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Development of novel bioadhesive niosomal formulation for the transcorneal delivery of moxifloxacin hydrochloride in the treatment of corneal ulcer

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ABSTRACT

Corneal ulcer is an open sore or epithelial defect with an inflammation of the cornea of the eye. Most of the corneal ulcers are caused by bacterial infections and are common in people who wear contact lenses. Moxifloxacin eye drops are frequently used for the treatment of infectious ulcers. However such formulations have a major drawback, that is the short duration of action and usually, require 4-6 times instillation daily. A bioadhesive polymer coated niosomal formulation of moxifloxacin was purposed to show a longer retention time on eyes and subsequent reduction in dosing frequency. Niosomes were prepared by solvent injection method using cholesterol and span 60. The coating of the niosomes was done using Carbopol 934or HPMC as bioadhesive polymer. The mean particle size of bioadhesive niosomes found to be below 200nm. Optimization of the coating was based on *in vitro* diffusion studies, *ex vivo* transcorneal permeation studies and bioadhesion studies. The retention time of the formulation was determined by *in vitro* and *ex vivo* bioadhesion testing. The antimicrobial assay confirmed the potency of the formulation against the gram-negative organism. The current study revealed that bioadhesive niosomal formulations have longer corneal retention time and have sustained drug release for a period of 24 hours.

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INTRODUCTION

Corneal ulcer or ulcerative keratitis is an inflammatory or infective condition of cornea involving disruption of its epithelial layer with involvement of the corneal stroma (Nicula and Szabo, 2016)

Most cases of corneal ulcer are due to bacterial infection that affects the cornea, often followed eye injury, trauma or other damage. Mostly infectious corneal ulcer is treated with topical antibiotics like Moxifloxacin (Mitra, 2003). The elimination of drug by lachrymation, non productive absorption by the conjunctiva and solution drainage is the major problems causing hindrance in the ophthalmic drug delivery. The residence time of conventional solutions in the ophthalmic cavity is limited to a few minutes and the overall absorption of topically applied drug is limited to 1-10% (Dave and Paliwal, 2014). Initially, ophthalmic ointments and gels were used to overcome the poor bio availability of eye drops. These preparations have the major disadvantage of providing blurred vision.

Niosomes are novel drug delivery system, in which the medicament is encapsulated in a vesicle. The vesicle is composed of a bilayer of non ionic surfactant and cholesterol (Gharbavi *et al.*, 2018). A bioadhesive material (polymer) coated niosomal formulation of anti-infective agent was purposed to show a longer retention time on eye and subsequent reduc-

tion in dosing frequency.

Niosomes coated with bioadhesive material can leads to a steady and sustained release of drug into ocular cavity without being eliminated at a faster rate. The enhancement in the retention time of the ophthalmic formulations leads to increase in transcorneal permeation of the drug and thereby enhancing the bio availability (Saikia and Gogoi, 2015).

Moxifloxacin hydrochloride is a fourth generation synthetic flouroquinolone derivative used for various ocular infections (Miller, 2008). Moxifloxacin is the prime choice for treatment of corneal ulcer either alone or in combination havingan antibacterial spectrumagainst Gram negative rods (*E. coli, Proteus species), Haemophilus influenza, Staphylococcus viridians, Staphylococcus aureus, Pseudomonas* and many other bacteria (Nagalakshmi *et al.*, 2015). Frequent dosing of generally 4-8 times a day is required for achieving the effective concentration in the eye. This leads to poor patient noncompliance and ineffective drug delivery. Therefore, there was a probable need of novel eye formulation for Moxifloxacin HCl with longer retention in the eye and less dosing frequency. Hence, the present study emphasized to search for an effective tool for solving low ocular retention and ocular permeation of Moxifloxacin by using the concept of bioadhesive niosomes (Figure 1).

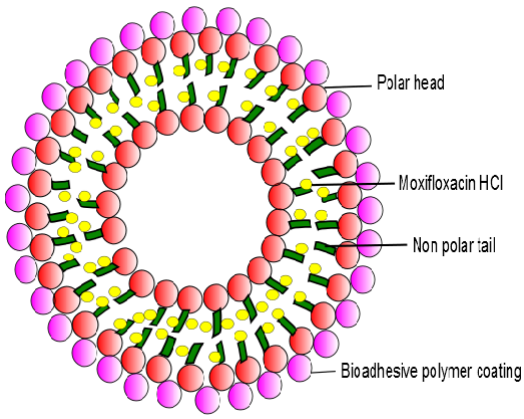

Figure 1: Bioadhesive polymer coated niosomes of Moxifloxacin HCl

MATERIALS AND METHODS

Materials

Moxifloxacin hydrochloride IP was gifted from MSN Pharmachem Private Limited. Cholesterol, nutrient agar media, nutrient broth media and sudan II were purchased from HiMedia laboratories Pvt. Ltd. Nasik. Span 60 and carbopol 934 were purchased from Oxford laboratory, Mumbai. HPMC 5CPS, chloroform and ethanol were purchased from Central drug house Ltd, New Delhi. Buffalo eye cornea was obtained from local slaughterhouse. Millipore water was used for all the practicalpurposes.

Experimental methods

Preparation of Moxifloxacin hydrochloride niosomes

Solvent injection method

Weighed accurately the required quantity of span 60 and cholesterol as per Table 1 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 phosphate buffer pH 7.4 (PB 7.4) maintained at 60-70^{0}C with continuous stirring in a magnetic stirrer at 1000 rpm until the solvent got evaporated. Stirring was continued for 1 hour at room temperature. The resultant solution was then placed in a bath sonicator for 10min (Kaur and Pawar, 2015).

Table 1: Composition of Moxifloxacin hydrochloride niosomes

Formulation code	Drug (mg)	Span 60 (mg)	Cholesterol (mg)	Chloroform (ml)	PB 7.4* (ml)
F1	20	25	75	5	17.5
F2	20	35	65	5	17.5
F3	20	45	55	5	17.5
F4	20	50	50	5	17.5
F5	20	55	45	5	17.5
F6	20	65	35	5	17.5

*PhosphateBuffer pH 7.4

Entrapment efficiency

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 absorbance was measured at 288nm using UV-Visible spectrophotometer. Niosomes prepared without drug was centrifuged in same manner and the supernatant solution was taken as blank. Entrapment efficiency was expressed as percentage of total drug entrapped.

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

T——— Amount for drug added.

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

Coating of niosome with bioadhesive polymer

The weighed quantity of polymer (HPMC or Carbopol) as per Table 2was dissolved in 2.5 ml of millipore water. The polymeric solution was then slowly added to the prepared niosomal dispersion (F4) and continued the stirring for 1 hour using a magnetic stirrer at room temperature.

Table 2: Composition of the bioadhesive niosomal formulations

Formulation Code	Niosomal Dispersion (ml)	HPMC (mg)	Carbopol (mg)	Distilled water (ml)
FC 1	17.5	40	-	2.5
FC2	17.5	80	-	2.5
FC3	17.5	120	-	2.5
FC4	17.5	-	40	2.5
FC5	17.5	-	80	2.5
FC6	17.5	-	120	2.5

Evaluation of bioadhesive niosomal formulations

Determination of Physical characteristics

All batches of prepared bioadhesive niosomal formulations were observed visually for physical appearance. The bioadhesive niosomal formulations were observed under a binocular microscope at 40X magnification to determine the characteristics.

Determination of pH and Viscosity

The viscosity of the prepared bioadhesive niosomal dispersions was determined by Brookfield viscometer model RVDVE with small sample adaptor. The pH of the prepared niosomes was determined by pH meter. The electrodes were completely dipped into the formulations and pH was noted.

***In vitro* drug release study**

The *in vitro* drug release studies of Moxifloxacin hydrochloride from bioadhesive niosomes were determined using membrane diffusion technique. The *in vitro* drug release was carried out using modified diffusion tube (diameter: 1.7 cm). The cellophane membrane was hydrated with Artificial Tear Fluid (ATF) for 12 h before being fastened between the donor and the receptor compartment. The donor medium was composed of 1 ml of the bioadhesive niosomal formulation equivalent to 1000μg of moxifloxacin hydrochloride. 40 ml of ATF was taken in the receptor compartment. The temperature of receptor compartment was maintained at 37 ± 0.5^0 C with continuous stirring at 200 rpm using a magnetic stirrer.2.5ml of aliquot samples were withdrawn from receptor compartment 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 at 288 nm after suitable dilutions. The procedure was repeated for marketed (0.5 % Moxifloxacin hydrochloride) eye drops. The cumulative amount of drug released across the cellophane membrane was determined as a function of time (Ahuja, 2008).

Preparation of dye entrapped niosomes

The dye entrapped niosomes were prepared with the incorporation of 50 mg of Sudan II along with span 60 and cholesterol and was dissolved in 5ml of chloroform. The rest of formulation process remains same. The bioadhesive polymer coating of the dye entrapped niosomes was carried out as per the composition in Table 2. The coating process remains the same as that of bioadhesive niosomes without dye.

***In vitro* Bioadhesion testing**

The bioadhesive potential of the prepared bioadhesive niosomes was evaluated in an agar plate (1% w/w), prepared in pH 7.4 phosphate buffer. 1ml of the prepared dye incorporated niosomal formulation was placed in the centre 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 ± 1^0 C. The residence time of the test samples on the plate was noted by visual appearance of the formulation over the plate. (Bachhav and Patravale, 2009).

***Ex vivo* Bioadhesion testing**

Fresh whole eye ball of buffalo were brought from the local butcher's shop in cold normal saline (4^0C). The cornea was excised and washed with cold normal saline and attached in a rectangular plastic plate (7x4 Cm) with a thread. 0.2ml of prepared bioadhesive formulations incorporated dye was added drop wise to the cornea. It was kept for 5 min. The plate was attached to a disintegration test apparatus and move up and down in ATF at 37 ± 1^0 C. The residence time of the test samples on the plate was noted by visual appearance of the formulation over the plate (Bachhav and Patravale, 2009).

Transcorneal permeation studies

Fresh whole eye ball of buffalo were brought from the local butcher's shop in cold normal saline (4^0C). The cornea was excised and washed with cold normal saline. Tie the cornea in the mouth of the diffusion cell. Fix the cornea in such a way that its

epithelial surface faced the donor compartment. 40 ml of artificial tear fluid (ATF) was taken in a beaker as receptor media. The temperature was maintained at 37 ± 1^0C. Measured quantity (0.5 ml) of the niosomal formulations (contains 500μg of moxifloxacin hydrochloride) was placed on the cornea or donor compartment. 2.5 ml samples were withdrawn from the receptor media at different time intervals, filtered and analyzed for drug content by using UV-Visible spectrophotometer at 288nm. The receptor compartment was immediately replaced with equal amount of fresh ATR. Similar procedure was done for marketed formulation of moxifloxacin hydrochloride eye drops, and compared the release kinetics (Rathore *et al.*, 2008).

Zeta potential and Size distribution

The optimized niosomal dispersions were characterized for zeta potential and average size distribution by zeta sizer, dynamic light scattering technology (Salopek *et al.*, 1992a**).** The size distribution was measured in Malvern particle size analyzer.

Antimicrobial assay

Antimicrobial assay was performed on Gram negative bacteria. E. coli was selected as Gram negative bacteria. Test tubes and petridishes were sterilized in hot air oven at 170^0C 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's were sub cultured to the sterilized broth media and incubated for 24 hours at 37^0C. The sub cultured broth media was transferred to the nutrient agar media.75 ml of the above agar media was poured into each petridishes. Agar plate was placed in a refrigerator for solidification. Small wells were made in each plate with a stainless steel sterilized borer of 6mm internal diameter. Each plate contains 4 wells, 50 μL antibiotic formulations was introduced into each well using a micropipette and refrigerated for 1hour at 4-8^0C. The plate was incubated for 24 hour at 37 $\pm0.5^0$C and zone of inhibition was measured (Jenkins and Schuetz, 2012).

Fourier Transform Infrared Spectroscopy (FTIR)

The compatibility and stability of Moxifloxacin HCl in Niosomal formulations were evaluated using FTIR peak matching method. The sample was prepared by triturating dried Niosomal preparation with approximately 300 mg of dry finely powdered potassium bromide. The mixture was ground thoroughly and was spread uniformly in a suitable die and compressed under vacuum at a pressure of about 800 MPa. The prepared disc was then mounted on a suitable holder in the FTIR spectrophotometer. The spectrum was recorded in the wavelength range of 400-4000 cm^{-1}

Vesicle morphology

The optimized niosome formulation was observed for its vesicle morphology using scanning electron microscope (Hitachi FESUM SU6600) (Naveed *et al.*, 2015; Pawar *et al.*, 2012).

RESULTS AND DISCUSSION

Solvent injection method

Moxifloxacin hydrochloride was prepared by solvent injection technique. The composition is mentioned in Table 1. The drug, cholesterol and surfactant was dissolved in chloroform and injected into aqueous vehicle. The aqueous vehicle was maintained at a temperature just above the boiling point of the organic solvent. When the organic solvent was injected into the aqueous system with continuous stirring, evaporation of volatile organic solvent resulting in the formation of lipid vesicle and the aqueous system got entrapped into the vesicle. Cholesterol induces change in fluidity and permeability of the bilayer. It gives rigidity and orientation order to niosomes and also helps to prevent the leakage. The non ionic surfactant, Span 60 was used as surfactant (Sahoo *et al.*, 2014). The moxifloxacin hydrochloride being lipophilic in nature will be entrapped in lipid bilayer (Kaur and Pawar, 2015; Nagalakshmi *et al.*, 2015).

Entrapment efficiency

Determined by centrifugation method

The percentage entrapment efficiency of various batches of Moxifloxacin hydrochloride niosomes were shown in Table 3. The moxifloxacin hydrochloride niosomal formulations showed increase in entrapment efficiency with increase in the concentration of surfactant up to formulation F4 (1:1 surfactant, cholesterol ratio). 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 (Kaur and Pawar, 2015).

Coating of niosome with bioadhesive polymer

The coating of niosomes with bioadhesive polymers was performed to increase the retention time of niosomes on the cornea and thereby to enhance the bio availability. The formulation F4 showing the highest entrapment efficiency was selected for coating with bioadhesive polymer. The formulations were prepared using HPMC and Carbopol 934as bioadhesive polymers in the ratios given in Table 2.

Table 3: Percentage entrapment efficiency of niosomal formulations

Formulation code	Percentage entrapment efficiency (Mean ±SD n=3)
F1	27.71±2.10
F2	29.90±0.90
F3	42.89±0.50
F4	50.50±0.66
F5	38.03±1.20
F6	32.60±0.95

Evaluations of bioadhesive niosomal formulations

Determination of Physical characteristics

All batches of the prepared bioadhesive niosomes were observed visually for physical appearance. The formulated niosomes were clear and slightly yellow in appearance. This indicated that there was no precipitation of polymer or drug. The images (Figure 2)from microscopic evaluation showed the niosomal vesicles with slight yellow color, suggesting the entrapment of drug in the vesicles.

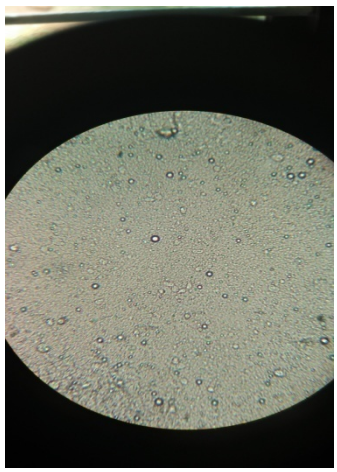

Figure 2: Binocular microscopic image of niosomes at 40X magnification

Determination of pH and Viscosity

The results were shown in Table 4. The pH of the formulations was found to be within the range of 6.9 to 7.2. The ideal pH of the ophthalmic preparations should be in the range of 6.3 to 7.3, in order to reduce the irritation on ophthalmic administration. The formulations coated with carbopol 934 (FC5 and FC6) showed higher viscosity when compared to that of HPMC (tab 4) due to the higher molecular weight of carbopol than the HPMC which promoted the formation of more intact matrix network. The formulation FC6 prepared using carbopol 934 as bioadhesive polymer showed maximum viscosity of 55cps.

Table 4: pH and Viscosity of the bioadhesive niosomal formulations

Formulation code	pH*	Viscosity (spindle no: 21)(Cps)*
FC1	7.0±0.2	30±1
FC2	7.1±0.2	35±1
FC3	7.2±0.1	40±2
FC4	7.1±0.1	40±2
FC5	7.0±0.2	50±3
FC6	6.9±0.2	55±3

(Mean ±SD n=3)

In vitro Bioadhesion testing

The bioadhesive potential of HPMC and Carbopol 934coated niosomal formulations were compared by using agar plate bioadhesion assembly and the results were shown in the Table 5. The results clearly indicated that the HPMC and Carbopol coated niosomes have bioadhesive property and the bioadhesion time increased with increase in the concentration of the polymer. Formulations FC1 to FC3 coated with HPMC showed increased bioadhesiveness with increase in polymer concentrations (0.2, 0.4 and 0.6% w/v of HPMC). Formulations FC4 to FC6 coated with Carbopol also showed increased bioadhesiveness with increase in polymer concentrations (0.2, 0.4 and 0.6% w/v of Carbopol). Carbopol coated niosomal formulations FC6 has maximum bioadhesion time of 210 minutes. The result indicated that carbopol coated niosomal formulations have more bioadhesive property due to higher hydrogen bonding capacity of carbopol as compared with HPMC coated niosomal formulations (Zubairu *et al.*, 2015).

Table 5: In vitro bioadhesion time of dyeincorporated bioadhesive niosomal formulations

Sl no	Formulation code	In vitro Bioadhesion time* (min)	Ex vivo Bioadhesion time* (min)
1	FC1	30±3	35±2
2	FC2	80±3	90±3
3	FC3	165±3	180±4
4	FC4	40±2	50±2
5	FC5	100±3	110±2
6	FC6	210±4	230±3

*n=3

Ex vivo Bioadhesion testing

The *Ex vivo* bioadhesive potential of HPMC and carbopol coated niosomal formulations was compared by using buffalo cornea bioadhesion assembly and the results were shown in the Table 5. The results indicated that carbopol coated niosomes has better bioadhesive property. The formulation FC6 showed maximum bioadhesive property (230 min). Carbopol is an anionic polyelectrolyte, which consist of a vinyl group and a carboxylic acid terminus. It has the ability to form strong hydrogen bond with the mucin present in the mucosal layer of cornea and thus it shows good bioadhesive property. HPMC has low hydrogen-bonding potential with the mucus membrane owing to its non-ionic character, and thus show lesser mucoadhesivity. The hydrophilic polymers have the feature to adhere with the mucosal surfaces, as a result of their ability to attract water molecules from the mucus gel layer (Dhawale *et al.*, 2018). The study revealed that mucoadhesive property increased with the increase in the polymer concentration (Bachhav and Patravale, 2009).

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 24hours. The results were shown in Figure 3.The *in vitro* drug release studies showed that formulation FC1 coated with 0.2% HPMC showed a Cumulative drug release (CDR) of 95.21±1.5 % and also sustained the drug release for a period of 7 hours. The formulations prepared with increasing concentrations of HPMC (FC2 and FC3) showed sustained release for 8 hours and 12 hours respectively with 94.38±1.41% and 94.211±1.01% release. These suggested that the drug release was sustained with increase in the concentration of HPMC.

The formulations FC4, FC5 and FC6, coated with 0.2 %, 0.4% and 0.6% w/v of carbopol showed a drug release of 94.77±0.76 %, 95.86±1.33% and 96.20±1.55% at the end of 12h, 18h and 24hours respectively. The results indicated that the release of moxifloxacin HCl was sustained with increasing concentration of Carbopol. The carbopol also showed greater ability to sustain the drug release when compared with HPMC. The marketed formulation showed a CDR of 95.25±1.95% within a period of 6hours. The HPMC and Carbopol have showed better sustained release when compared with marketed formulation. It was revealed that the coating of the niosomes with bioadhesive polymer helps to deliver the drug in a sustained release manner when compared to conventional marketed eye drops. The better mucoadhesive property of carbopol in comparison with HPMC resulted in sustaining the drug release for 24 hours. This might be due to the higher molecular weight of carbopol 940 and more hydrogen bonding (Bachhav and Patravale, 2009).

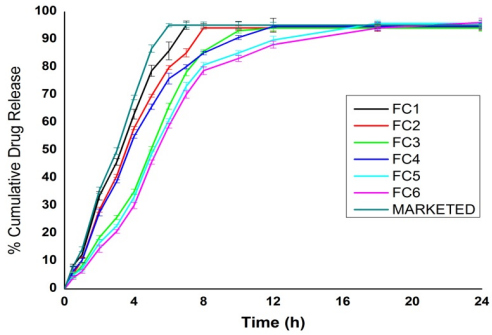

Figure 3: In vitro drug release of bioadhesive moxifloxacin hydrochloride niosomal formulations (FC1 to FC 6) (n=3)

Transcorneal permeation studies

Based on various evaluations such as viscosity, *in vitro* release studies, *in vitro* bioadhesion studies and e*x vivo* bioadhesion studies formulations FC3 and FC6 were selected for further transcorneal permeation studies. It was compared with marketed eye drops(Figure 4). The *ex vivo* drug release studies showed that formulation FC3 coated with 0.6% HPMC showed a % CDR of 97.96±1.5 % and sustained the drug release for a period of 18 hours. Whereas formulation FC6 coated with 0.6% Carbopol showed a CDR of 98.01±1.7 % and sustained the drug release for a period of 24 hours. The drug release from marketed formulation was found to be completed at the end of 10 hours (95.21±2.14%). The *ex vivo* drug permeation pattern of HPMC and carbopol coated niosomes revealed that the coating of the niosomes with bioadhesive polymer helps to deliver the drug in a sustained release manner when compared to conventional marketed eye drops (Rathore *et al.*, 2008).

Zeta potential and Size distribution

The optimized niosomal dispersions were characterized for zeta potential by zeta sizer using dynamic light scattering technology. Zeta potential of all the formulations was found to be negative. This might be due to the presence of free carboxyl groups in cholesterol and span 60. The higher zeta potential value was observed (Table 6) for carbopol coated niosomal formulation FC6 (-47.6mV). The zeta potential of HPMC coated niosomal formulation (FC3) was less when compared with carbopol coated niosomal formulation. The zeta potential

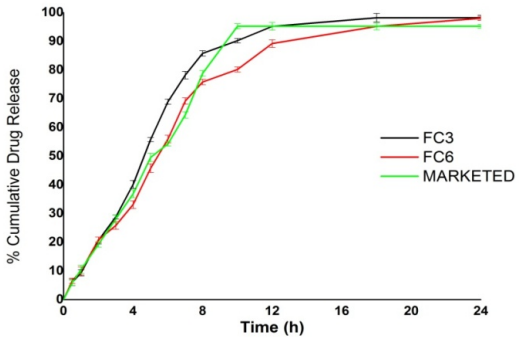

Figure 4: Ex vivo Trans corneal drug release of bioadhesive Moxifloxacin hydrochloride niosomal formulations FC3, FC6 and marketed (n=3)

value suggested sufficient kinetic stability of the niosomes. Higher the positive or negative zeta potential value, larger will be its colloidal stability. A zeta potential between +30 and -30 mV indicates an unstable suspension, whereas zeta potential of more than ±40 exhibits greater stability. Therefore, the Carbopol coated bioadhesive niosomes showed better stability.

The average size distribution of formulation FC3 was found to be 131.31±5.33 nm and average size distribution of formulation FC6 was found to be 125.45±8.21 nm (Table 6). The transcorneal permeation of niosomes will be enhanced when the size of the vesicles is less than 500nm. Both the formulations (FC3 and FC6) showed average vesicle size less than 500nm (Salopek *et al.*, 1992b).

Table 6: Zeta potential and Size distribution of the formulations FC3 and FC6

Sl no	Formulation code	Zeta potential (mV)*	Average size distribution* (d.nm)
1	FC3	-28.5±2.1	131.31±5.33
2	FC6	-47.6±2.3	125.45±8.21

*n=3

Antimicrobial assay

Antimicrobial assay was performed to evaluate the relative potency of the niosomal formulations. The results were shown in Table 7. The study was performed using formulations FC3, FC6,pure drug solution, marketed moxifloxacin eye drops, minimum inhibitory concentration (MIC) of the drug and niosomes without drug. The zone of inhibition of MIC concentration of moxifloxacin was found to be 0.9 cm. The MIC concentration is the minimum concentration of drug showing antimicrobial activity

Table 7: Zone of inhibitionof bioadhesive moxifloxacin hydrochloride niosomal formulations and marketed product 0.5%

Sl no	Formulation code	Zone of inhibition (Cm)*
1	FC3	1.5±0.05
2	FC6	1.6±0.1
3	Pure drug solution	1.5±0.1
4	Marketed	1.6±0.2
5	MIC	0.9±0.05
6	Blank niosome	0.0

*n=3

Table 8: FT-IR spectrum of optimized niosomal formulation FC6

Moxifloxacin HCl (Cm-1)	Formulation FC6 (Cm-1)	Characterization
3496	3470	-N-H
3527	3529	-OH
1623	1621.4	-C=O
1600	1621.4	aromatic C=C stretching

against the micro organism. The zone of inhibition of the drug formulation should be more than that of MIC. FC3, FC6 and plain drug solution (1mg/ml) has zone of inhibition of 1.5 cm and higher. The zone of inhibition of blank niosomal formulation was found to be zero and therefore there was no antimicrobial activity for excipients and polymers. The optimized formulation has the antimicrobial activity more than that of the MIC concentration.

Based on viscosity', *in vitro* release study, *in vitro* &*ex vivo* bioadhesion studies and *ex vivo* permeation study formulation FC6 was selected as optimized bioadhesive niosomal formulation.

Fourier Transform Infrared Spectroscopy (FT-IR)

The drug polymer compatibility study was carried out by FT-IR spectroscopy. The spectrum obtained from formulation FC6 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 formulation FC6 (Table 8 and Figure 5). This Blearly suggested the absence of any drug polymer incompatibilities.

Vesicle morphology

The image from SEM analysis revealed that the

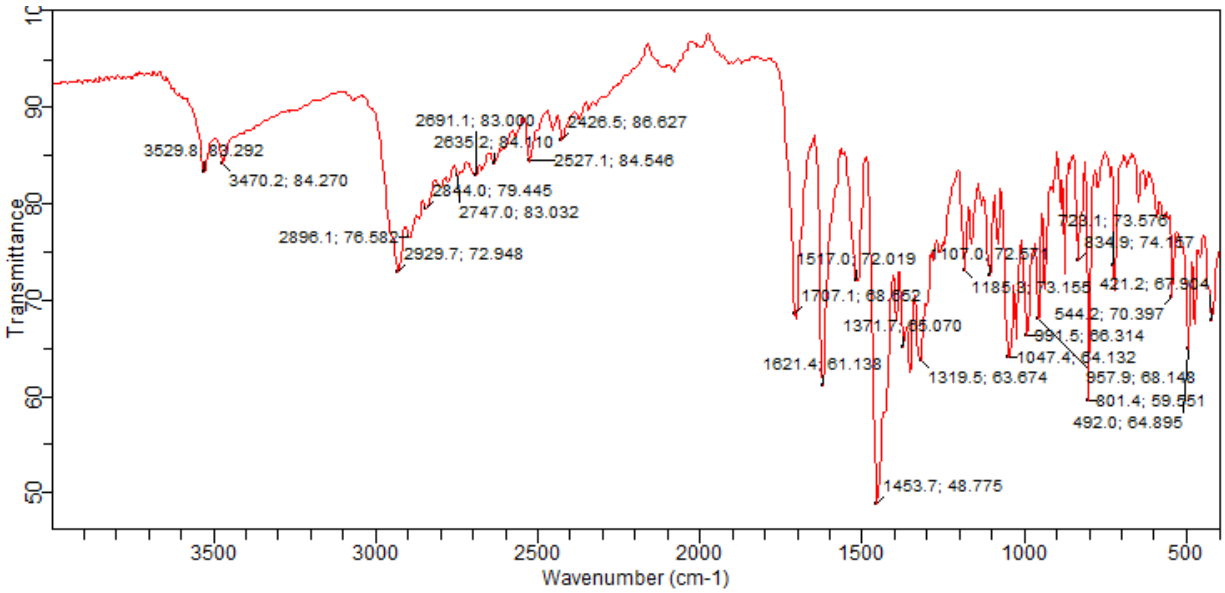

Figure 5: FT-IRspectrum of optimized niosomal formulation FC6

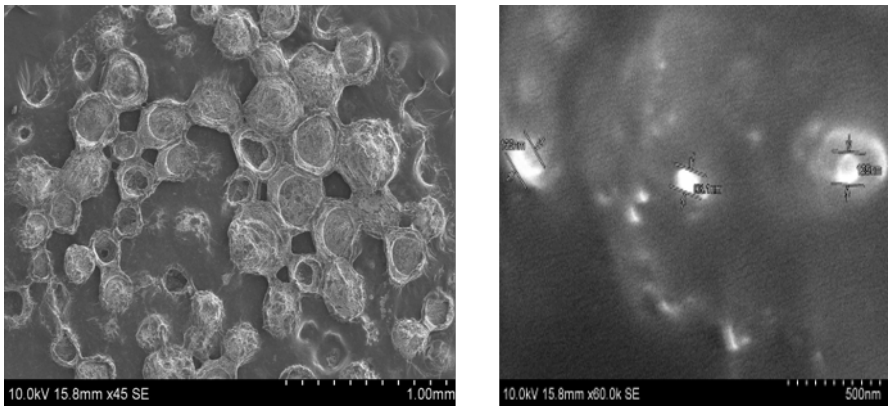

Figure 6: SEM image of optimized coated niosomal formulation(FC6) at a) 45Kmagnification b) 60K magnification

optimized bioadhesive niosomal formulation FC6 appeared to be round vesicular morphology and less than 200nm size range. Aqueous filled vesicles were observed in SEM image (Figure 6).

CONCLUSION

The novel bioadhesive niosomal formulation of moxifloxacin hydrochloride prepared by solvent injection method was found to be capable of increasing the corneal retention of the drug. It also showed enhanced permeation and a sustained drug release for a period of 24 hrs. The niosomes coated with carbopol 934 showed good bioadhesiveness and ability to sustain the drug release. Hence the novel bioadhesive niosomal formulation (FC6) was found to be a good replacement for conventional eye drops. It can reduce the frequency of drug instillation and helps in maintaining the effective drug concentration for 24hrs.

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