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FORMULATION AND *IN VITRO* EVALUATION OF NIOSOMAL DRUG DELIVERY SYSTEM OF QUININE SULPHATE

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ABSTRACT

Quinine sulphate is the antimalarial drug used to treatment for Malaria. Subjugated inherent defects associated with convention dosage form of quinine sulphate such as severe side effects like chest pain, jaundice, abdominal pain, blurred vision, nausea. Niosomal drug delivery system of Quinine sulphate by thin film hydration method by using cholesterol and various non-ionic surfactant such as span 60, span 20 at different ratio (1:1, 1:2), then it was evaluated for various parameters. By formulating oral quinine sulphate niosomes to overcome, Reduce the dose and dose frequency, Minimize the side effects, Prolong the action of drugs, Provide sustained drug release, better patient compliance.

KEYWORDS: Niosomes, quinine sulphate, cholesterol, span 60 or span 20.

1. INTRODUCTION

Niosomes are vesicular systems comprising of bilayer made up of nonionic surfactants and excellent carrier for loading both hydrophilic and lipophilic drugs. It has been widely explored for antigen delivery because of their bio compatibility, nontoxic, high antigen encapsulation efficiency, high stability in the gastric environment and high permeability across the intestine. niosomes are prepared by using the various types of nonionic surfactants such as Spans and Tweens. These span and tween are amphiphilic molecules with a hydrophilic (head) and hydrophobic (tails). Cholesterol in the niosome formulation to produce the rigidity to the bilayer membrane. Other components such as charging lipids can be used to form niosome to induce a specific charge on the surface of this niosomal particles.[1][2][3]

Quinine is a anti malarial drug which are used alone or with other medication to treat malaria. It is also gametocidal against all species except P. falciparum. The sporozoites, pre-erythrocytic stage and the persistent tissue forms has no effect. The antimalarial action is uncertain. Quinine forms a hydrogen-bonded complex with double stranded DNA causing inhibition of DNA replication, transcription to RNA and protein synthesis and interferes with the cellular oxidation of glucose, and depresses many enzyme actions. But in in several draw back such as like high dose is give per day like 300 to 600 mg twice per day and it produce lot of side effects like the, jaundice, nausea, loss of vision, flu symptoms etc. These factors necessitated niosomal formulation of quinine sulphate and dosage form to reduce the dosage frequency and give better patient compliance. The present research work carried out to formulate & evaluate sustained release Quinine sulphate niosomes and it was planned to evaluate the various parameters such as morphological studies, Particle size analysis, Drug entrapment efficiency, Drug content determination, *In-vitro* drug release studies, Zeta-potential analysis.[4][5][6][7]

2. MATERIALS AND METHODS

Quinine sulphate, span 60 and span 20 was obtained from the LOBA CHEMICALS, Mumbai, India: diethyl ether and cholesterol was obtained from the NICE CHEMICALS, Kerala, India: All the above ingredients used were of analytical grade.

2.1. PREPARATION OF NIOSOMES

Noisome containing quinine sulphate are prepared by hand shaking method using different ratio of surfactants (Span 60, Span 20) and cholesterol was kept at constant. In this method the cholesterol, span 60 and diethyl ether is taken in a round bottom flask. The solvent is evaporated under reduced pressure in vacuum evaporator of round bottom flask, which leaves a mixture of solid surfactant and cholesterol on the walls of round bottom flask. This layer is rehydrated with phosphate buffer of pH 6.8 containing drug upon continuous shaking which results in swelling of surfactant layer. Milky white suspension formed. Different batches of noisome were prepared in order to select an optimized formula as per general method described above and proportion of surfactant and cholesterol for the preparation of niosome is given in table 1.[8]

Table 1: composition of surfactant and cholesterol for preparation of noisome.

FORMULATION CODE	NON-IONIC SURFACTANT	DRUG (mg)	DIETHYL ETHER (ml)	CHOLESTEROL: SURFACTANT
FS1	SPAN 20	100	20	1:1
FS2		100	20	1:2
FS3	SPAN 60	100	20	1:1
FS4		100	20	1:2

Sr.no	Formula	FS1	FS3
1	CHOLESTEROL	100mg	100mg
2	SPAN 60		100mg
3	SPAN 20	100mg	
4	QUININE SULPHATE	100mg	100mg
5	ETHER	10m1	10ml
6	PHOSPHATE BUFFER 6.8	20ml	20m1

2.3 PARTICLE SIZE

Niosomes containing drug was placed on a glass slide. A cover slip was placed over the niosomes suspension and evaluated the average vesicle size and shape by an ordinary optical microscope using a pre-calibrated ocular eye piece micrometer. [41]Mean particle sizes of all empty niosomes formulation and drug loaded niosomal formulations were determined by using optical microscopy.[9]

2.4 PERCENTAGE ENTRAPEMENT EFFICIENCY

Drug entrapment efficiency was calculated by using centrifugation method. 10ml of niosomal suspension was taken and centrifugation at 15,000 rpm for 20mins. The supernatant liquid was collected and suitably diluted with phosphate buffer (pH 6.8). Then the absorbance was taken at 310nm with the help of UV double beam spectrophotometer using pH 6.8 as the blank. Above formula is used to calculate the drug entrapment efficiency.[10]

$$\text{Total entrapment efficiency} = \frac{\text{Amount of drug in supernatant liquid}}{\text{Amount of drug}} \times 100$$

2.5 DRUG CONTENT

The UV Spectrophotometric approach was used to assess the quality of quinine sulphate in niosomes. A 10ml of methanol dissolved in niosomes comprising of 10mg of medication equivalent were taken for testing. UV Spectrophotometers with blank calculation at λ_{max} 310 nm were measured and the drug amount was calculated after sufficient dilution absorption. The percentage drug content of quinine sulphate in different niosomal formulation

calculated.[11]

2.6. In-vitro DRUG RELEASE STUDIES[12]

In-vitro drug release could be achieved by using dialysis tubing. The niosomes is placed in prewashed dialysis tubing which can be hermitically sealed. The dialysis sac is then dialyzed against a suitable dissolution medium at room temperature; the samples are withdrawn from the medium at suitable intervals, analyzed for drug content using suitable method (UV spectroscopy).

2.7. ZETA POTENTIAL

Zeta potential is done for the determining of colloidal properties of the formulations. The suitably diluted niosomes derived from proniosomes dispersion was determined using zeta potential analyzer based on electrophoretic light scattering and laser Doppler velocimetry method. The temperature was set at 25˚C. mean zeta potential, charge on vesicle and standard deviation was directly obtained from the measurement.[13]

3. RESULT AND DISCUSSION

The research study was aimed to formulate Quinine Sulphate niosomes to sustain the action of drug for over the period of 8 hours. The niosomes were prepared by Thin Film Hydration method. Different non-ionic surfactants (span 60, span 20) & cholesterol in the ratio of 1:1, 1:2 used for encapsulating the drug and also to release the drug in sustained manner. Diethyl Ether was used as a solvent. Phosphate buffer pH 6.8 was used as a hydrating medium for loading the drug.

Preformulation studies such as solubility analysis, melting point and FT - IR studied were carried out before the formulation. After formulation, the niosomes were evaluated for various parameters like morphological analysis, particle size analysis, percentage entrapment efficiency, drug content analysis, *in vitro* analysis, and zeta potential analysis.

3.1 FT-IR spectra

FT - IR spectral analysis showed that the formulation peaks and patterns of the spectra were similar both in pure drug and highest proportion of excipients. This indicated that there was no chemical interaction between Quinine Sulphate and other excipients used in the formulations and the data and spectrum was shown in below **Table 1 to 4.**

Table 1: FT-IR Spectral Data and spectrum of Quinine Sulphate.

S. No	WaveNumber (cm^{-1})	Characteristics
1.	3291.94	O-H Stretching
2.	2969.21	C-H Stretching
3.	1620.09	C=C Stretching
4.	1509.19	Aromatic C=C
5.	1473.51	CH_2 methylene bending
6.	1243.04	C-N Stretching
7.	1082.96-1028.95	C-O Stretching

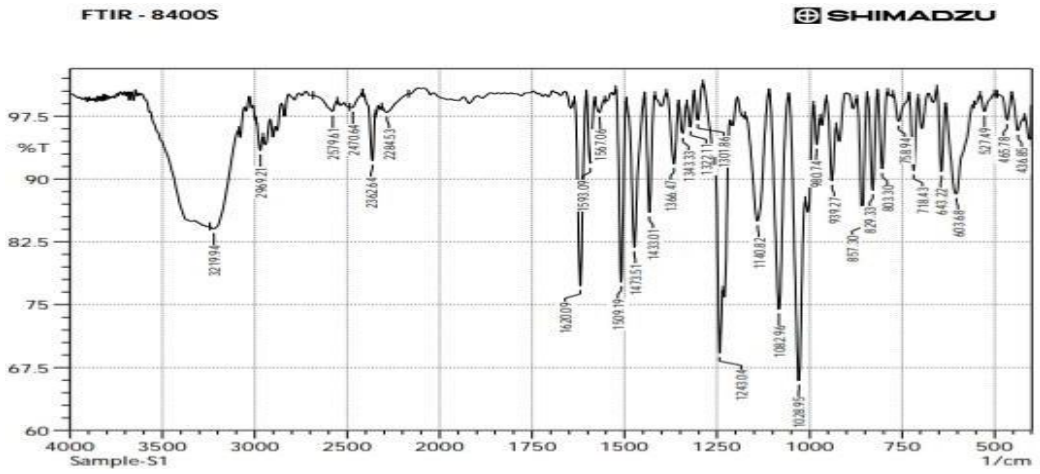


Table 2: FT-IR Spectral Data and spectrum of Quinine Sulphate + cholesterol

S.No	Wave Number (cm^{-1})	Characteristics
1.	3385.80	O-H Stretching
2.	2934.49	C-H Stretching
3.	1619.13	C=C alkene
4.	1509.19	Aromatic C=C
5.	1433.98	CH_2 methylene bending
6.	1242.07	C-N Stretching
7.	1082.96-1027.02	C-N Stretching

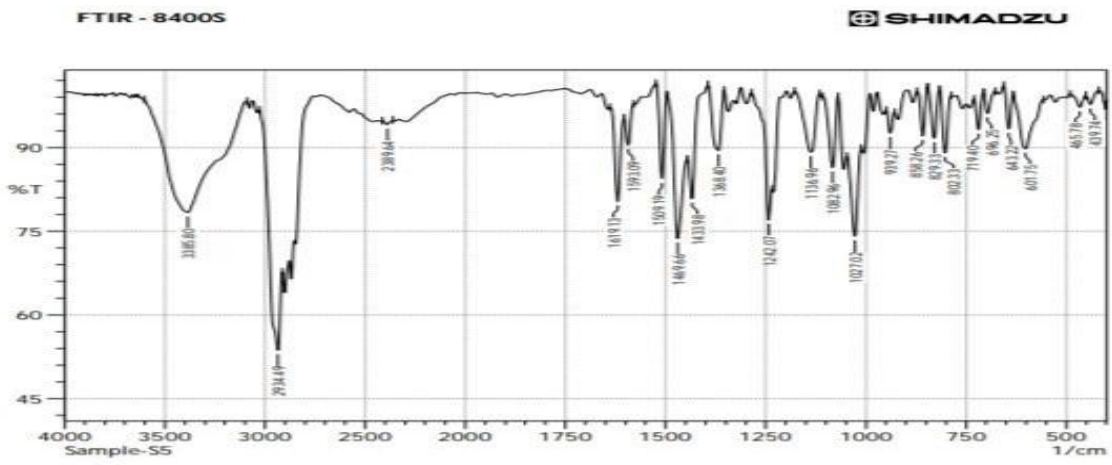


Table 3: FT-IR Spectral Data and spectrum of Quinine Sulphate + span 60

S.No	Wave Number (cm^{-1})	Characteristics
1.	3431.13	O-H Stretching
2.	2920.03	C-H Stretching
3.	1739.67	C=O Stretching
4.	1466.76	CH2 methylene bending
5.	1172.64	C-O Stretching
6.	1032.81	C-O Stretching of Secondary alcohol

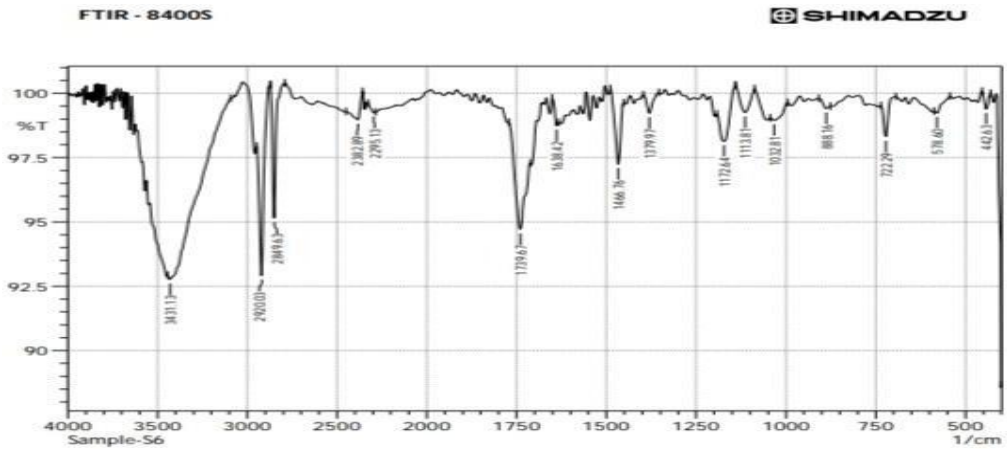
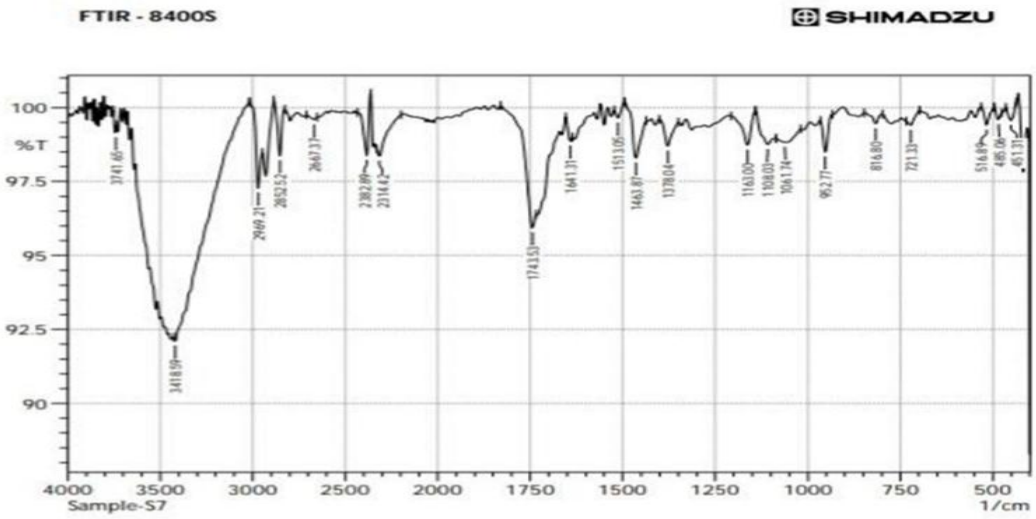


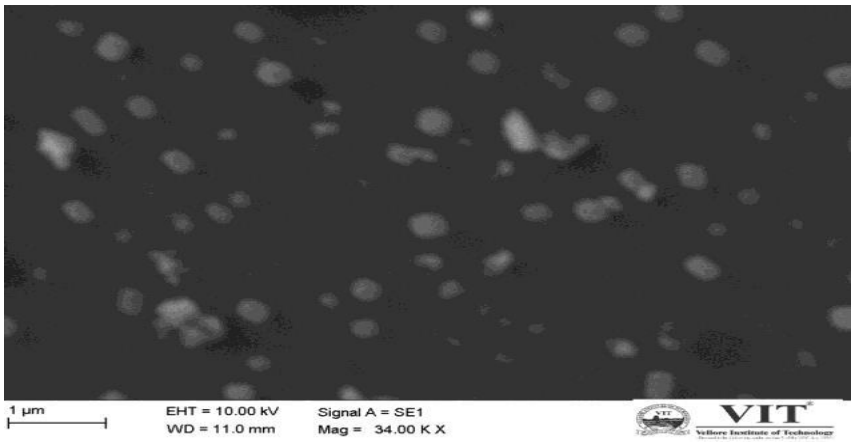
Table 4: FT-IR Spectral Data and spectrum of Quinine Sulphate + span 20.

S. No	Wave Number (cm^{-1})	Characteristics
1.	3418.59	O-H Stretching
2.	2969.21	C-H Stretching
3.	1743.53	C=O Stretching
4.	1641.31	C=C alkene stretching
5.	1378.04	CH_2 methylene bending
6.	1163.00-1108.03	C-O Stretching of Secondary alcohol
7.	1061.74	C-N Stretching of amine



3.2 Morphology

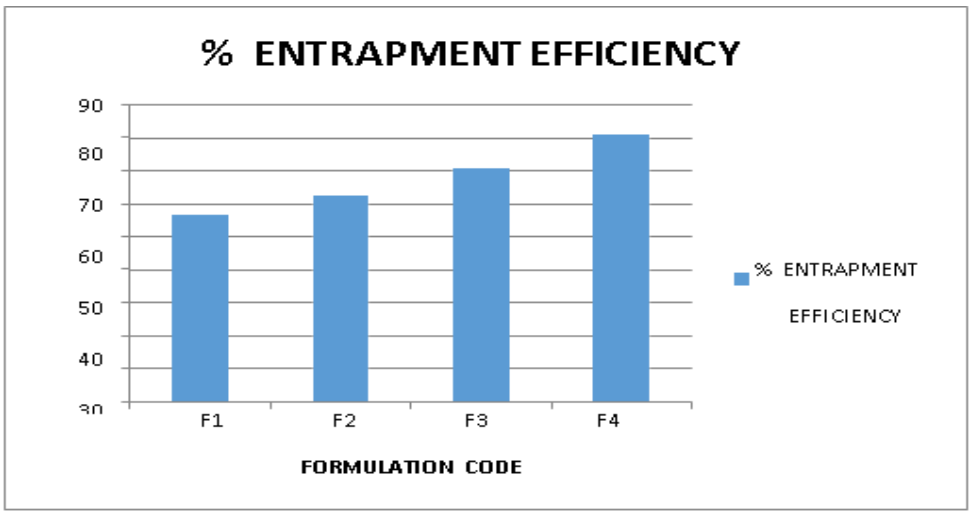
The morphological characteristics of niosome was evaluated by SCANNING ELECTRON MICROSCOPY for one optimized sample (FS4). Based on the SEM images, the particles are almost spherical and homogeneous. The result showed that the Quinine sulphate niosome have a spherical shape with smooth surface and discrete without any aggregation or agglomeration was shown below.



3.3 Percentage Entrapment Efficiency

The percentage drug entrapment efficiency of niosomes were prepared by thin film hydration method. The formulation was formulated varying the cholesterol ratio. It was found to be that percentage drug entrapment efficiency of formulation FS1, FS2, FS3 and FS4 were 60.67% w/w, 63.39% w/w, 75.66% w/w and 80.09% w/w respectively.

Higher surfactant concentration of span 60 showed higher entrapment efficiency than others, which might be due to the high fluidity of the vesicles.



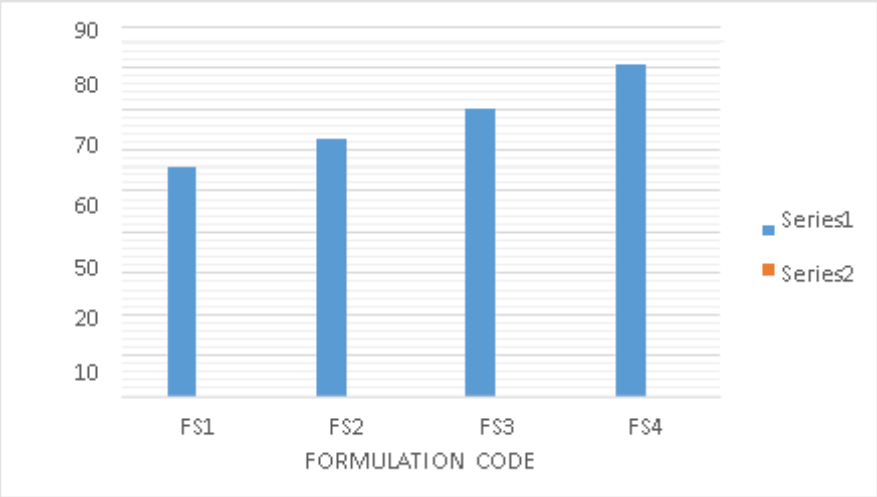
The entrapment efficiency was increased with increasing surfactant concentration. Type of surfactant also has an impact on entrapment efficiency, span 60 shows more entrapment efficiency than span 20.

Span 60> Span 20

High conc of non-ionic surfactant > lowest conc. of non-ionic surfactant.

3.4 Drug content

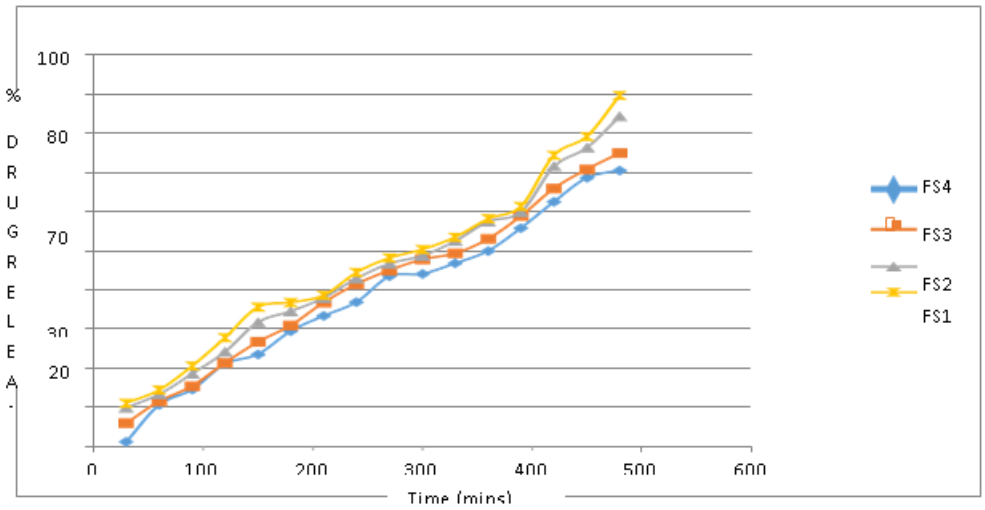
The percentage drug content of niosomes was found to be 56.82 % w/w, 62.27 % w/w, 70.77% w/w 80.97% w/w for FS1, FS2, FS3 and FS4 respectively.



Formulation with higher concentration of span 60 showed more drug concentration other. Drug content was increased with increasing surfactant concentration.

3.5 *IN-VITRO* Release studies

In-vitro release studies were performed to evaluate the release of drug from the prepared Quinine sulphate niosomes. The percentage drug release for all formulation FS1, FS2, FS3 and FS4 were found to be 89.65, 84.32, 74.92 and 70.496 respectively in 8 hrs.The formulation FS1 show faster release than formulation FS2 and FS3 due to concentration of surfactant. The formulation FS2 show faster release than formulation FS3. While the concentration of surfactant was increase to decrease the release of drug. The prepared niosomes of FS1 to FS4 showed sustained release of drug. When increased ratio of surfactants (span 20, span60) also sustain the release of drug was released in hand shaking method



3.6 Zeta potential

Zeta potential electrophoretic mobility of the FS4 niosomes formulation was measured by using Malvern zeta sizer nano 2s and result was shown below. Mean value of zeta potential was showed as -29.1mV. mean value of electrophoretic mobility was showed as -0.000226 cm^2/vs.

Measurement Results

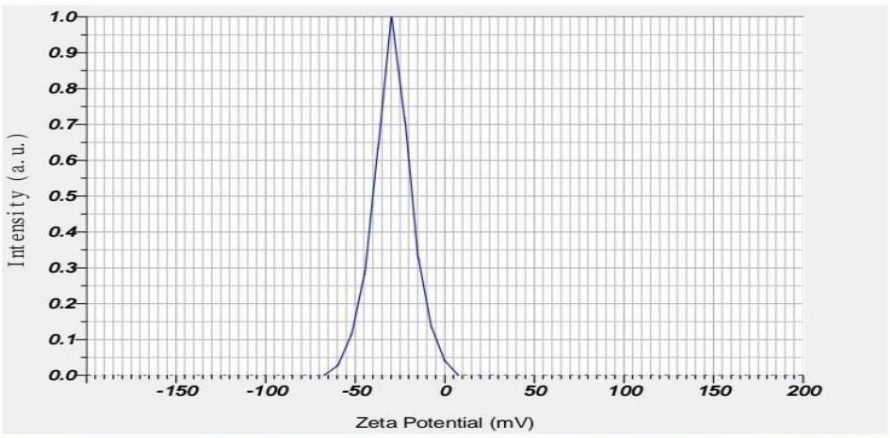
Measurement Results

Measurement Type	:	Zeta Potential
Sample Name	:	vznfe
Temperature of the Holder	:	25.0 °C
Dispersion Medium Viscosity	:	0.894 mPa·s
Conductivity	:	0.194 mS/cm
Electrode Voltage	:	3.4 V

Calculation Results

Peak No.	Zeta Potential	Electrophoretic Mobility
1	-29.1 mV	-0.000226 cm2/Vs
2	--- mV	--- cm2/Vs
3	--- mV	--- cm2/Vs

Zeta Potential (Mean)	:	-29.1 mV
Electrophoretic Mobility Mean	:	-0.000226 cm^2/Vs



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CONCLUSION

This study concluded that quinine sulphate was successfully formulated as a niosomal drug delivery system by thin film hydration method. in cholesterol ratio was constant and non-ionic surfactant concentration (span 20, span 60) were gradually increased (1:1, 1:2).

The morphological characters of prepared niosomes were determine with the help of scanning electron microscope. SEM result showed formulation were spherical in nature. It was analyzed by Malven particle size analyzer.

The particle size results that 2formulation (FS2, FS3) are uniform in size. The percentage entrapment efficiency and % drug content were higher in formulation with span 60 compared in span 20 % entrapment efficiency, % drug content were higher un higher concentration of non-ionic surfactant.

The in vitro release showed the concentration of surfactant was increased the drug release rate was retarded. Higher concentration of span 60 showed sustained drug release. Over a period of 8 hours compared to others. The zeta potential study was performed for one optimized formulation FSH.

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