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DEVELOPMENT AND CHARACTERIZATION OF MOXIFLOXACIN LOADED NIOSOMAL *IN- SITU* GEL FORMULATIONS

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ABSTRACT

Niosomes are a bilayered non-toxic, non-immunogenic nanoparticular delivery system; it is being used for drug delivery. It obtained in the hydration of artificial non-ionic surfactants, without or with addition of cholesterol or additional lipids. The intention of the current study was to organize and evaluate the *in-situ* niosomal gel loaded with Moxifloxacin for the ophthalmic drug delivery system. Moxifloxacin is in the fluoroquinolone family of medications used to treat a number of bacterial infections. This includes pneumonia and tuberculosis. Moxifloxacin loaded niosomes investigate the connection among the non-ionic drug / surfactant ratio with the adding of cholesterol was successfully organized with the thin film hydration method. Niosomes have been identified by drug entrapment efficiency, drug content, particle size and in-vitro diffusion study. The niosomal in situ gel is a viable alternative to conventional eye drops by virtue of its ability to enhance bioavailability through its longer precorneal residence time and ability to sustain drug release.

KEYWORDS: Niosomes, in-situ gel, Moxifloxacin, non-ionic surfactants.

INTRODUCTION

Drug delivery of drugs efficiently on the eye is extremely complicated. Ocular dosage forms are designed to be instilled onto the external surface of the eye, administered inside or adjacent to the eye. The sequence of complex defence mechanism of the eye makes it secure and it is very tough to deliver successful concentration of the drug in target area of the eye.[1,2] Eye drops, ointments are the most conventional ophthalmic preparations. As a result of tear flow, drainage of nasolacrimal, there is quick loss from corneal layer in case of eye drops and ointments. As per a study, a very small amount (around 10) of the drug is accessible for its therapeutic effect.[3,4] This makes frequent dosing a necessity. To amplify the bioavailability of drug, this research focuses upon the expansion of nisomal in-situ gelling procedure of moxifloxacin which enhances the corneal diffusion and expands the retention time in ocular cavity. Niosomes are microscopic particles whose size is measured in nanometers (nm). Niosomal *in situ* gels for controlled release of the drug, to prolong the residence time,and to increase the bioavailability of the drug.[1]

Moxifloxacin is an antibiotic drug. Moxifloxacin is in the fluoroquinolone family of medications used to treat a number of bacterial infections. This includes pneumonia, tuberculosis, and sinusitis. It usually results in bacterial death through blocking their ability to duplicate DNA.[5-6] It is a broad-spectrum antibiotic that is active against both Gram-positive and Gram negative bacteria. It functions by inhibiting DNA gyrase, a type II topoisomerase, and topoisomerase IV, enzymes necessary to separate bacterial DNA, thereby inhibiting cell replication. Moxifloxacin is available as powder for eye drops, oral suspension, and tablet on the market.[7]

In the present investigation, the main aim was to develop a niosomal -loaded *in situ* gel formulation for ophthalmic drug delivery. The objective of this work was to improve precorneal retention time, thereby increasing therapeutic activity in a controlled release manner. Reducing the frequency of dosage will improve patient compliance.[8,9]

MATERIALS AND METHODS

Materials

Moxifloxacin Hydrochloride was obtained as a Gift Sample Span 20, Span 40, Span60 Cholesterol was purchased from Yarrow Chem Products. Chloroform, Methol Was purchased from Finar. All chemicals of analytical or pharmaceutical grade were used without further purification.

METHOD

Preparation of niosomes

Thin film hydration method

In this technique, cholesterol and span of different degree with different ratio were dissolved in chloroform and methanol, the drug was disintegrated in the solvent and

the solvent was evaporated at a temperature of 60°C, using a rotary vacuum evaporator. The combination of a thin layer of cholesterol and surfactant was mixed in the round bottom flask. The aqueous phase of the phosphate buffer solution pH 7.4 (10 ml) was added to the round bottom flask 60°C and stirred for about 15 minutes, which results in a fine dispersion of the mixture and the niosome is produced.[10-12]

Preparation of moxifloxacin niosomal in situ gel

Poloxamer based in situ ophthalmic gel were prepared by the modified cold method. Briefly, poloxamer (P407) and required amount of HPMC K4M was slowly added to the calculated amount of cold acetate buffer (pH 6.5) with continuous mixing using a thermostatically controlled magnetic stirrer. The partially dissolved poloxamer solutions were stored in a refrigerator and stirred periodically until clear homogenous solutions were obtained (approximately 24 h). The ophthalmic formulations were prepared by dissolving the appropriate amount of moxifloxacin, 0.5% (w/v), in the calculated amount of acetate buffer during the mixing step.[13-15]

Table 1: Composition of niosomes.

Drug(mg)	Cholesterol(mg)	Span20(mg)	Solvent (Chloroform: Methanol) (2:1)
50	100	100	15
50	95	105	15
50	90	110	15
50	85	115	15

Evaluation of the formulations

Determination of pH: The ophthalmic formulations should have a pH 6.6-9.0 to avoid irritation. pH of the niosomal formulations were determined using pH meter.[16]

Drug entrapment efficiency: The portion of the encapsulated moxifloxacin hydrochloride was obtained by ultra-centrifugation 1ml of the niosomal suspension at 18000 rpm for 1hour using a cooling centrifuge at 4°C . The supernatant was removed and the formed niosomal pellets were re-suspended in phosphate buffer saline (PBS) pH 7.4 to ensure the complete removal of all free moxifloxacin hydrochloride. The supernatant (free moxifloxacin hydrochloride) was collected and measured using UV spectrophotometer at 287 nm using PBS pH 7.4 as blank.[17,18] It was calculated using the following equation.

%Entrapment efficiency = Entrapped amount of drug /Total amount of drug added ×100

Particle size and zeta potential: The normal particle size of the drug loaded niosomes and the zeta potential of the whole formulation was determined by malvern zeta sizer nano ZS (Malvern Instrument Ltd., worcestershire, UK). The entire sample were diluted with bidistilled water to reach an appropriate concentration before measurement.[19,20]

Appearance and pH

Clarity testing was performed on all developed formulations by visual observation of the samples to examine the presence of any transparent or coloured particulate matters or turbidity. The pH of the various gels was determined by calibrated pH meter.[21-23]

Drug content

Uniform distribution of active ingredients is important to achieve dose uniformity. The drug content of various gels was determined by placing the sample (2 ml) of the in-situ gel in a 100 ml volumetric flask and diluting the same with STF of pH 7.4. The UV absorbance of the resulting sample was then measured at 287 nm and using the standard curve percentage drug content was determined.[24]

Rheological evaluation

The rheological study of the formulation was measured by taking the sample in 150 ml beaker. Viscosity of the sample was measured using Brookfield viscometer LV-III, using appropriate spindle.[25]

Gelation Temperature

GT was measured by a magnetic bar method. In brief, 10 ml of the formulation was taken in 20 ml beaker. The formulation was stirred using the magnetic bar and gradually heated at the rate of 1 °C/min. The temperature at phase transformation of the formulation was noted when the movement of magnetic bar was hindered.[26]

In vitro drug release studies: In vitro drug release studies of drug from niosomes were carried out using membrane diffusion technique. In vitro diffusion cell was made using dialysis membrane as a semi permeable membrane. The diffusion cell consists of a test tube with both ends open. One end of the test tube was closed using presoaked dialysis membrane and the other end was open to introduce the niosomes formulation. an accurately measured amount of moxifloxacin niosomes formulation equivalent to 2 mg was suspended in 1ml PBS (pH 7.4) and then transferred it to test tube, having a diameter of 2.5cm that was covered with a dialysis membrane (12000-14000 molecular weight cut off). The test tube was suspended in the dissolution flask

of a USP dissolution apparatus containing 75 ml PBS pH 7.4. The temperature of the solution was maintained at 37±0.5 °C and the glass tube was allowed to rotate at a constant speed (50 rpm). aliquots of the medium was withdrawn every hour and replaced with fresh PBS (pH 7.4). The samples were analyzed using U/Visible spectrophotometer at 287 nm.[22]

Table 2: Evaluation parameters of formulations.

Formulation Code	Entrapment Efficiency	Particle Size (nm)	Zeta Potential (mV)	pH
MN 1	43.13	3652	-15.2	7.35
MN 2	41.92	3296	-14.8	7.38
MN 3	39.23	2305	-14.9	7.42
MN 4	46.24	3793	-22.4	7.38
MN 5	42.42	3403	-21.5	7.39
MN 6	40.09	2668	-22.6	7.41
MN 7	48.45	3961	-30.3	7.33
MN 8	45.67	3581	-29.0	7.40

Determination of Entrapment Efficiency, Particle Size, Zeta Potential, pH

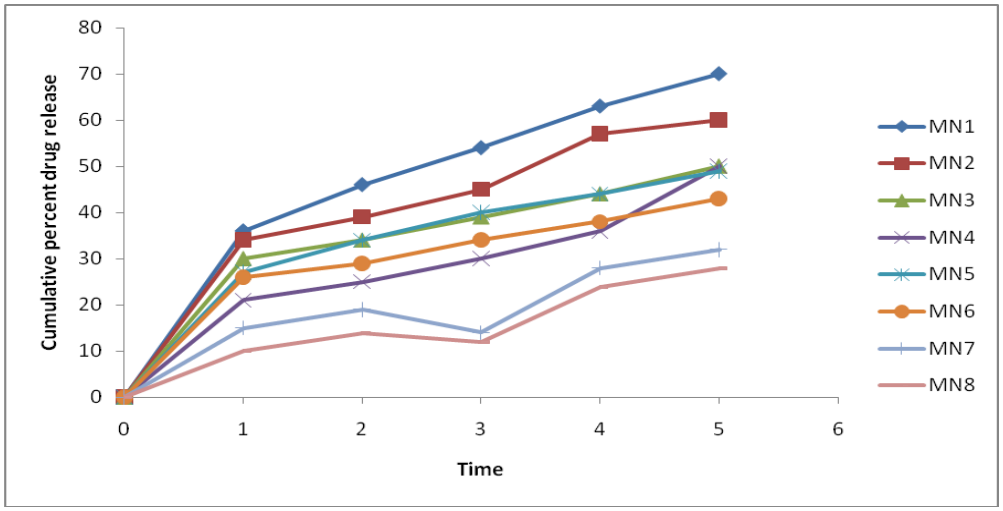

Figure 1: Release profile of different formulations.

CONCLUSION

Ocular efficacy and ocular bioavailability are directly related. They can be further improved by enhanced penetration of corneal drug and also prolonging the cessation time of the precorneal drug. A significant increase in precorneal abode time of the drug can be achieved and subsequently, higher bioavailability through the use of administration systems based upon the concepts of in-situ Niosomal gel. Therefore, Niosomal in-situ eye gel have an advantage over the other forms of ophthalmic dosage (eye drops, suspensions, ointments) to increase penetration and bioavailability of the cornea. Present study concludes effective delivery of the Moxifloxacin by the means of niosomes, however there is need of some more in-vivo experiments' on it.

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