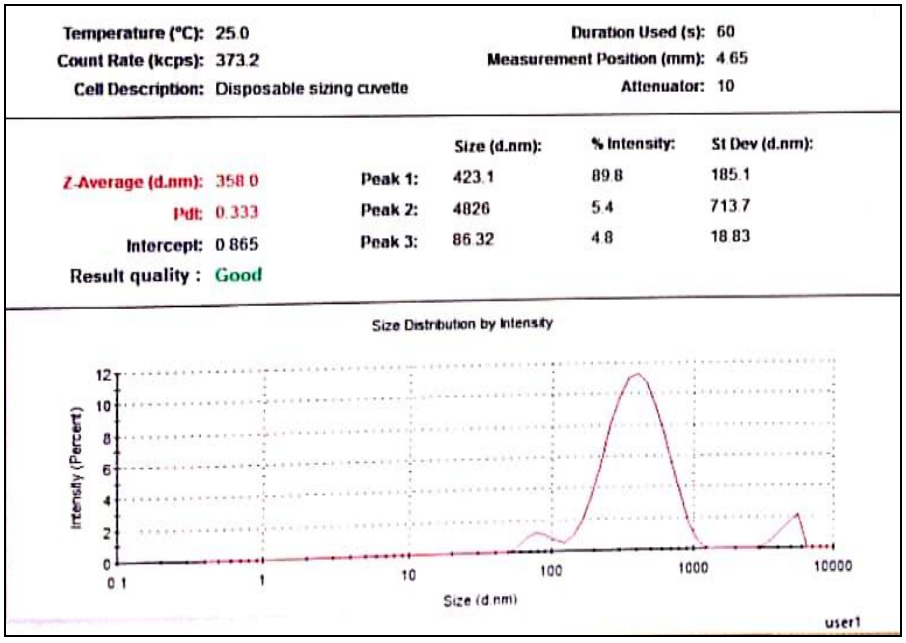

Figure 6: Average size distribution of bioadhesive niosomal formulation FC3.

The average size distribution of formulation FC3 was found to be 358.0 nm. The transcorneal permeation of niosomes will be enhanced when the size of the vesicles is less than 500nm.

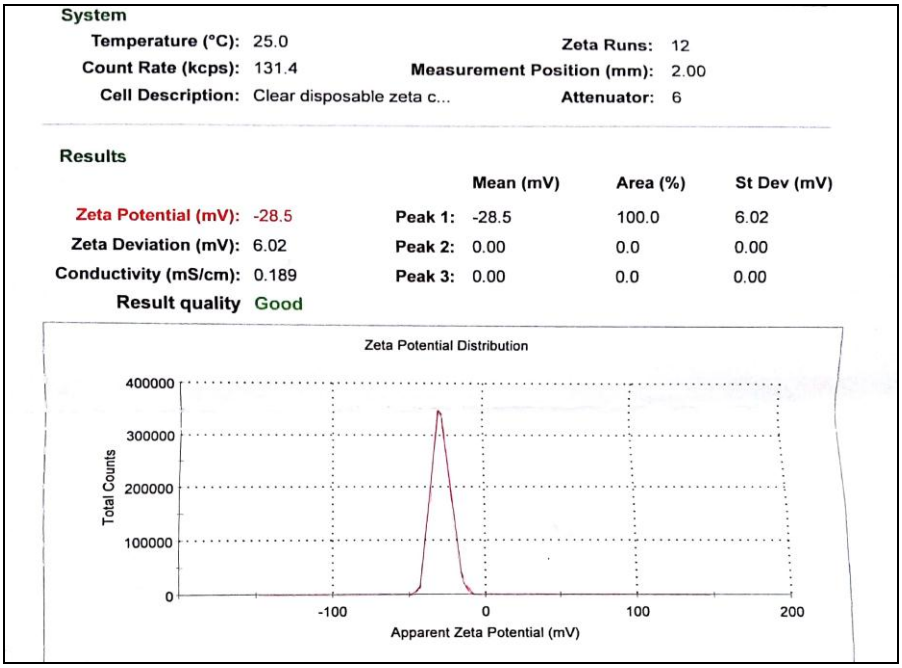

Figure 7: Zeta potential of bioadhesive niosomal formulation FC3.

Zeta potential of all the formulation was found to be negative. This might be due to the presence of free carboxyl groups in Cholesterol and Span 60. The zeta potential of HPMC 3CPS coated niosomal formulation (FC3) -28.5mV. The zeta potential value suggested sufficient kinetic stability of the niosomes. More the positive or negative zeta potential value, larger its colloidal stability.

Antimicrobial assay

Antimicrobial assay was performed to evaluate the relative potency of the niosomal formulations.

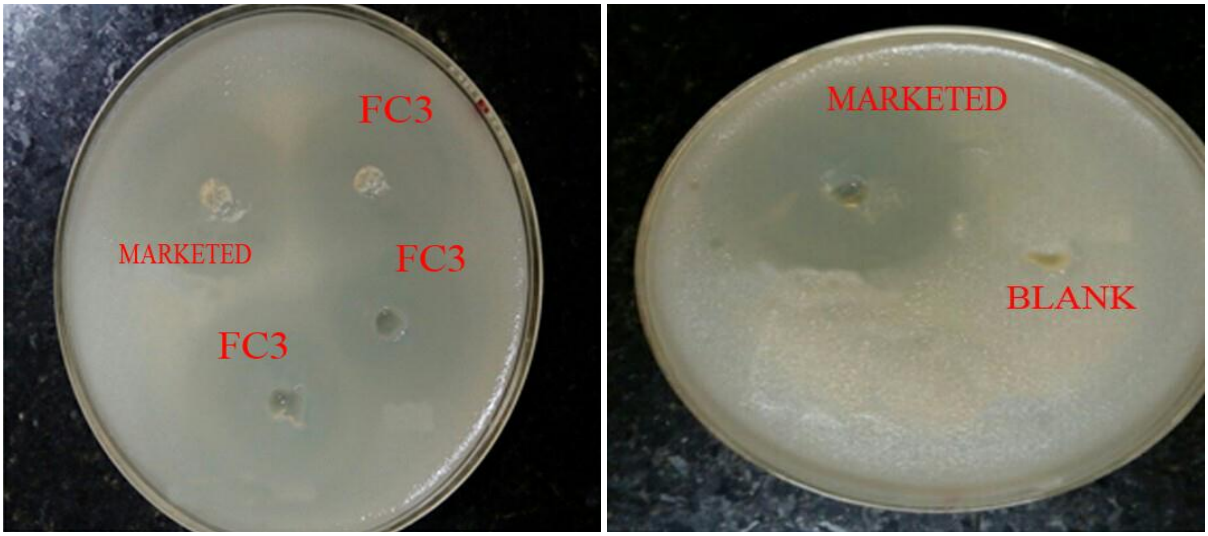

Figure 8: Zone of Inhibition of Bioadhesive Niosomal Formulations and Marketed Product.

Table 10: Zone of inhibition of bioadhesive Ofloxacin Hydrochloride niosomal formulations and marketed product (Oflox 0.3%).

Sl no	Formulation code	Zone of inhibition (cm)
1	FC3	1.6
2	Marketed	1.9
5	Blank niosome	No Zone of Inhibition

The study was performed in optimized formulation (FC3), niosome without drug and marketed Ofloxacin Hydrochloride eye drop.

FC3 has zone of inhibition of 1.6cm.It concluded that there was no loss of drug in the formulated niosomes. The zone of inhibition of marketed product was found to be 1.9cm. The zone of inhibition of blank niosomal formulation was found to be zero and therefore there was no antimicrobial activity for excipients and polymers.

Based on viscosity, *in vitro* release study, *in vitro* bioadhesion study formulation FC3 was selected as optimized bioadhesive niosomal formulation.

Vesicle morphology

The optimized niosome formulation FC3 was observed for its vesicle morphology and surface characteristics using scanning electron microscope.

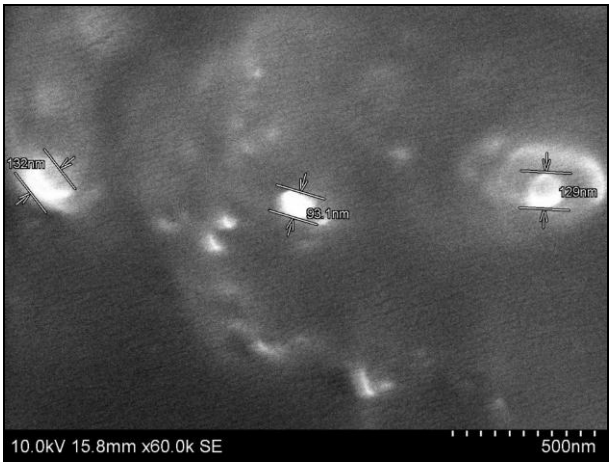

Figure 9: SEM image of optimized coated niosomal formulation at 60K magnification.

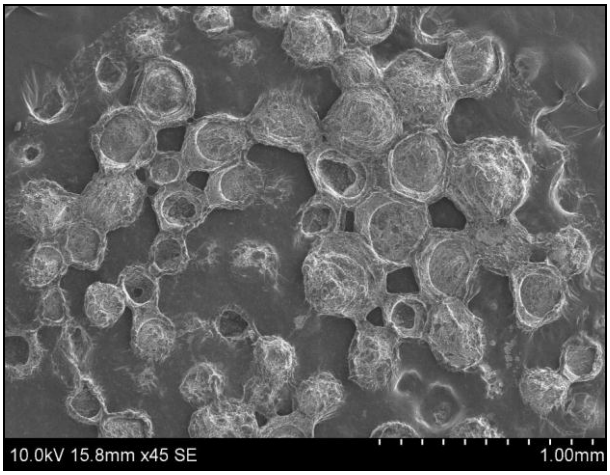

Figure 10: SEM image of optimized coated niosomal formulation at 45K magnification.

The image from SEM analysis revealed that the niosomes appear to be round vesicular morphology and less than 200nm size range. Aqueous filled vesicles were observed in SEM image.

Drug release kinetics of the Bioadhesive Niosome

Table 11: *In vitro* drug release of bioadhesive Ofloxacin Hydrochloride niosomal FC3 kinetic parameters

Time (Hour)	Log time	Square root of time	%CDR	Log %CDR	% Drug remain to be permeated	Log % drug remain to be permeated
0		0	0	0	100	2
1	0.000	1.000	8.46	0.9273	91.54	1.9616
2	0.301	1.414	15.67	1.1950	84.33	1.9259
3	0.477	1.732	22.24	1.3471	77.76	1.8907
4	0.602	2.000	29.34	1.4674	70.66	1.8491
5	0.699	2.236	38.55	1.5860	61.45	1.7885
6	0.788	2.449	45.02	1.6534	54.98	1.7402
7	0.845	2.646	50.23	1.7009	49.77	1.6969
8	0.903	2.828	57.37	1.7586	42.63	1.6297
9	0.954	3.000	65.43	1.8157	34.57	1.5386
10	1.000	3.162	74.02	1.8693	25.98	1.4146
11	1.041	3.317	81.23	1.9097	18.77	1.2734
12	1.079	3.464	88.32	1.9460	11.68	1.0674

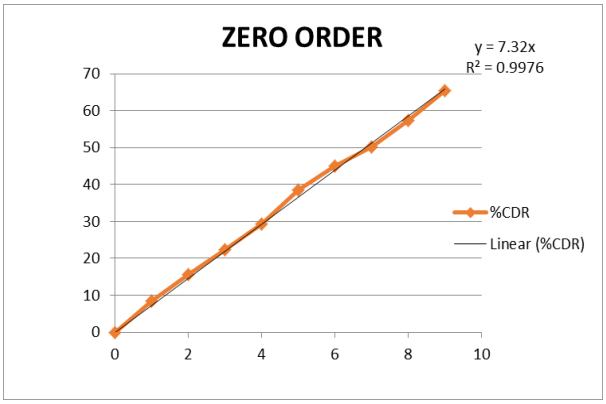

Figure 11: Zero order kinetics (% CDR vs. Time).

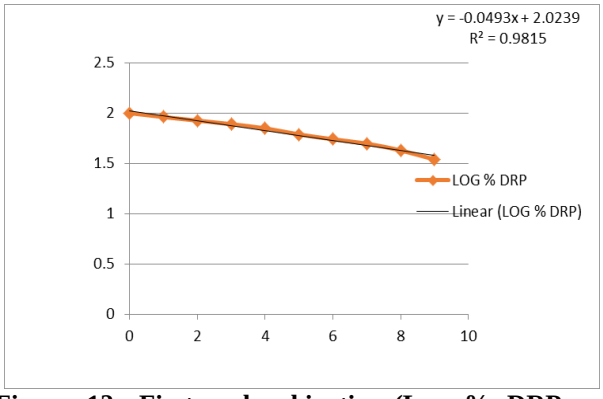

Figure 12: First order kinetics (Log % DRP vs. Time).

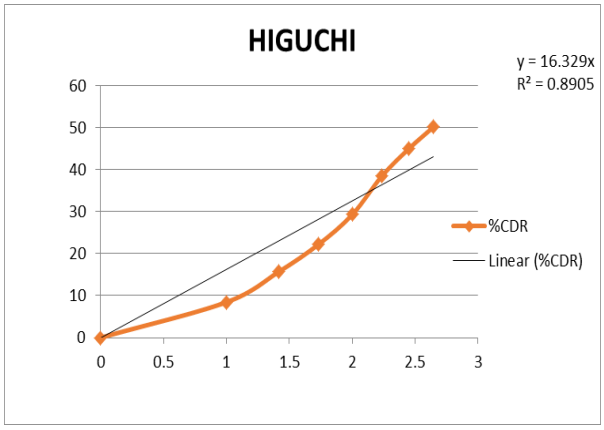

Figure 13: Higuchi model for the formulation FC3 (%CDR vs. Log time).

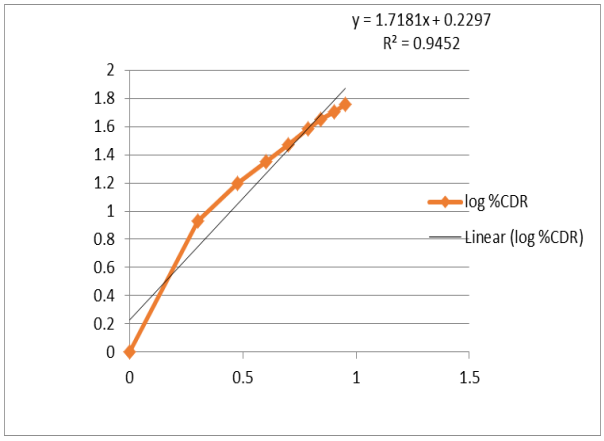

Figure 14: Korsemeyer Peppas model for the formulation FC3 (Log %CDR vs. Log time).

Table 12: Regression coefficients of various kinetic models.

Zero order	First order	Higuchi model	Korsmeyer-Peppas model	
R^2	R^2	R^2	R^2	N
0.997	0.989	0.890	0.945	1.718

Ex vivo drug permeation data was subjected to goodness of fit by linear regression analysis according to zero order, first order kinetic equation, Higuchi and Korsmeyer Peppas model (fig) to ascertain the mechanism of drug release. The result of linear regression analysis of data including regression coefficient are listed in Table 12. Regression coefficient (R^2) obtained for first order kinetics and zero order kinetics was 0.989 and 0.997 respectively. The results indicate that the drug release follows nearing zero order kinetics. The coefficients obtained from Higuchi model was 0.890, indicating diffusion played a predominant role in the drug release procedure. The value evidenced that initial drug concentration in the matrix is much higher than drug solubility, drug diffusion takes place only in one dimension (Edge effect should be avoided), drug particles are much smaller than thickness of system, swelling of matrix and dissolution are less or negligible and drug diffusivity is constant.

Slope obtained from Korsmeyer-Peppas equation was the 'n' value and found to be 1.718 indicated that release was super case II transport results from a combination of diffusion effect and non fickian transport mechanism. Case II transport occurs when the sorption is entirely controlled by stress-induced relaxations taking place at a sharp boundary separating an outer swollen shell, essentially at equilibrium penetrant concentration.

SUMMARY

Ophthalmic drug delivery is one of the most interesting and challenging endeavors facing the pharmaceutical scientist. The anatomy, physiology, and biochemistry of the eye render this organ highly impervious to foreign substances. Drug delivery to the eye can be broadly classified into anterior and posterior segments. Conventional systems like eye drops, suspensions, and ointments cannot be considered optimal in the treatment of vision-threatening ocular diseases. However, more than 90% of the marketed ophthalmic formulations are in the form of eye drops. These formulations mainly target the diseases in the anterior segment of eye. Topical ocular medications do not reach the posterior segment of the eye. Posterior segment (retina, vitreous, choroid) can be treated by high drug dosage regimen given intravenously or by intravitreal administration or implants or by periocular injections. Currently, the posterior segment drug delivery is a rapidly growing interest area in ophthalmic drug delivery. In the present study, attempts were made to prepare sustained release bioadhesive Ofloxacin Hydrochloride niosomes using Cholesterol and Span 60 by solvent injection method. The coating of the niosomes was done using bioadhesive polymer HPMC 3CPS. Different parameters were evaluated for the prepared formulations include drug-polymer compatibility studies, rheological studies, drug entrapment efficiency, in vitro drug release study, in vitro bioadhesion studies, antimicrobial assay and zeta potential. The drug polymer compatibility studies were carried out by FT-IR spectroscopy and revealed the absence of drug polymer interactions. The pH of the formulation was within the range of ophthalmic preparations and therefore there were no ocular irritations. Niosomes prepared with cholesterol: surfactant ratio of 1:1 showed maximum entrapment efficiency. The in vitro drug release of formulations showed sustained release of the drug over 12hr. The in vitro bioadhesion testing confirmed the bioadhesion property of the formulated coated niosomes. The formulation FC3 showed better bioadhesion property. The drug release kinetic study confessed the release was nearing zero order kinetics. The Stability studies revealed that the prepared bioadhesive niosomal formulation was stable during storage. The zeta potential value revealed that the formulations having negative zeta potential and have good stability. The SEM analysis showed that the particle size of the niosomal formulations were below 400nm and round vesicle shape in morphology. Antimicrobial assay confirmed the potency of the formulation. The Ofloxacin

Hydrochloride bioadhesive niosomal formulation showed zone of inhibition similar to that of marketed product. Based on the above in vitro drug release and in vitro bioadhesion evaluation bioadhesive niosomal formulation FC3 (niosome coated with 0.6% HPMC 3CPS) were concluded as optimized formulation. The novel bioadhesive niosomal formulation of Ofloxacin Hydrochloride was found to be capable of enhancing the ocular retention time of the drug. It also showed enhanced sustained drug delivery for a period of 12 hours. Hence this novel formulation was found to be a good replacement for conventional eye drops with decreased dosing frequency and an effective drug level in eyes.

CONCLUSION

The novel bioadhesive niosomal formulation of Ofloxacin Hydrochloride was found to be capable of enhancing the ocular retention time of the drug. It also showed enhanced sustained drug release for a period of 12 hours. In the present study, attempts were made to prepare sustained release bioadhesive Ofloxacin Hydrochloride niosomes using Cholesterol and Span 60 by solvent injection method. The coating of the niosomes was done using bioadhesive polymer HPMC 3CPS. Different parameters were evaluated for the prepared formulations include drug-polymer compatibility studies, rheological studies, drug entrapment efficiency, in vitro drug release study, in vitro bioadhesion studies, Antimicrobial assay, Zeta potential and Stability studies. The drug polymer compatibility studies were carried out by FT-IR spectroscopy and revealed the absence of drug polymer interactions. The pH of the formulation was within the range of ophthalmic preparations and therefore there were no ocular irritations. Niosomes prepared with cholesterol: surfactant ratio of 1:1 showed maximum entrapment efficiency. The in vitro drug release of formulations showed sustained release of the drug. The in vitro bioadhesion testing confirmed the bioadhesion property of the formulated coated niosomes. The formulation FC3 showed better bioadhesion property. The drug release kinetic study confessed the release was nearing zero order kinetics. The Stability studies revealed that the prepared bio adhesive niosomal formulation was stable during storage.

REFERENCES

1. Anubha K, Kanchan G, Pravin, Inderbir. Mucoadhesive Polymers for Enhancing Retention in Ocular Drug Delivery: A Critical Review, 2014; 1(1): 1-2.
2. Arora S, Prashar B, Dhamija H, Chandel A, Thakur V. Niosomes: The Unique Vesicular Drug Carriers. Journal of Drug Delivery & Therapeutics, 2012; 2(1): 1-2.
3. Indian Pharmacopoeia, Government of India; Indian Pharmacopoeia Commission, Ghaziabad, 2007; 6(1): 854-56.
4. A. R. Shabaraya, Ankit S, Krishnananda K, D Shripathy. A Novel Approach of Artesunate Pellets for the Treatment of Malaria. International Journal of Pharmaceutical Sciences and Drug Research, 2018; 10(6): 442-46.
5. Kaur V, Pawar P. Formulation and evaluation of moxifloxacin hydrochloride niosomes for controlled ophthalmic drug delivery. Journal of Pharmaceutical Technology, Research and Management, 2015; 3(1): 11-28.
6. G Lakshmana, G Vijaya, B Sravani, PS Prasanna, D Anand, Bhanu P, Bhagya S, D Prasanna, M Prasad, R Syam. Design and Development of Ofloxacin Insitu Gel Using Mucoadhesive Polymers. Scholars Academic Journal of Pharmacy, 2017; 6(5): 212-20.
7. Yahaya Z, Lalit M, Zeenat I, Sushama T. Design and development of novel bioadhesive niosomal formulation for the transcorneal delivery of anti-infective agent: In-vitro and ex-vivo investigations. Asian Journal of Pharmaceutical Sciences, 2015; 10: 322-30.
8. Branko S, Dragan K, Suzana F. Measurement and application of zeta-potential. Rudarsko-geoloSko-naftni zbornik, 1992; 4: 147-52.
9. Laboratory methodologies for bacterial antimicrobial susceptibility testing. Guideline 2.1, OIE Terrestrial Manual. 2012; 1: 1-11.
10. Ghatage SL, Navale SS, Mujawar NK, Patil S, Patil V. Antimicrobial screening. Indian Journal of Drugs, 2014; 2(3): 84-88.
11. Kaur V, Pawar P. Formulation and evaluation of moxifloxacin hydrochloride niosomes for controlled ophthalmic drug delivery. Journal of Pharmaceutical Technology, Research and Management, 2015; 3(1): 11-28.
12. Sabitha K, Sajeeth CI, Santhi K. Chitosan nanoparticles: A Novel Vehicle for the Enhanced Ocular Delivery of Moxifloxacin Hydrochloride. Research Journal of Pharmaceutical, Biological and Chemical Sciences, 2012; 3(2): 534-47.
13. Ghatage SL, Navale SS, Mujawar NK, Patil S, Patil V. Antimicrobial screening. Indian Journal of Drugs, 2014; 2(3): 84-88.
14. Hina KS, Kshirsagar RV, Patil SG. Mathematical models for drug release characterization: a review. World Journal of Pharmacy and Pharmaceutical Sciences, 2015; 4(4): 324-38.
15. Brahmankar DM, Jaiswal SB. Biopharmaceutics and pharamacokinetics – a treatise. Vallabh Prakashan publisher, New Delhi, 2009; 3: 241-46.