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FORMULATION AND EVALUATION OF NIOSOMAL GEL OF GATIFLOXACIN

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ABSTRACT

The objective of the work was to formulate niosomes of a drug meant for infections caused due to Gram-positive and Gram-negative bacteria. Gatifloxacin sesquihydrate was white crystalline odorless powder. When tested for its solubility in various solvents, it was determined that drug sample was slightly soluble in water and 0.1 HCl, soluble in methanol, ethanol and Buffer 7.4 pH etc. melting point observed 182-185°C. Gatifloxacin sesquihydrate solution was scanned in the U.V. range of 200-400 nm. The spectrophotometric method of analysis of Gatifloxacin at λ_{max} 292 nm was found. The standard curves were prepared in Methanol at λ_{max} 292 nm. The data were regressed to obtain the straight line. The correlation coefficient was 0.996 while the concentration range of 2-10 µg/ml. Partition coefficient value of Gatifloxacin was 2.54 revealed its Lipophilic nature. The IR spectrum of drug substance was authenticated using IR spectroscopy. Niosomes were prepared by the thin-film hydration method. Gatifloxacin loaded niosomal dispersion was off-white in color and fluid in nature. It was stable and did not show sedimentation. pH was found to be in the range of 5.1-6.8. Vesicle size found 1.42 to 2.13µm, Percentage drug content found 91.26 to 99.14% and viscosity was 2.255 to 3.333. The values of zeta (ζ) potential of the drug loaded niosomal formulation were in the range of-20.29 to -27.77mV. Formulations F5 and F6 had 90.21 and 95.25% of drug release respectively. It can be concluded that for better stability, the formulations should be stored at low temperature in refrigerator.

KEYWORDS: Gatifloxacin sesquihydrate, Niosomes, gel, Evaluation.

INTRODUCTION

The basic goal of novel drug delivery system is to achieve a steady state blood or tissue level that is therapeutically effective and non toxic for an extended period of time.[1] Conventional drug delivery involves the formulation of the drug into a suitable form, such as compressed tablet for oral administration or a solution for IV administration.[2] A Niosome is a non-ionic surfactant-based Vesicle (biology and chemistry).[3] Niosomes are formed mostly by non-ionic surfactant and cholesterol incorporation as an excipient[4] oher excipients can also be used.[5] Niosomes are vesicular system similar to liposome that can be used as carriers of hydrophilic, amphiphilic and lipophilic drugs.[6] Niosomes are noval drug delivery system in which the medication is encapsulated in vesicles.[7] Niosomal delivery systems are a desirable form of drug delivery because of the obvious advantages over other delivery systems.[8] Niosomal drug delivery offers controlled release of the drug into the patient, it enables a steady blood-level profile, resulting in reduced systemic side effects and, sometimes, improved efficacy over other dosage forms.[9]

To develop a Niosomal Gel of gatifloxacin for formulate and evaluate the prepared gel for its pH, viscosity, drug content and spreadability. Also investigate the effect of permeation of gel formulations.

MATERIAL AND METHOD

Gatifloxacin sesquihydrate was a kind gift from Zydus Cadila, Ahmedabad, India. $NaH_2PO_4H_2O$, lecithin, Span 20, chloroform, carbopol 940 was used. Systronics UV-2203 UV/Vis double beam spectrophotometer, centrifuge (Remi, India), Optical Microscopy, Scanning Electron Microscopy (SEM) also used.

Methods

Preformulation Study

Determination of Solubility: A fixed amount of drug was taken, and then distilled water was added and observes the solubility visually. Solubility study should be performed for gatifloxacin to determine in which solvent it is soluble, for that various solvents like water, methanol, 0.1N NaOH, 0.1N HCl, Ethyl acetate was used, for determining the solubility the drug should be dissolved in individual solvent in 1:10 ratio (Drug: Solvent) and visually observed for its solubility.

Melting Point: The Melting point was determined by the capillary method using Digital Melting point apparatus. The capillary tube was fused and filled by pressing the open end gently into pure drug sample and packed by tapping the bottom of the capillary on a hard surface so that the drug packed down into the bottom of the tube. When the drug was packed into the bottom of the tube, the tube was placed into the slot of the apparatus, the apparatus was started and the temperature was noted at which the drug melt.

Preparation of Ph 7.4 Buffer: Prepare 800 mL of distilled water in a suitable container. Add 20.214 g of Na_2HPO_4-$7H_2O$ to the solution. Add 3.394 g of $NaH_2PO_4H_2O$ to the solution. Adjust solution to final desired pH using HCl or NaOH Add distilled water until volume is 1 L.

Analytical estimation by UV Spectrophotometer

Determination of Wavelength of Maximum Absorbance (λ_{max}): 10 mg of drug was weighed accurately and transferred to 100 ml of volumetric flask. Then 0.1M pH 7.4 phosphate buffers, was added to dissolve the drug completely. The volume was made up to 10 ml with pH 7.4 phosphate buffers, The prepared sample was 100 µg / ml. 10 ml of above solution was then transferred to another 100 ml volumetric flask and diluted it upto the mark with pH 7.4 phosphate buffers,. This sample was 10 µg / ml.

Preparation of Calibration Curve

Preparation of stock solution: Gatifloxacin (10 mg) was dissolved in 1ml pH 7.4 phosphate buffers, and volume was made upto 10 mL volumetric flask using pH 7.4 phosphate buffers. 1mL of stock solution (1 mg/mL) was further diluted with pH 7.4 phosphate buffers, up to 10 mL. This solution (100µg/mL) was further diluted to pH 7.4 phosphate buffers, to obtain solutions of 2 to 10 µg/mL. Absorption of each solution was measured at 292 nm. Using Systronics UV-2203 UV/V is double beam spectrophotometer and pH 7.4 phosphate buffers, as a reference standard.

Gatifloxacin (10 mg) was dissolved in 1mL distilled water and volume was made upto 10 mL volumetric flask using distilled water. 1mL of stock solution (1 mg/mL) was further diluted with distilled water to 10 mL. This solution (100µg/mL) was further diluted to distilled water to obtain solutions of 2 to 10 µg/mL. Absorption of each solution was measured at 292 nm using Systronics UV-2203 UV/Vis double beam spectrophotometer and distilled water as a reference standard.

Scanning of drug in the range of 200-400 nm

Preparation of dilutions from stock solution: From this stock solution 2, 4, 6, 8, 10 ml was pipette out in 100 ml calibrated volumetric flask and dilutions of 2, 4, 6, 8, 10 µg/ml was obtained. The absorbance of these solutions was taken on double beam U.V. spectrophotometer using λ_{max} at 292 nm. The absorbance values were plotted against concentration (µg/ml) to obtain the standard calibration curve. Same procedure was fallowed for distilled water.

Partition Coefficient: Normally one of the solvents chosen is water while the second is hydrophobic such as n-Octenol. Hence both the partition and distribution coefficient are measures of how hydrophilic ("water loving") or hydrophobic ("water fearing") a chemical substance. A partition coefficient can also be used when one or both solvents are a solid though. In medical practice, partition coefficients are useful for example in estimating distribution of drugs within the body.

Drug and Excipients Compatibility Study by FT-IR Spectra Analysis: FT-IR Spectroscopy can be used to investigate and predict any physicochemical interactions between different components, in a formulation and therefore it can be applied to selection of suitable chemically compatible excipients. While selecting the ingredients, we would choose those which are stable, compatible and therapeutically acceptable. The aim of compatibility study was to test, whether there is any interaction between the excipients and the drug and compatibility between the drug and excipients.

Formulation of Niosomes

Different batches of niosoms of gatifloxacin were prepared by changing the proportions of drug surfactant and lecithin using thin-film hydration technique. Span 20, Lecithin and gatifloxacin were dissolved in a mixture of chloroform in a round bottom flask. The rotary flash evaporator was used to evaporate solvent until thin, dry and uniform film is formed. The thin dry lipid film thus formed was hydrated using phosphate-buffered saline (pH 7.4) at a temperature slightly above the glass transition temperature (Tg) of Span 20 (49±1°C). The formed niosomal suspension was first sonicated to convert into desired size unilamellar vesicles and then subjected to centrifugation at 3000 rpm and 4°C for 15 min using laboratory centrifuge (Remi, India) to affect sedimentation of unentrapped drug as sediment at the bottom of the centrifugation tube. Supernatant was decanted and characterized for vesicle size and percentage of drug entrapment (PDE) while the drug sediment was used to measure

unentrapped drug in order to ascertain mass balance. The formulation process parameters were optimized to achieve maximum possible drug entrapment with desirable size range.

Optimization of Process-Related Variables in Niosome Formulation

The process-related variables of sonication time, hydration medium, hydration time, speed of rotation of flask evaporator and charge-inducing agents were investigated in vesicle formation with Span 20 and lecithin with a fixed amount of Gatifloxacin by trial and error method.

Method of formulation of niosomal Gel of Gatifloxacin

Dissolve 0.5 g of carbopol 940 in water were mixed together using a magnetic stirrer, at 100 rpm. By keeping Gatifloxacin loaded Niosomes in constant amount in all the formulations. Gatifloxacin loaded Niosomes was poured into the polymer solution. The solution was kept under stirring and then the pH was adjusted. The formulated gels were taken for further analysis.

Methods of Characterization of Niosomes

Optical Microscopy: A drop of niosomal suspension was placed on the microscopic glass slide. Photographs of sonicated and nonsonicated formulations were taken at 40x magnification using the digital camera attached to the eye piece of the microscope. Shape and lamellar nature of the nonsonicated vesicles was confirmed with the photographs.

Scanning Electron Microscopy (SEM): The morphology of the niosomes was investigated by SEM. The representative SEM photographs of the niosomal suspension are shown in Figure SEM images showed that niosomal suspension were finely spherical and uniform; no entire drug crystals were observed visually.

Vesicle Size Determination: Vesicle size of sonicated formulation was determined by optical microscopy using a pre-calibrated eye piece. Eyepiece was calibrated using stage micrometer at 40x magnification. Size of each division of eyepiece micrometer was determined using the formula:

$$\textbf{Size of each division} = \frac{\text{Number of divisions of stage micrometer}}{\text{Number of divisions of eye piece micrometer}} \text{ X } 100$$

The average diameter of 100 vesicles was counted for 3 times at different time intervals after 4 hours for the prepared formulation.

Determination of Viscosity: Viscosity of the formulations was determined using Ostwald viscometer. The time taken for water and formulations to flow from point A to B was calculated and substituted in the formula and the viscosity was calculated as:

$$\textit{viscosity of sample}(\eta 1) = \frac{\rho 1 * t1}{\rho 2 * t2} \times \eta 2$$

Where,

ρ1 – density of sample

ρ2 – density of water

η1 – viscosity of sample

η2 – viscosity of water

t1 – time taken by the sample to flow from point A to B

t2 – time taken by water to flow from point A to B

Determination of Drug Entrapment in Vesicles: Niosomal formulations were centrifuged at 15,000 rpm for 15 min at 4ºC using a refrigerated centrifuge to separate niosomes from non-entrapped drug. Concentration of the free drug in the supernatant was determined by measuring absorbance at 292 nm with a UV spectrophotometer. The percentage of drug entrapment in niosomes was calculated using the following formula. This process was repeated thrice to ensure that free drug was completely removed.

$$\% \text{ Drug entrapment} = \frac{\text{Total drug - Drug in supernatant}}{\text{Total drug}} \times 100$$

***In -vitro* Release Studies**

In vitro release was studied using a dialysis bag as a 'donor compartment'. Niosomes containing entrapped Gatifloxacin obtained after centrifugation of 2 ml of the formulation were resuspended in 1 ml of PBS, pH 7.4, and used for the release study. The dialysis membrane was soaked in warm water for 10 min, one end was sealed with a clip, the niosome preparation or drug in solution was pipetted into the bag and the bag was sealed with another closure clip to prevent leakage. The dialysis bag was placed in 50 ml of PBS, pH 7.4, at 37 ± 2^{o}C. The medium, which acted as the receptor compartment, was stirred at 100 rpm. Samples of medium (5 ml) were withdrawn hourly and replaced with fresh buffer and Gatifloxacin absorbance at 292 nm was measured using PBS as blank. Results were the mean values of three runs.

$$\% \text{ Drug release} = \frac{\text{Conc. obtained from graph } (\mu g/ml) \text{ X Total vol. of dissolution medium X } 100}{\text{Amount of drug present in 1 ml of niosomal formulation X } 100} \text{ X Dilution factor}$$

Method of Evaluation of Niosomal Gel

Measurement of pH: The pH of the gel formulations is delivered by using digital pH meter. Before measurement pH meter should calibrated then readings taken by dipping the glass rod into the gel formulations.

Viscosity Measurement: The viscosity of gel formulations determine by Brookfield viscometer. 25.0 g gel was taken in beaker and spindle number 4 was rotated at 50 rpm and viscosity of the sample determine by calculation.

Spreadability: The spreadability of gel formulations determine by using spreadability apparatus. 1.0 g of gel sample placed on the lower slide and upper slide was placed on the top of the sample. The spreadabilit determine by the formula where spreadability, is weight tied to upper slide, is length travel by upper slide, and is time taken.

***In-vitro* Permeation Studies:** The *In-Vitro* permeation studies of niosomal gel carried out with Franz diffusion (FD) cell using egg membrane followed by hydration for 30 minutes in PBS pH 7.4 at room temperature to remove the extraneous debris and leachable enzymes. Then excised egg membrane placed between donor and receptor compartments of the FD cell. Gel place in donor compartment and PBS pH 7.4 fill in receptor compartments as media. Temperature of cell was maintained at 37°C ± 0.5°C. The assembly kept on magnetic stirrer and samples withdrawn at time intervals of 1, 2, 3, 4, 6, 8, 12, and 24 h and replaced with equal volume of fresh media. Samples analyzed by UV spectrophotometer at 292 nm and calculate cumulative % of drug release.

Stability Studies

Niosomal formulation will selected on the basis of entrapment efficiency *and in vitro* release studies. Stability studies will assessed by keeping niosomal suspension and niosomal gel in sealed glass vials and storing them in two different storage conditions, that is, refrigeration temperature and room temperature for a period of 30 days. The samples withdrawn at different time intervals over a period of one month and the residual content was determined spectrophotometrically.

RESULTS AND DISCUSSION

Preformulation

Physical Appearance: The drug Gatifloxacin sesquihydrate powder was examined for its organoleptic properties like colour and odour and it was observed that Gatifloxacin sesquihydrate was white crystalline odorless powder.

Solubility study: The sample was qualitatively tested for its solubility in various solvents. It was determined in various solvent e.g. Slightly Soluble in water and 0.1 N HCl, Soluble in methanol and Ethanol, Sparingly soluble in NaOH. at room temperature.

Melting point determination: Melting point of Gatifloxacin sesquihydrate was observed at 182-185°C.

Preparation of calibration curves: Gatifloxacin sesquihydrate solution was scanned from 200-400 nm using UV Visible spectrophotometer. The standard curve prepared in Methanol at λ_{max} 292 nm. The data were regressed to obtain the straight line. The correlation coefficient greater than 0.996 was observed in all the cases, which indicated that, the drug follows Beer-Lambert's law in the concentration range of 2-12 µg/ml.

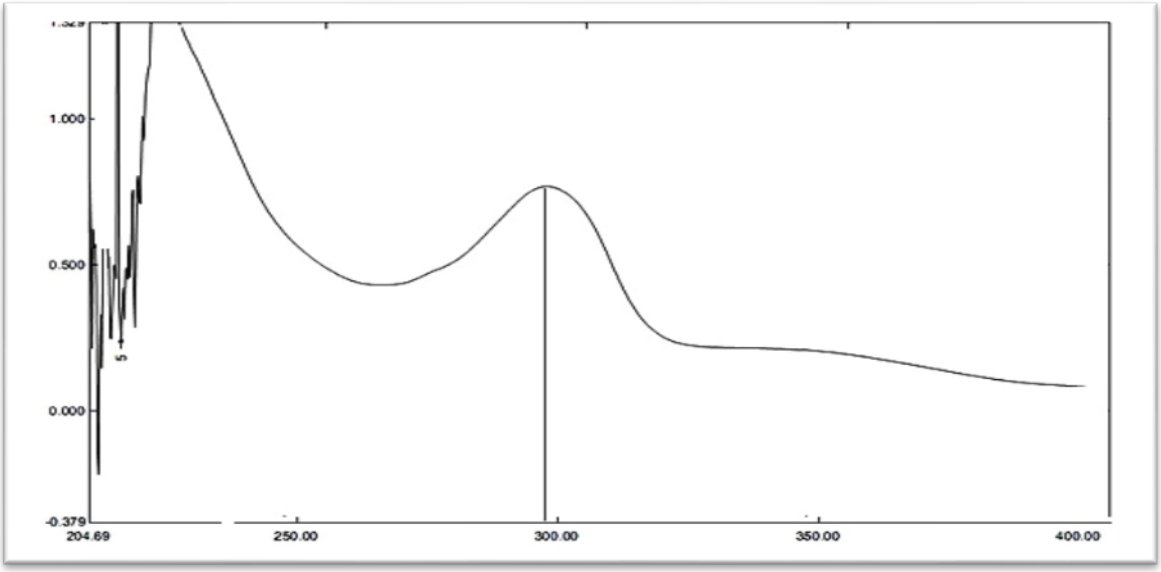

Figure 7: Absorption spectra of Gatifloxacin (10 µg mL^{-1})

Preparation of Calibration Curve of Gatifloxacin in Methanol

Table no. 6: Standard Curve of Gatifloxacin.

Concentration [X] (µg/ml	0	2	4	6	8	10
Absorbance [Y] at 292 nm	0	0.99	0.191	0.286	0.376	0.483

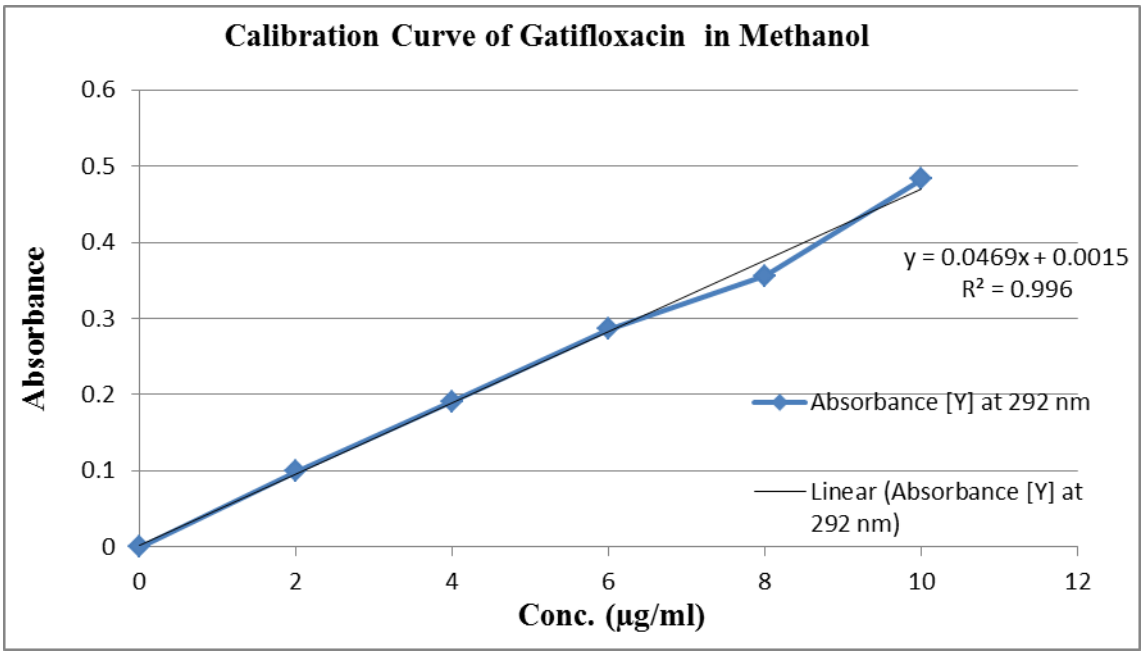

Figure 8: Calibration curve of Gatifloxacin in Methanol at 292 nm.

The calibration curve of drug was prepared in methanol. The slope and intercept of the calibration curve were 0.018 and 0.001 respectively. The correlation coefficient 'r^2' values were calculated as 0.996 as shown in table.

Partition coefficient: Partition coefficient study was carried out and found 2.54. Partition coefficient value of Gatifloxacin also revealed its Lipophilic nature.

Fourier-Transform Infra Red spectroscopy (FTIR): The IR spectrum of drug substance was authenticated using IR spectroscopy. The presence of characteristic peaks associated with specific structural characteristics of the drug molecule was noted. Various peaks of the drug are shown in figure and shown in table with its band frequencies.

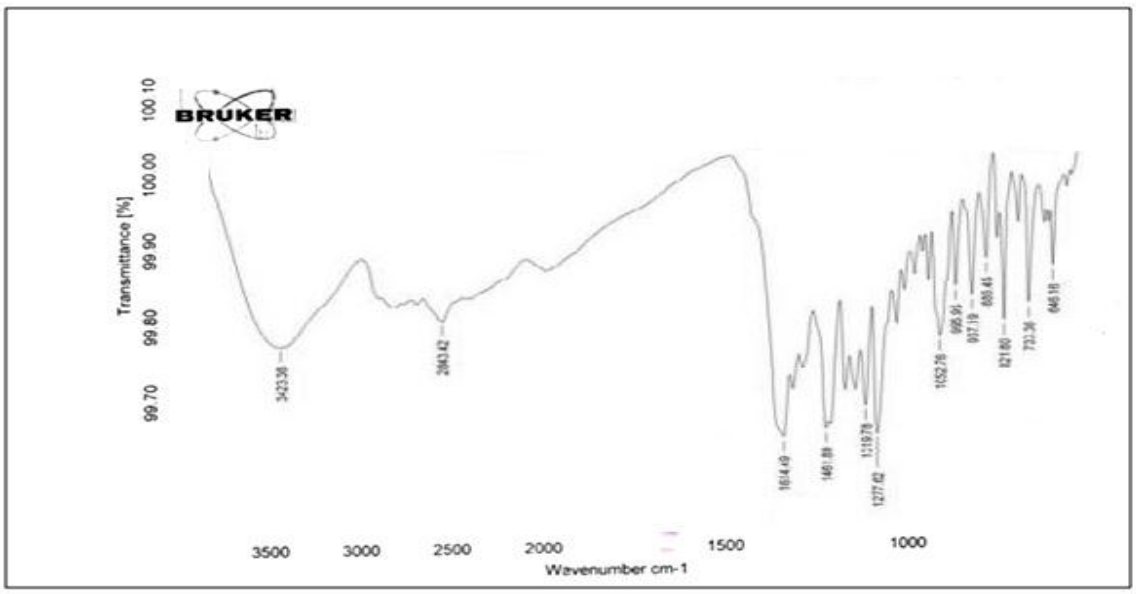

Figure 9: FT-IR of Gatifloxacin drug sample.

Table no. 8: Important band frequencies in IR spectrum of Gatifloxacin sesquihydrate.

S. No	Functional Group	Frequency (cm^{-1})
1.	-COOH (O-H Stretch)	3000
2.	-COOH (C=O Stretch)	1685
3	-CH3 (C-H Stretch)	2870
4.	Aromatic C-H (C-H Stretch)	900 – 750

Optimization of Process-Related Variables in Niosome Formulation

Table no. 9: Optimization of Process-Related Variables in Niosome Formulation.

S. No	Batch No.	Lecithin : Span 20 µM ratio	Hydration medium	Hydration volume (ml)
1	F1	1:1	PBS pH 7.4	10
2	F2	1:2	PBS pH 7.4	10
3	F3	1:3	PBS pH 7.4	10
4	F4	1:4	PBS pH 7.4	10
5	F5	1:5	PBS pH 7.4	10
6	F6	1:6	PBS pH 7.4	10

Evaluation of Niosomal Formulation

Developed niosomal formulations were characterized with respect to particle size, shape, entrapment efficiency, and in vitro drug release profile.

Surface Morphology of Gatifloxacin Niosomes: Gatifloxacin niosomes shape and lamellar structure were determined by optical microscopy method specified for optimized formulations F3, F4 and F6 in figure below:

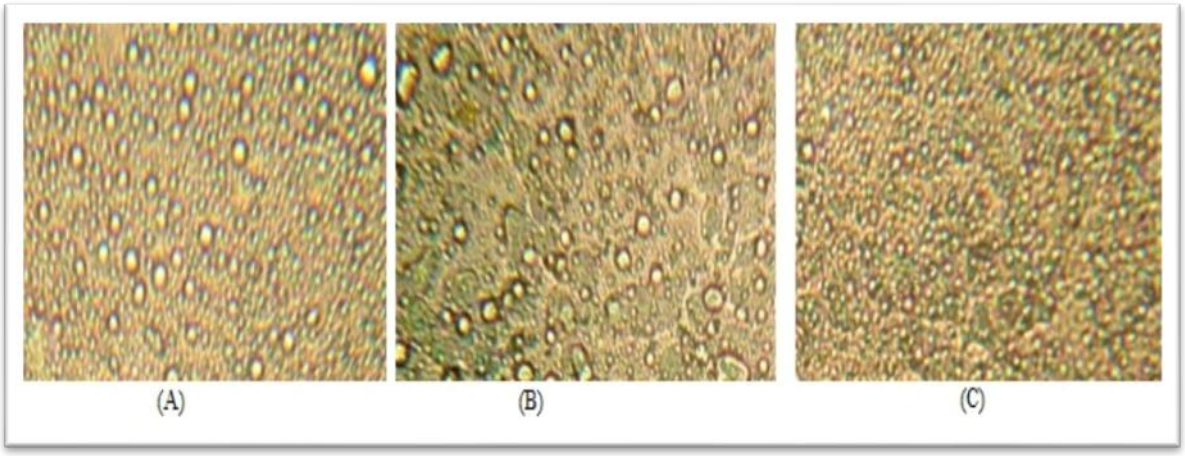

Figure 11: Photomicrographs of formulations (A) F3, (B) F4 & (C) F6.

Photomicrographs revealed that niosomes formulated with span 20 were spherical and sonicated vesicles exist without aggregation upto 15 days when compared with non-sonicated vesicles.

Physical Parameters, Drug Content, pH, Vesicle size and Viscosity of niosomal

Gatifloxacin loaded niosomal dispersions were off-white colored fluid. All were stable without showing sedimentation. pH was found to be in the range of 5.1-6.8. Summarize data of all the six batches of factorial design is shown in table. Viscosity of niosome formulations was determined using Ostwald viscometer.

Table no. 11: Drug content in niosomal formulation.

Formulation code	Appearance	pH	Vesicle size (µm)	%Drug content ± S.D.	Viscosity (centipoise)
F1	Off-white	5.3	1.42 ± 0.53	98.31 ± 0.45	3.196
F2	Off-white	6.4	1.75 ± 0.52	91.26 ± 0.61	3.067
F3	Off-white	6.3	1.84 ± 0.73	93.31 ± 0.89	3.177
F4	Off-white	6.8	1.83 ± 0.12	98.17 ± 0.92	2.255
F5	Off-white	5.5	1.54 ± 0.43	98.52 ± 1.10	3.148
F6	Off-white	5.1	2.13 ± 0.24	99.14 ± 0.87	3.333

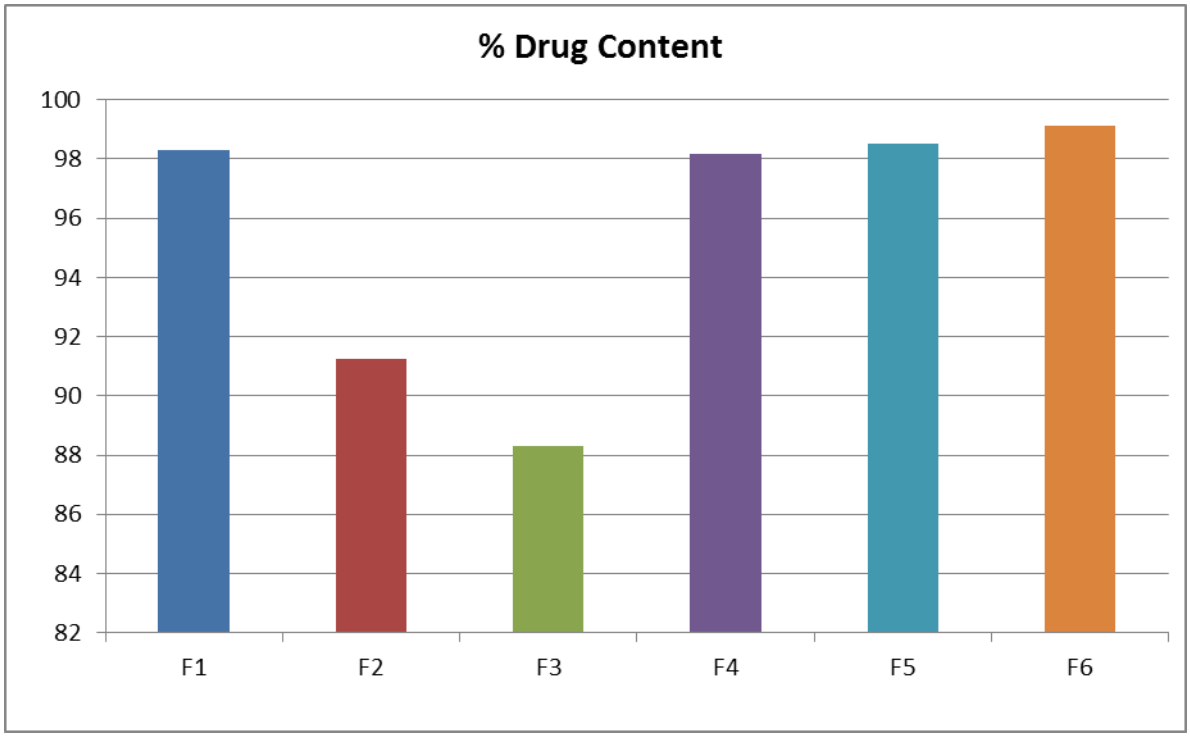

Figure 12: %Drug Content in Niosomal Formulation.

Zeta Potential, Polydispersibility index and Entrapment efficiency of niosomes

Table no. 12: Evaluation of Gatifloxacin Niosomal batches.

Formulation code	Polydispersibility Index	Entrapment Efficiency (%) ± S.D	Zeta Potential (Mv) ± S.D
F1	0.411	75.52 ± 1.13	-7.77 ± 1.55
F2	0.389	73.60 ± 1.39	-4.84 ± 0.79
F3	0.420	69.05 ± 1.14	-5.29 ± 1.03
F4	0.385	79.60 ± 2.26	-5.44 ± 0.92
F5	0.325	78.09 ± 1.94	-6.07 ± 1.75
F6	0.370	74.84 ± 1.60	-6.57 ± 0.16

***In-vitro* Release Studies of Niosome Formulations**

In-vitro release was studied using a dialysis membrane.

Table no. 14: *in-vitro* Release from Niosome Formulation.

Time in hours	Cumulative % Drug release					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	35.01	30.35	27.53	25.32	06.42	12.12
2	45.32	34.76	37.83	31.82	13.12	23.82
3	56.38	42.23	54.42	37.36	19.09	28.12
4	63.78	49.19	60.48	45.12	25.32	34.14
5	76.68	52.65	64.12	54.82	33.86	40.72
6	87.38	57.73	68.83	61.32	41.42	48.82

7	89.49	64.18	71.12	68.21	49.32	55.64
8	90.62	69.38	77.34	74.14	57.72	64.78
9	91.38	75.47	81.13	79.26	65.82	72.72
10	92.14	81.01	88.38	81.12	73.81	80.76
11	92.57	86.26	89.11	83.46	82.32	88.13
12	92.94	87.32	89.88	85.56	90.21	95.25

*Each value was an average of three determinations

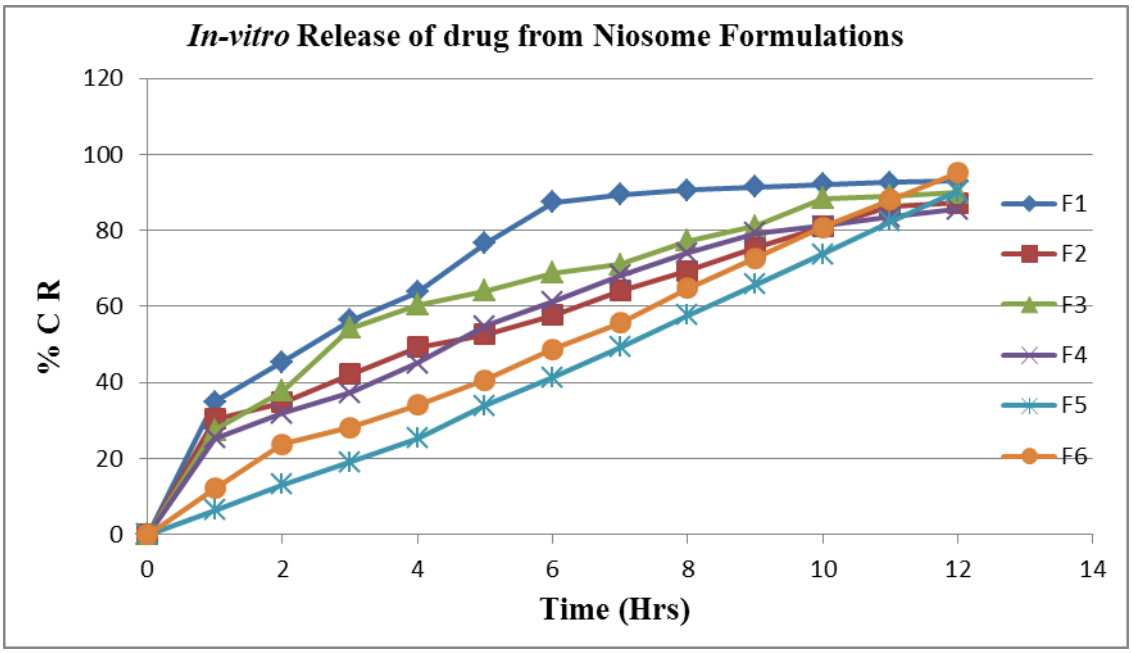

Figure 15: *In-vitro* Release of drug from Niosome Formulations.

7.5 Formulation of Niosomal gel

Table no. 15: Formulation of Niosomal gel of Gatifloxacin.

Formulation	GF-1	GF-2	GF-3	GF-4	GF-5
Niosome (g)	0.4	0.4	0.4	0.4	0.4
Carbaol 940 (g)	0.5	0.5	0.5	0.5	0.5
Distilled water (g)	100	100	100	100	100

7.6 Evaluation of Niosomal Gel on the basis of following parameter

Table no 16: Evaluation of Niosomal gel of Gatifloxacine.

Formulation code	Clarity	Phase Separation	Washability	Homogeneity	Grittiness
GF-1	Clear	No	Washable	Yes	No
GF-2	Clear	No	Washable	Yes	No
GF-3	Clear	No	Washable	Yes	No
GF-4	Clear	No	Washable	Yes	No
GF-5	Clear	No	Washable	Yes	No
GF-6	Clear	No	Washable	Yes	No

Table no. 17: Evaluation of Niosomal gel of Gatifloxacine on following parameter.

Formulation code	pH	Spread ability(cm)	% Drug Content	Viscosity (cp)	%Permeation
GF-1	7.0	5.6 ± 0.5	99.32 ± 1.2	83 ± 1.8	78%
GF-2	7.2	5.7 ± 0.3	98.02 ± 1.3	98 ± 2.0	89%
GF-3	7.6	5.8 ± 0.1	96.01 ± 1.1	100 ± 1.2	87%
GF-4	7.0	6.0 ± 0.6	99.64 ± 1.7	100 ± 0.8	89%
GF-5	7.1	6.1 ± 0.3	99.81 ± 0.4	116 ± 1.1	91%
GF-6	7.2	6.1 ± 0.4	99.01 ± 0.2	118 ± 1.5	93%

Stability Studies

Table no 18: Stability of Niosomal gel of Gatifloxacine at Different Conditions.

Formulation code	Phase separation		pH		Drug content (%)	
	4°C	**40 °C**	**4°C**	**40 °C**	**4°C**	**40 °C**
GF-1	No	No	6.9	7.0	100±1.1	95±2.0
GF-2	No	No	7.4	7.3	100±1.8	99±1.9
GF-3	No	No	7.4	7.2	98±1.9	98±1.8
GF-4	No	No	7.2	7.1	99±0.6	92±1.0
GF-5	Yes	Yes	7.1	7.4	101±1.9	97±2.1
GF-6	Yes	Yes	7.5	7.5	99±1.4	98±1.2

DISCUSSION

The objective of the work was to formulate niosomes of a drug meant for infections caused due to Gram-positive and Gram-negative bacteria. Preformulation testing is the first step in the rational step in the development of dosage forms of a substance. It can be defined as an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. The overall objective of preformulation testing is to generate information useful to the formulator in developing stable and bioavailable dosage forms that can be produced. The drug Gatifloxacin sesquihydrate powder was examined for its organoleptic properties found it was observed that Gatifloxacin sesquihydrate was white crystalline odorless powder. When tested for its solubility in various solvents, it was determined that drug sample was slightly soluble in water and 0.1 HCl, soluble in methanol, ethanol and Buffer 7.4 pH etc. melting point observed 182-185°C. Gatifloxacin sesquihydrate solution was scanned in the U.V. range of 200-400 nm using Shimadzu UV Visible spectrophotometer. The spectrophotometric method of analysis of Gatifloxacin at λ_{max} 292 nm was found to be reproducible and highly sensitive. The standard curves were prepared in Methanol at λ_{max} 292 nm. The data were regressed to obtain the straight line. The correlation coefficient greater than 0.996 was observed in all the cases, which indicated that, the drug follows Beer-Lambert's law in the concentration range of 2-10 µg/ml. Partition coefficient

studies are carried out to find extent of drug transfer in the aqueous and the other non aqueous layer. Partition coefficient value of Gatifloxacin was 2.54 revealed its Lipophilic nature. The IR spectrum of drug substance was authenticated using IR spectroscopy. The presence of characteristic peaks associated with specific structural characteristics of the drug molecule was noted. -COOH (O-H Stretch) 3000; -COOH (C=O Stretch) 1685 and CH_3 (C-H Stretch) 2870. Drug and polymer compatibility study reveals that there is no incompatibility between drug and polymer thus can be used for further formulation and evaluation purposes. Niosomes were prepared by the thin-film hydration method. The thin films were hydrated with 10 ml of phosphate buffered saline (PBS) pH 7.4 and the formulations were sonicated 3 times at 50 Hz in a bath-sonicator for 15 min with 5 min interval between successive times. Vesicle suspensions were also sonicated for 5 min and 2 min.

Gatifloxacin niosomes shape and lamellar structure were determined by optical microscopy method specified for optimized formulations. Photomicrographs revealed that niosomes formulated with Span 20 were smooth and spherical in shape. Sonicated vesicles exist without aggregation upto 15 days when compared with nonsonicated vesicles. Gatifloxacin loaded niosomal dispersion was off-white in color and fluid in nature. It was stable and did not show sedimentation. pH was found to be in the range of 5.1-6.8. Vesicle size found 1.42 to 2.13µm, Percentage drug content found 91.26 to 99.14% and viscosity was 2.255 to 3.333. The values of zeta (ζ) potential of the drug loaded niosomal formulation were in the range of-20.29 to -27.77mV. Values of zeta (ζ) potential showed that the drug loaded niosome had sufficient charge and mobility to inhibit aggregation of vesicles. Polidispersibility index and entrapment efficiency was also excellent. Formulations F5 and F6 had 90.21 and 95.25% of drug release respectively. Niosomal Gatifloxacin formulations with fast drug release in the initial hours may be due to the release of adsorbed drug from the lipophilic region of niosomes which will help to achieve the optimal loading dose. When the concentration of lecithin was high in span 20 the drug release was higher initially.

Formulated niosomal preparation incorporated in gels in fixed amount. That gel formulations were evaluated and found all formulations were clear, washable, homogeneous and free from grittiness and also no phase separation found. All gels were found under pH range 7.0 to 7.6, Spreadability under the rage 5.6 to 6.1cm, % drug content 96.01 to 99.81 %, viscosity of gels was 83 to 118 cp and % permeation found in rage 78 to 93%. Excellent % Permeation Gel

formulation GF-6 was found 93%. Drug stability concerns about drug product safety, efficacy, and quality, found it to appropriate. The percentage drug loss from the formulations, pH and phase separation was used as a measure of storage stability. These properties help in breaking or bursting of vesicles after penetration to skin. It can be concluded that for better stability, the formulations should be stored at low temperature in refrigerator.

CONCLUSION

From the trial-and-error optimization design, drug loaded Gatifloxacin Niosomes were successfully evaluated. Preformulation study confirms purity of drug and compatibility of drug with excipients using FT-IR study. Span 20 was found significant with the experimental results. It was confirmed that the increasing the concentration of span 20 increases the stability of niosomes. From characterization parameters and stability study, it was concluded that the formulation has acceptable morphology and particle size, no any chemical interaction and was stable at refrigerated condition respectively. An extensive investigation is needed with reference to depth of penetration into the skin, determination of zeta potential and confirmation of configuration of phospholipids in lipid bilayer. There is a need to develop suitable formulation for commercial exploitation.

CONFLICTS OF INTERESTS

There are no Conflicts of interests.

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