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FORMULATION DEVELOPMENT AND EVALUATION OF NANOGEL LOADED WITH MONTELUKAST SODIUM NIOSOMES

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Keywords:

Niosomes, Niosomal gel, Montelukast sodium, Non-ionic surfactant vesicles, Vesicular drug delivery system

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ABSTRACT: Niosomes are vesicular carriers in the drug delivery system that are reported in the seventies. They are formed by self -assembly of non –ionic surfactant and cholesterol upon hydration with aqueous media resulting in lamellar structures that encapsulates both polar and non polar drugs. In the present research work, Montelukast sodium niosomes were prepared by using non –ionic surfactant span 60 and cholesterol in 1:1 concentration by thin-film hydration method using a rotary vacuum evaporator. The prepared Montelukast sodium niosomes were incorporated into the nanogel prepared by varying concentration of carbopol 934 to check the effect of polymer concentration on gel property. Niosomal gels were optimized and evaluated for various parameters such as homogeneity, grittiness, pH, viscosity, spreadability, extrudability drug content, skin irritation, *in-vitro* diffusion, zeta size, zeta potential, Etem study for vesicle size and stability study. Nanogel was successfully formulated by using Montelukast sodium niosome dispersion. The average sizes of niosome vesicles were found to be 496.2 nm, and polydispersity index (PI) was found to be 0.680, zeta potential study reveals that formulation was stable.

INTRODUCTION: Non-ionic surfactant based vesicles are termed as Niosome, were first reported in the seventies as a feature of the cosmetic industry but have since been studied as drug targeting agents [1]. Niosome is formed from the self-assembly of non-ionic surfactants in aqueous media leading to closed bilayer structures (unilamellar or multi-lamellar) capable of encapsulating both hydrophilic and lipophilic substances [2, 4].

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The assembly into a closed bilayer is rarely spontaneous and usually involves some input of energy such as physical agitation or heat [5]. Non-ionic surfactants orient as planar bilayer lattices, which forms closed or sealed vesicular shape wherein polar or hydrophilic heads align facing aqueous media while hydrocarbon segments are so aligned that their interaction with aqueous media is minimized (*i.e.*, every bilayer for thermodynamic reasons folds over itself to be a continuous membrane and forms a vesicle so that hydrocarbon-water interface remains no more exposed [3, 6].

Niosomes are dispersed uniformly into gel base (hydrogel) to form niosomal gel. It has gained considerable attention in recent years as one of the most promising vesicular drug delivery systems owing to their unique potential via combining the

characteristics of a hydrogel system with niosomes. Several polymeric hydrogel niosomes systems have been prepared and characterized in recent years, but among them, carbopol 934 has been studied extremely for preparing of niosomal gel [1, 3, 4].

Niosomes can reduce side effects, modify drug pharmacokinetics, increase bioavailability, increase the residence time of drug, and site-specific drug delivery, especially in trichomoniasis, bacterial vaginosis, non–gonococcal urethritis, whose symptoms are seen superficially on the external body surface. Niosomal gel seems an interesting drug delivery system in the treatment of parasitic infection especially protozoal infections [2, 5, 6].

The structural component of niosomes included non-ionic surfactants, cholesterol, additives, and drug. Montelukast sodium is an anti-asthmatic (leukotriene receptor antagonist). Montelukast sodium is an orally available leukotriene receptor antagonist which is widely used for the prophylaxis and chronic treatment of asthma and has been linked to rare cases of clinically apparent liver injury. Not use for the treatment of bronchospasm in acute asthma attacks.

Montelukast is usually administered orally. Montelukast blocks the action of leukotriene D4 on the cysteinyl leukotriene receptor CYSLT1 in the lungs and bronchial tubes by binding to it. It reduces the bronchoconstriction which caused by the leukotriene and results in less inflammation [7]. These problems can be improved by reformulating the drug delivery *via* a different route like skin. However, conventional topical dosage forms, most of which are present in the gel form, usually have quite limited therapeutic efficacy due to the low bioavailability as a small fraction of drug cross the skin barrier. Nowadays, niosomes play an increasingly important role by acting as a carrier for the delivery of drugs across the skin. The present work is based on the use of Montelukast sodium in the treatment of urticaria.

MATERIALS AND METHODS: All the material and chemicals were of analytical grade and produced from the authentic source. Montelukast sodium was gifted by Morphen laboratories Pvt. Ltd. Mumbai, India. Span 60, cholesterol carbopol 934, propylene glycol, glycerol, triethanolamine, disodium hydrogen phosphate, potassium hydrogen phosphate, sodium chloride, chloroform, methanol, egg membrane. The whole research activity was conducted during the year 2019 at Shri D.D. Vispute College of Pharmacy & Research Center, Panvel, Navi Mumbai, Maharashtra.

Formulation of Niosomes:

By Thin Film Hydration Method [8]: Niosomal ingredients like non–ionic surfactant and cholesterol in 1:1 concentration were dissolved in a volatile organic solvent like chloroform in a round bottom flask and sonicated for complete solubilization of ingredients.

The volatile organic solvent is removed by evaporation under vacuum reduced pressure (400 mm/hg) at 60 °C temperature for about 1 h using rotary flash vacuum evaporator with 120 rpm speed; leaving a thin layer of solid mixture deposited on the wall of the flask. The dried layer was hydrated using aqueous media like phosphate buffer saline (PBS) pH 6.8 with gentle shaking at 60 °C temperature for about 1 h; it resulted into the formation of niosomal dispersion containing multilamellar vesicles. The niosomal dispersion was further sonicated for 2 min. to form uniform unilamellar vesicles. The dispersion containing vesicles was further refrigerated for 24 h.

Separation of Unentrapped Material:

Egg Membrane: Egg membrane separates the unwanted material along with free unentrapped drug from dispersion. The niosomal dispersion was exhaustively dialyzed by placing it in a sealed egg membrane tubing (previously washed and soaked in PBS pH 6.8 for about 12 h) which is suspended in a beaker containing dialysis medium like PBS pH 6.8, which is constantly stirred on a magnetic stirrer until entire free material is separated from niosomal dispersion [9,10].

Formulation of Niosomal Gel:

By Dispersion Method: The formulation of niosomes was incorporated into the gel base prepared by the Dispersion method by using various concentrations of Carbopol 934. Appropriate quantity of Carbopol 934 was weighed sprinkled onto the distilled water with continuous stirring and further it was soaked and hydrated for 2 h.

Other ingredients like Propylene Glycol (10% w/w) and Glycerol (30% w/w) along with required quantity of API entrapped in Niosomes were added subsequently with continuous stirring and dispersed uniformly.

The gel was neutralized to pH 7 by using triethanolamine (TEA), and the final weight was adjusted with distilled water. The gel was sonicated for 30 min and kept undisturbed overnight to remove entrapped air.

TABLE 1: FORMULATION AND COMPOSITION OF NIOSOMAL GEL

Formulation Code	Carbopol 934	Propylene Glycol	Glycerol
F1Nv1	1%	5%	30%
F1Nv2	1.5%	5%	30%
F1Nv3	2%	5%	30%
F1Nv4	2.5%	5%	30%
F1Nv5	3%	5%	30%
F1Nv6	3.5%	5%	30%

Characterization of Vesicles:

Determination of Particle Size Zeta Potential and Poly Dispersity Index: Particle size, zeta potential, and polydispersity index were measured for optimized niosomes using the dynamic light scattering (DLS) technique at 250 °C using the particle size system (Horiba scientific nano partica analyser Sz 100, Mumbai India). The drug-loaded niosomal colloidal dispersion was diluted with purified water before being subjected for measurement [11].

Determination of Percentage Entrapment Efficiency: The amount of Montelukast sodium entrapped in niosome was estimated by centrifugation method. 2 ml of suspension was placed in centrifugation tube and centrifuged at 14000 rpm for half-hour. Montelukast sodium in niosome was determined after separating non-entrapped Montelukast sodium.

Subsequently, vesicles were dissolved in distilled water, and the amount of drug was analyzed by using UV spectrophotometer (Shimadzu) at 230 nm. Entrapment efficiency is stated as the percent of drug trapped in vesicles. It is a determination by following equation [12].

Entrapment efficiency = (amount of drug entrapped / Total amount of drug added) × 100

Vesicle shape and Size: Niosomes vesicles can be envisioned by optical and transmittance electron microscopic (TEM). The morphological description of niosome vesicles, such as shape and surface feature, was anticipated by TEM. A droplet of niosome suspension was positioned over the slide, and photo was taken at 100 × resolution[13].

Evaluation of Niosomal Gel:

Homogeneity: Niosoms gels placed in transparent beakers were tested for homogeneity by visual inspection. It was also tested for their appearance and presence of any aggregates [14].

Grittiness: Niosome gels were evaluated microscopically to check the presence of any visible particulate matter.

pH: The pH of the niosomal gels was determined by using digital pH meter which was previously calibrated by standard solution prepared by standard capsules of pH 4, 7 and 9.2 respectively. pH measurement of the gels was carried out by dipping the pH-electrode of a digital pH meter completely into the gel formulation for 10 min prior to taking the readings in order to allow the pH values to stabilize. The measurement was carried out in triplicate, and the average of the three readings was recorded. The electrode was washed thoroughly between each reading [16].

Viscosity: The viscosity of the niosomal gels was determined by Brookfield viscometer with spindle no. 64, rotated at 5 rpm for 5 min at 25 °C temperature.

Spreadability: The spreadability of niosomal gels was determined on the basis of "maximum slip and minimum drag" principle, the excess quantity of gel formulation was placed in between two glass slides of length 7.5 cm each. A 1000 g weight is allowed to rest on the upper slide for 1 min to expel air between the slides and to provide uniform distribution of the gel. The weight was removed and the excess of gel adhering to the edges of the slides was scrapped off.

The lower slide (immovable) was fixed on the wooden board. The upper slide (movable) was attached with a string that was tied with a pan. The string was passed over a pulley, and the pan was hung from the string. Thereafter 80 g weight was added to the pan, and the upper slide was subjected to pull with the help of string. The time required to separate the 2 slides *i.e*. the time in which the upper slide slips over the lower slide is noted and taken as a measure of spreadability. The experiments were done in triplicate [18, 19]. The following formula is used to calculate the spreadability.

$$S = m \times l\, t$$

Where, S is the Spreadability m is that the weight tied to the upper slide (g) l is the length of a glass slide (cm) t is the time taken to separate the slide completely from each other (s)

Extrudability: The extrudability of niosomal gels was determined by the amount of gel extruded from the tube on the application of pressure. The formulation was filled in a clean lacquered collapsible aluminium tube of capacity 5 g with 5 mm orifice, and the tube is pressed firmly at the crimped end, and the clamp was applied to prevent any rollback.

The amount of extruded gel was collected carefully and weighed accurately. Extrudability was then determined by measuring the amount of gel extruded (in percentage) through the orifice when a pressure was applied to the tube. The experiment was performed in triplicate [20, 21, 22, 24].

Drug Content Uniformity: To ensure uniform distribution of drug (entrapped in niosomes) into the gel, a fixed quantity of the gel samples was collected from a different location (top, middle and bottom) of the tube and weighed accurately 0.250 g of formulation and transferred in a 250 ml volumetric flask each and diluted with 100 ml methanol (as it also breaks the niosomal structure).

Flask was shaken vigorously for 30 min on a mechanical shaker to disperse the gel and sonicated for about 10-15 min for complete extraction of the drug. Then these solutions were filtered and were analyzed by UV-Vis spectrophotometer. Drug content was determined from the standard calibration curve of drug [25].

***In-vitro* Diffusion Study:** *In-vitro* diffusion studies of niosomal gels was carried out by using a set of Franz diffusion cells, to study the release rate of drug from formulation.

The receptor chamber was filled with receptor medium (PBS pH 6.8). The receptor medium was stirred continuously and its temperature was kept at 37 °C ± 0.5 °C by circulating water through a jacket surrounding the cell body throughout the experiment.

An egg membrane which was already soaked in receptor medium for 12 h was clamped between two chambers 0.250 g of formulation was placed in the donor cell. Subsequently, 1 ml samples were collected after a particular time interval from the receptor cell. The same volume of fresh medium was added after each collection to keep the volume constant. The withdrawn aliquots were diluted if required and subjected to spectrophotometric analysis using fresh receptor medium as blank. The concentration of drug released at a particular time interval was determined by using an equation generated from standard calibration curve [26].

Drug Release Kinetics Modelling: For the determination of the release mechanism, the data obtained from the results of *in-vitro* diffusion studies were fitted with several kinetics models as follows [22, 26]:

Zero Order Model:

$$C_0 - C_t = K0\ t \text{ and } C_t = C_0 + K_0\ t$$

Where C_t is the amount of drug released at time t, C_0 is the initial concentration of drug at time t = 0, K_0 is the Zero-order rate constant. First-order model

$$\log C = \log C0 - K1\ t/2.303$$

Where, C is the percent of drug remaining at time t, C_0 is the initial concentration of the drug at time t = 0, K1 is the first-order rate constant. Higuchi model

$$Q = KH\ t1/2$$

Where, Q is the cumulative amount of drug released in time t, KH is the Higuchi dissolution constant. Korsmeyer-peppas model

$$\log (Mt/M\infty) = \log KKP + n \log t$$

Where, M_t is the amount of drug released at time t, M_∞ is the amount of drug released after the time ∞, n is the diffusional exponent or drug release exponent, KKP is the Korsmeyer-peppas release rate constant. Hixson-crowell model

$$W_0\ 1/3 - W_t\ 1/3 = KHC\ t$$

Where, W_0 is the initial amount of drug at time t = 0, W_t is the remaining amount of drug at time t, KHC is the Hixson-crowell constant.

Skin Irritation Test: Test for skin irritation of niosomal gels was performed on human volunteers of different age. Gel was applied on an area of 2 square inch to the back of hand or 9 cm^{-2} area near to the elbow and covered with cotton for 24 h and observed for lesions, irritation or any reaction [17].

Stability Study: The stability study of the formulation was performed as per International Council for Harmonisation (ICH) guidelines.

Freshly prepared formulations were divided into groups and kept at specified storage conditions as per ICH guidelines. The sample was withdrawn periodically and tested for various evaluation parameters mentioned above. The stable formulation must retain the evaluation parameters at specified storage conditions over a period of time [16].

RESULTS AND DISCUSSION:

Drug-Excipient Compatibility Study by Fourier Transform Infra-Red (FTIR) Spectro-scopy: IR Spectrum of pure drug and excipient along with the mixture of drug and excipients were recorded by FTIR, and the compatibility of drug and excipients was checked by comparing the spectra. The FTIR of all the samples is represented in **Fig. 1** To **Fig. 5**. Along with the spectrum peaks in **Table 2** to **Table 6**. All the characteristics peaks were found in the sample. The FTIR study concluded that there was no interaction between Montelukast sodium and any of the excipients.

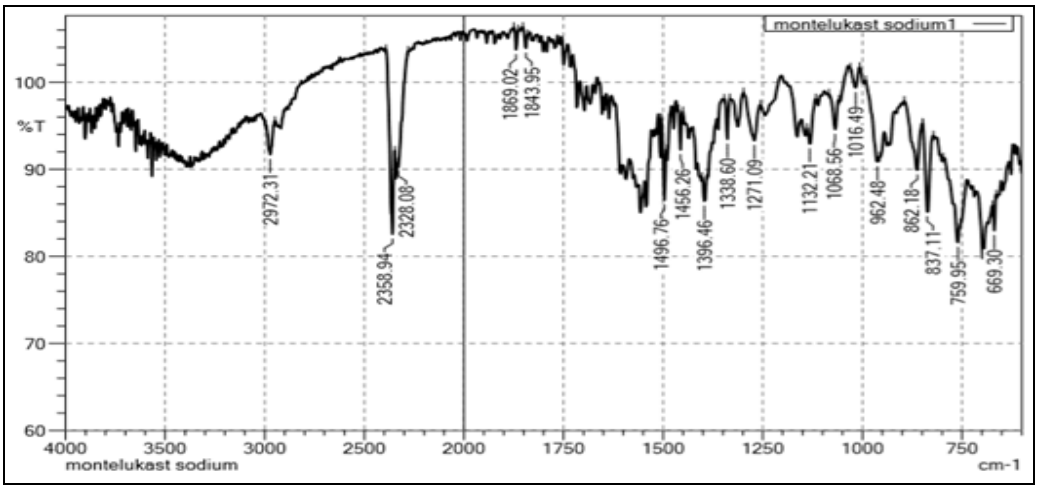

FIG. 1: IR SPECTRA OF MONTELUKAST SODIUM

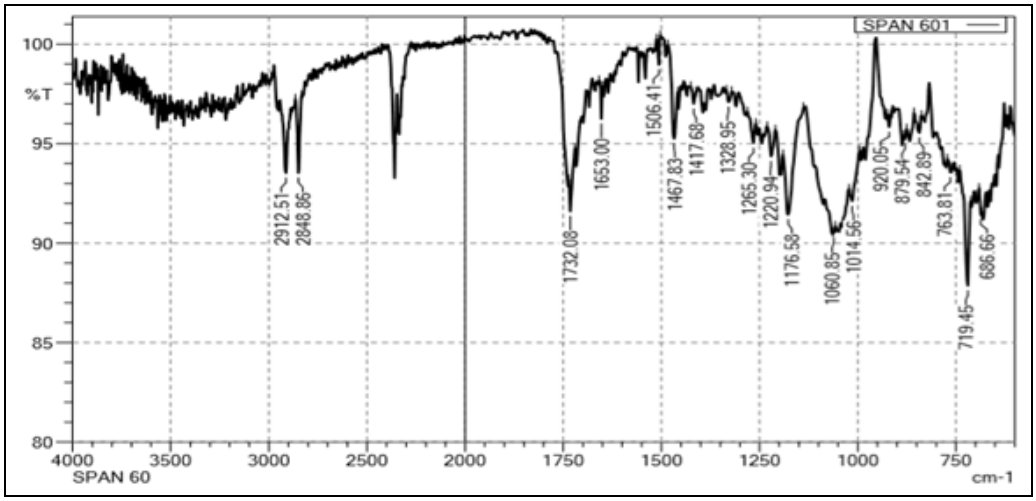

FIG. 2: IR SPECTRA OF SPAN 60

TABLE 2: IR SPECTRUM PEAKS OF MONTELUKAST SODIUM

Peaks (cm^{-1})	Groups	Type of Vibrations	Frequency
669.30, 759.95, 837.11, 862.18, 962.48	C-H	Alkenes (out -of -plane bend)	1000-650
		Aromatic (out-of-plane bend)	900-690
1016.49, 1068.56, 1132.21, 1271.09	C-O	Alcohol	1300-1000
,1338.60	C-N	Amines	1350-1000
2972.31	C-H	Alkanes	3000-2850

TABLE 3: IR SPECTRUM PEAKS OF SPAN 60

Peaks (cm^{-1})	Groups	Type of Vibrations	Frequency (cm^{-1})
719.45, 763.81, 842.89, 879.54	C-H	Aromatic (out-of-plane bend)	900-690
1014.56, 1060.85, 1176.58, 1220.94, 1265.30	C-O	Alcohols, Ethers, Esters	1300-1000
1732.08	C=O	Ester	1750-1730
2912.51	C-H	Alkanes	3000-2850

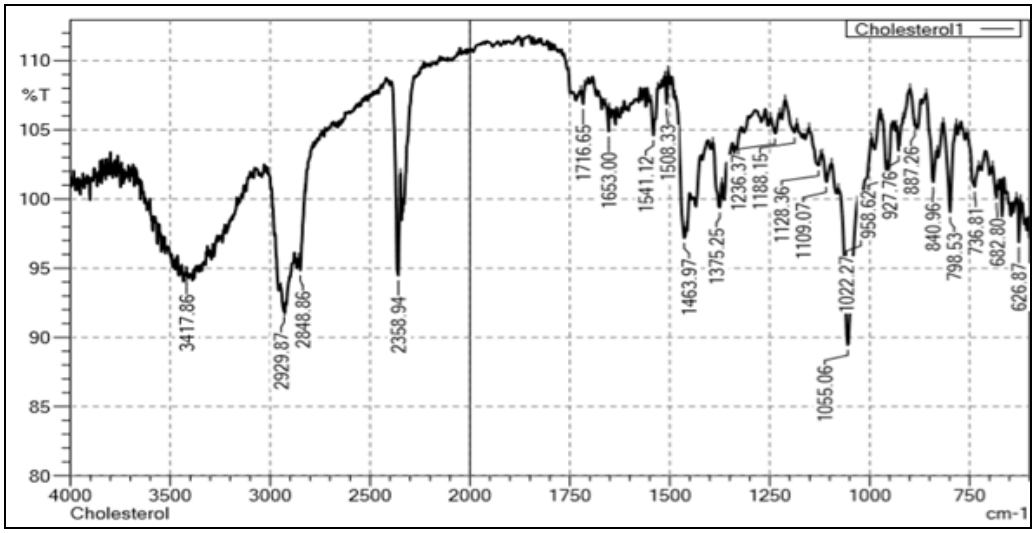

FIG. 3: IR SPECTRA OF CHOLESTEROL

TABLE 4: IR SPECTRUM PEAKS OF CHOLOESTEROL

Peaks (cm^{-1})	Groups	Type of Vibrations	Frequency (cm^{-1})
682.80, 736.81, 798.53, 840.96,	C-H	Alkenes (out-of-plane bend)	1000-650
887.26, 927.76, 958.62		Aromatic (out-of-plane bend)	900-690
1055.06, 1022.27, 1109.07,1128.36,	C-O	Alcohol	1300-1000
1188.15, 1236.37			
2929.87	C-H	Alkanes (stretch)	3000-2850

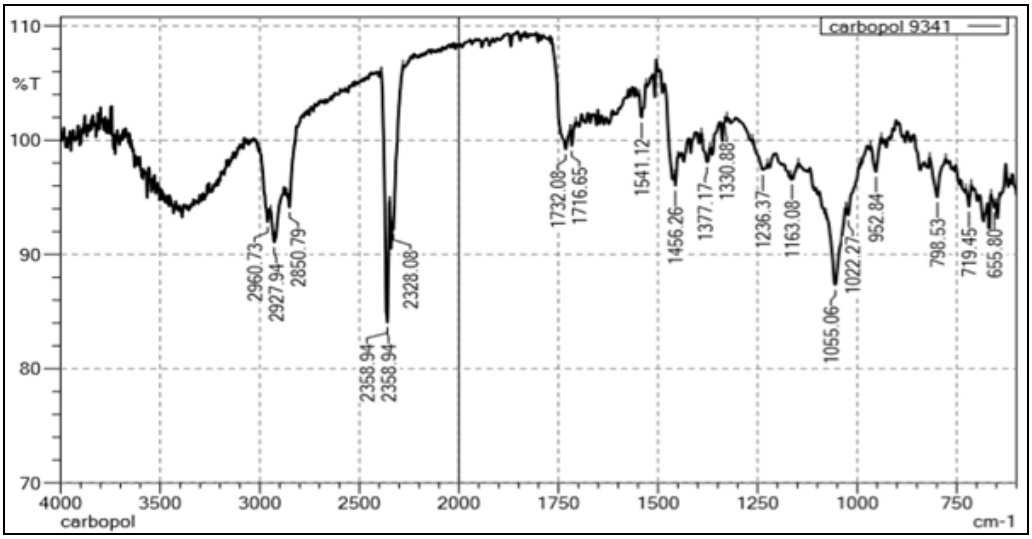

FIG. 4: IR SPECTRA OF CARBOPOL 934

TABLE 5: IR SPECTRUM PEAKS OF CARBOPOL 934

Peaks (cm^{-1})	Groups	Types of vibration	Frequency (cm^{-1})
1022.27, 1055.06, 1163.08, 1236.37	C-O	Carboxylic acid	1300-1000
1716.65	C=O	Carboxylic acid	1725-1700
2850.79, 2927.94, 2960.73	C-H O-H	Alkane Carboxylic acid	3000-2850, 3400-2400

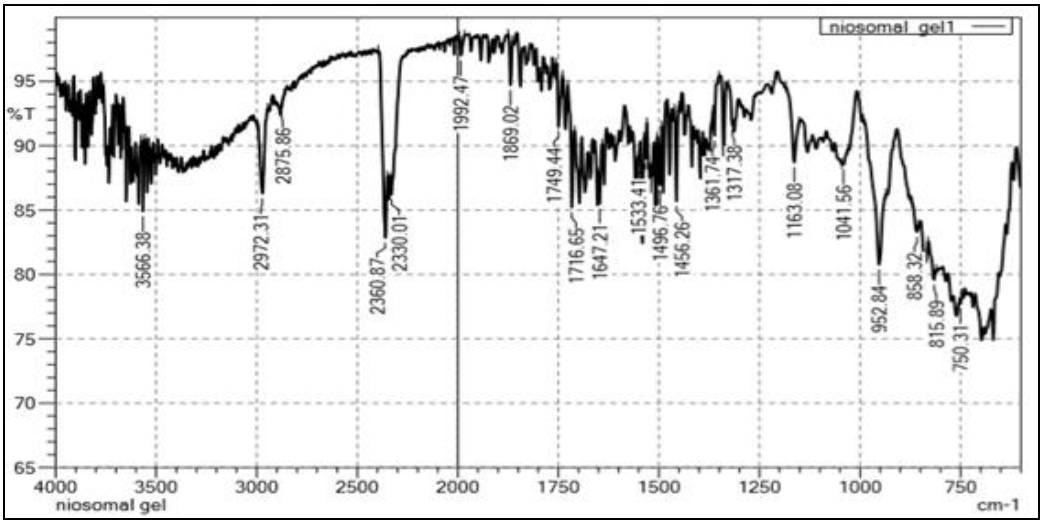

FIG. 5: IR SPECTRA OF API AND EXCIPIENTS USED IN FORMULATION

TABLE 6: IR SPECTRUM PEAKS OF API AND EXCIPIENTS USED IN FORMULATION

Peaks (cm^{-1})	Groups	Types of Vibration	Frequency (cm^{-1})
750.31, 815.89, 858.32,	C-H	Alkenes (out-of-plane bend)	1000-650
952.84		Aromatic (out-of-plane bend)	900-690
1041.56, 1163.08, 1317.08,	C-O	Alcohol, Ether, Esters, Carboxylic acid	1300-1000
1361.74	C-N	Amines	1350-1000
1716.65	C=O	Ester	1750-1730
2875.86	C-H	Alkane (stretch)	3000-2850
	O-H	Carboxylic acid	3400-2400
2972.31	O-H	Aicohol, Carboxylic acid	3400-2400
	N-H	Primary and secondary Amines (stretch)	3500-3100

Visual Images and Surface Morphology by TEM: The formulated optimized niosomes containing Montelukast sodium visualized by TEM and the TEM image was shown in **Fig . 7**.

The TEM image showed multilamellar vesicular structure. It was observed that after subjecting to 2 cycles of sonication, the size of vesicle is reduced **Fig. 8** and after 4 cycle sonication structure **Fig. 9**.

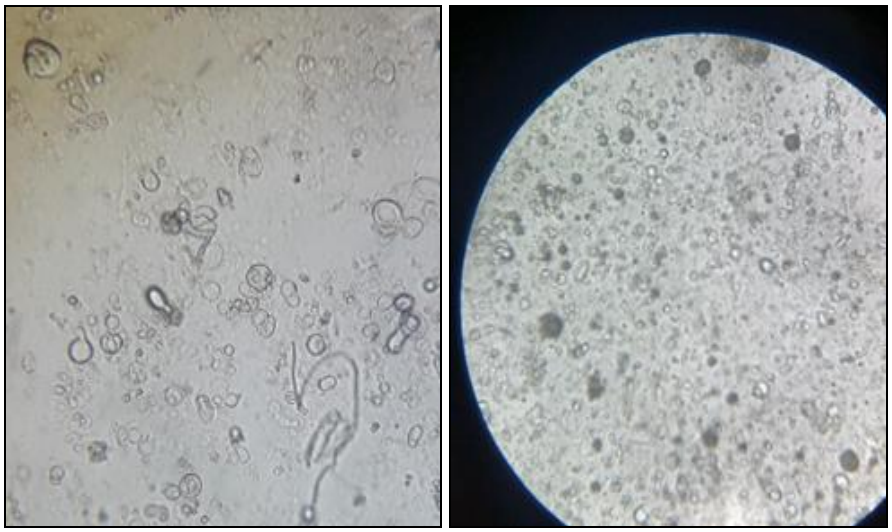

FIG. 6: IMAGE IN OPTICAL MICROSCOPE

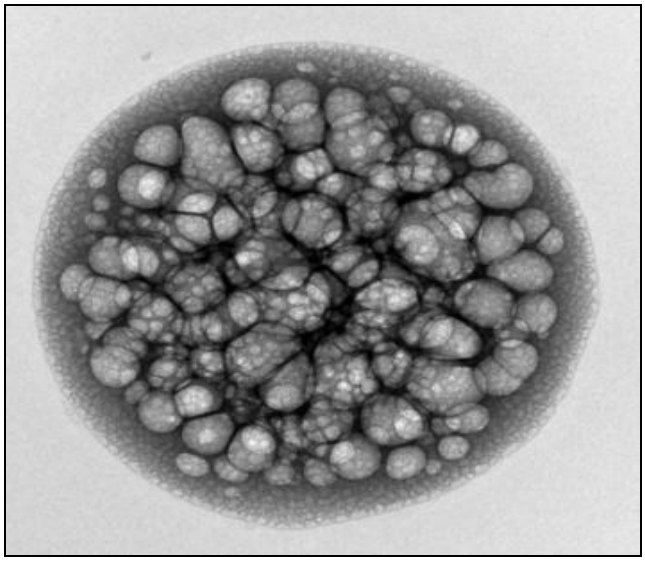

FIG. 7: TEM IMAGE OF VESICLE BEFORE SONICATION CYCLE

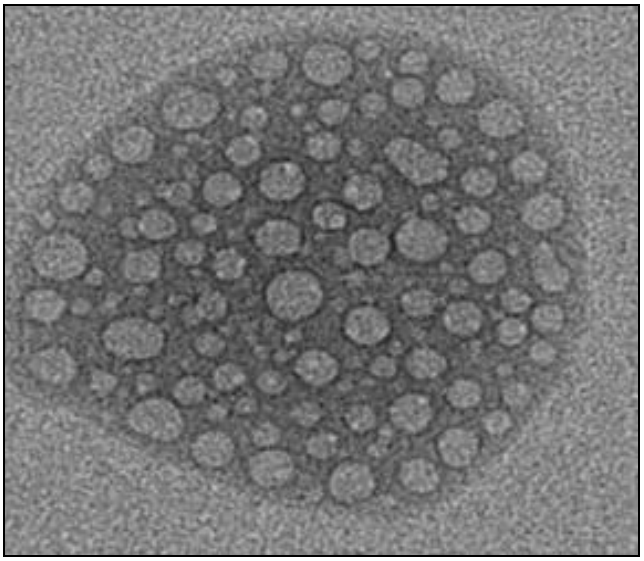

FIG. 8: TEM IMAGES OF VESICLE AFTER 2 CYCLES OF SONICATION

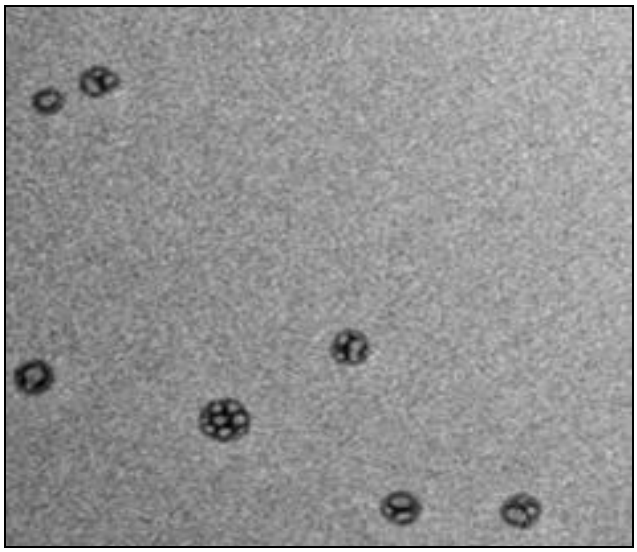

FIG. 9: TEM IMAGE OF VESICLE AFTER 4 CYCLES OF SONICATION

Zeta potential: The zeta potential of the niosomes was determined using a zeta sizer, and the zeta potential of the niosome was found to be -2.0 mV which indicates that niosomes were stable.

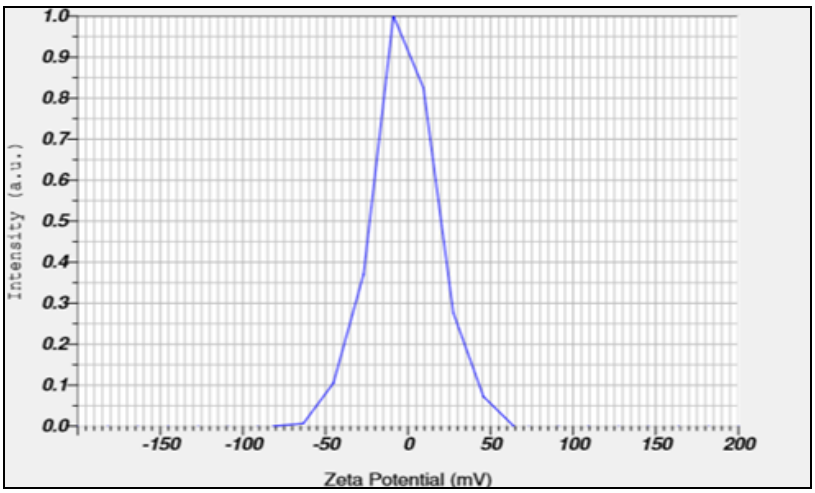

FIG. 10: ZETA POTENTIAL OF FORMULATION N1

Vesicle Size Measurement: The average sizes of niosome were found to be 496.2 nm & the polydispersity index (PI) was found to be 0.680.

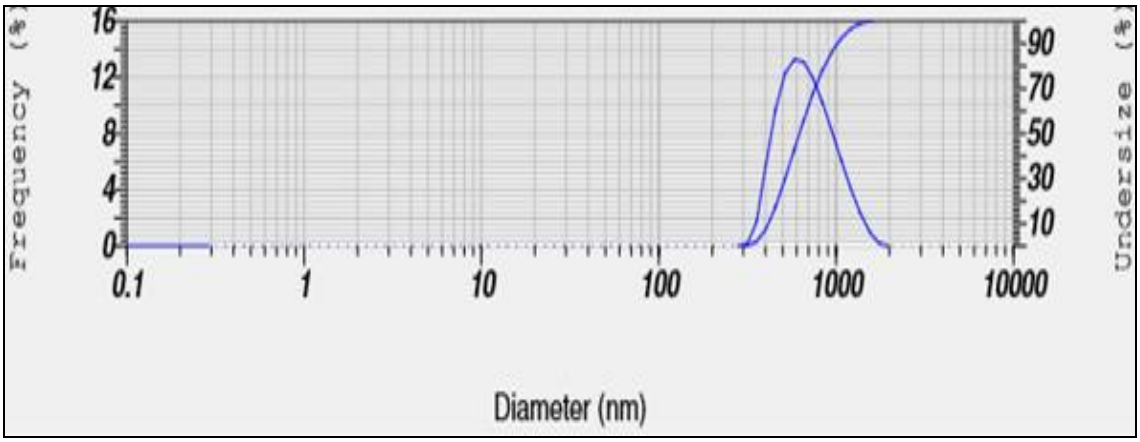

FIG. 11: PARTICLE SIZE ANALYSIS OF MONTELUKAST SODIUM LOADED NIOSOME

Entrapment Efficiency: Percentage entrapment of montelukast sodium niosome was found to be in the range of 48%-81% as shown in **Fig. 7.** The entrapment efficiency was found to be higher for N1 formulation (81%). Ratio of span 60 and cholesterol used for the niosome preparation seems to have influence on entrapment efficiency. Among all the surfactant used, span 60 showed better results. The ratio of 1:1 of span 60 and cholesterol showed higher entrapment efficiency.

TABLE 7: ENTRAPMENT EFFICIENCY

Formulation code	Entrapment efficiency
N1	81.17%
N2	48.52%
N3	79.49%
N4	75.00%
N5	62.66%
N6	49.41%
N7	57.35%
N8	56.40%

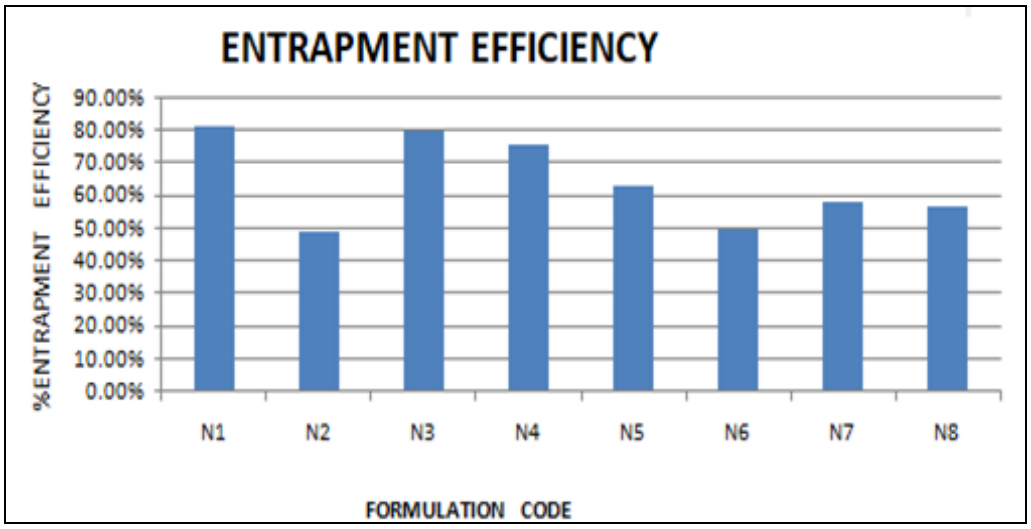

FIG. 12: GRAPH OF ENTRAPMENT EFFICIENCY

***In-vitro* Drug Release of Optimized Niosomal Gel:** The results of all the evaluation parameters (homogeneity, grittiness, pH, viscosity, spreadability, extrudability, drug content uniformly, skin irritation, and *in-vitro* diffusion study) of niosomal gels are tabulated in **Table 8**.

TABLE 8: RESULTS OF EVALUATION PARAMETER OF NIOSOMAL GEL

Formulation Evaluation	NG1	NG2	NG3	NG4	NG5	NG6
Homogeneity	+++	+++	+++	+++	++	+
Grittiness	+++	+++	++	+	_	_
PH	6.9	7.2	6.86	6.7	7.06	6.9

Viscosity(p)	194600	102100	685600	517800	422900	401200
Spreadability (g.cm/sec)	+++	+++	+++	++	-	-
Extrudability (%)	95	96	89	87	73	71
Drug Content Uniformity(%)	70%	80%	73.75%	65%	55%	72.5%
Skin Irritation	No	No	no	No	No	No
+++Excellent, ++Good, + Satisfactory, -Poor, -- Fail.						
***In-vitro* Diffusion (%)**	**NG1**	**NG2**	**NG3**	**NG4**	**NG5**	**NG6**
0 h	0	0	0	0	0	0
1 h	32.9	17.62	31.72	24.67	16.45	11.75
3h	24.2	33.57	38.27	28.87	32.40	21.52
4 h	15.35	35.43	41.42	35.35	53.05	36.07
5 h	35.4	59.67	45.80	53.70	68.25	50.92
6 h	23.1	70.30	59.63	78.30	73.17	69.6
7 h	33.9	67.02	62.02	96.35	86.40	80.42
8 h	45.39	47.20	63.25	104.17	94.00	92.62

Formulation NG1, NG2, NG3, and NG4 was found to be best in case of homogeneity as compare to other niosomal gel. NG5, NG6 showed the presence of aggregates and lumps. No particulate matter was seen in the first four formulations under optical microscope. NG5 and NG6 showed the particulate matter; hence it fails the test. All the formulated niosomal Gels were found to be in acceptable range *i.e.* neutral to skin. NG1 and NG2 were found to have appropriate viscosity suitable for topical application. NG3 and NG4 were slightly more viscous. Viscosity NG5 and NG6 were found to be very low. Spreadability of NG1, NG2, NG3 and NG4 was found to be good as compared to NG5 and NG6. Lesser the time taken for separation of two slides indicates more slip and better spreadability. The least resistance to the separation of the slides indicates good spreadability.

All the formulation exhibit good extrudability in range 70% - 90%. The extrusion of the gel from the tube is an important parameter for its application on skin and for patient acceptance. The drug content was found to be in the range 70% - 90%, which is an acceptable range. No irritation was observed on volunteers indicating that all the formulation passes the skin irritation test. Since all the values of the evaluation parameter are in the accepted range, the method used for preparation is considered suitable, and formulation NG2 showed better results; hence it is selected as an optimized formulation.

Drug Release Kinetic Modelling: The *in-vitro* release data were fitted in various release kinetic models to predict the release mechanism of the drug from the niosomal gel.

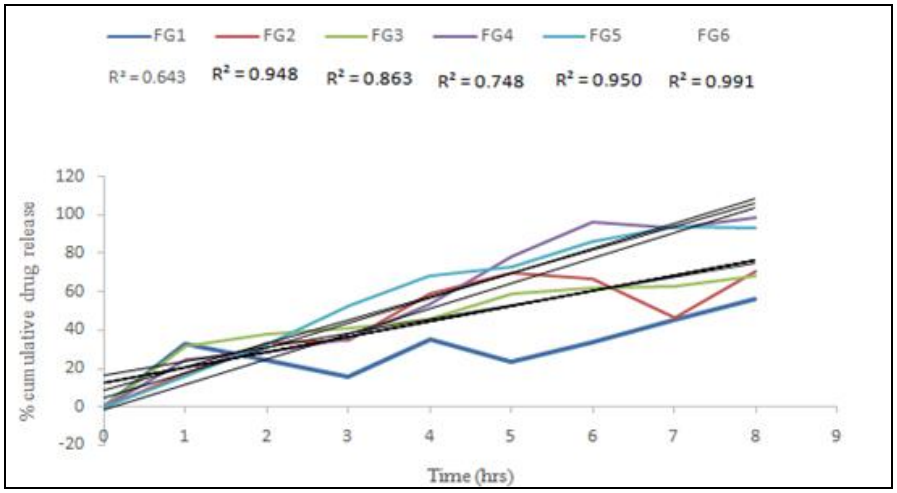

FIG. 13: ZERO ORDER KINETICS

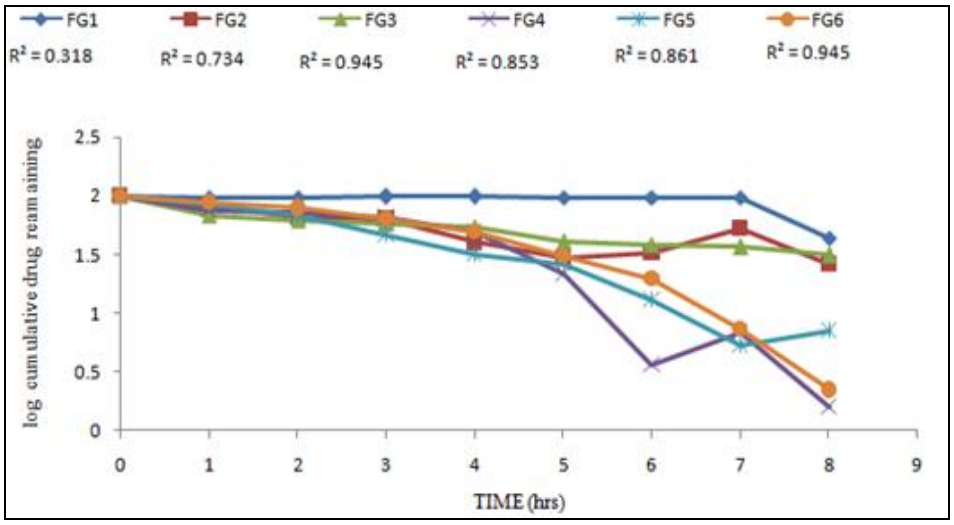

FIG. 14: FIRST ORDER KINETICS

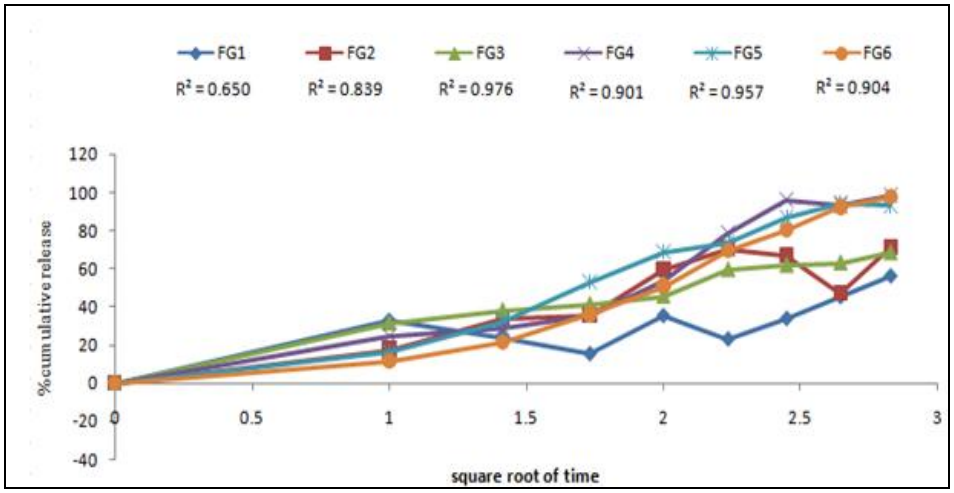

FIG. 15: HIGUCHI MODEL KINETIC RELEASE

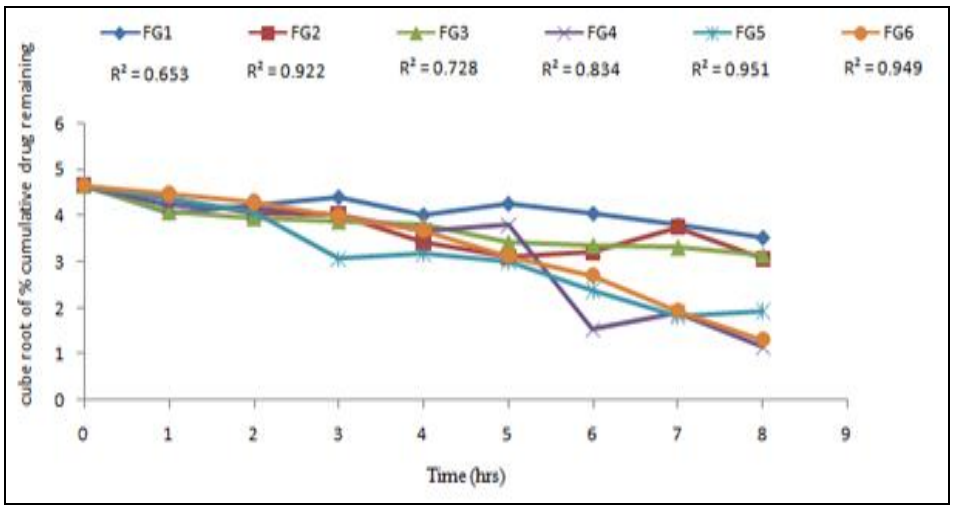

FIG. 16: HIXSON –CROWELL MODEL KINETIC RELEASE

The results reveal that all the formulation were best fitted in Higuchi release kinetic model as the graph plots show the highest linearity. Hence, all the formulation follows Higuchi kinetic release. But the formulation FG2 showed the highest R^2 value among all the formulations indicating the best Higuchi model release kinetic. It shows that a constant amount of drug is released unit time from the niosomal gel.

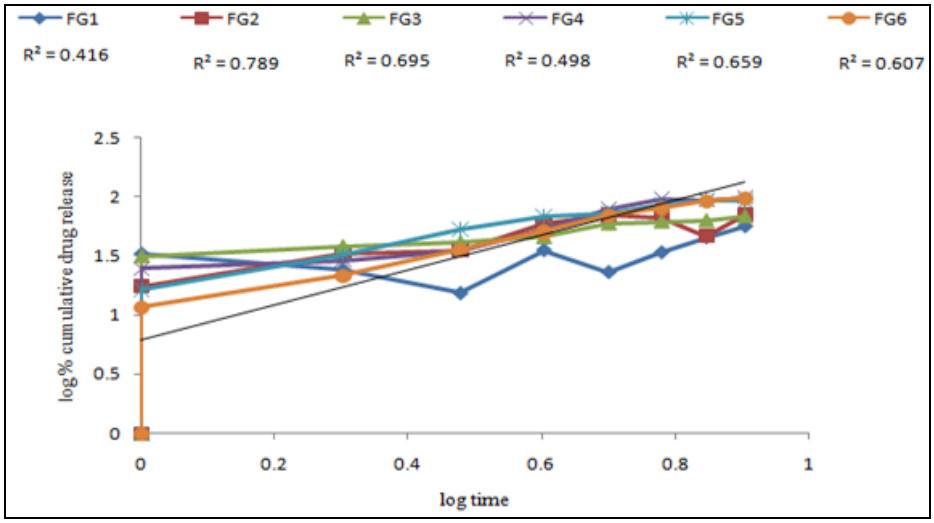

FIG. 17: COMPARATIVE *IN-VITRO* RELEASE STUDY OF NIOSOMAL GEL NIOSOMAL VESICLES PURE DRUG

TABLE 9: COMPARATIVE STUDY OF *IN-VITRO* RELEASE OF OPTIMIZED FORMULATION OF NIOSOMES VESICLES, NIOSOME GEL AND PURE DRUG

Time (h)	Niosomal Gel	Niosome Vesicles	Pure Drug
0	0	0	0
1	17.625	8.22	17.625
2	33.57	25.05	23.875
3	35.43	40.85	42
4	59.67	42.875	44.05
5	70.30	56.675	69.625
6	67.02	70.75	64.57
7	47.20	73.35	59
8	71.05	68.40	56.25

Stability Study: The stability study of the niosomal gel was performed as per ICH guidelines. Freshly prepared formulations were divided into groups and kept at specified storage conditions as per ICH guidelines. The sample was withdrawn periodically and tested for various evaluation parameters. The results of the stability study are tabulated in **Table 10**.

The stability study of the niosomal gel was performed as per ICH guidelines. Freshly prepared formulations were divided into groups and kept at specified storage conditions as per ICH guidelines. The sample was withdrawn periodically and tested for various evaluation parameters. The results of the stability study are tabulated in **Table 10**.

TABLE 10: STABILITY STUDY OF OPTIMIZED FORMULATION OF NG2 NIOSOMAL GEL

Formulation		NF2			
Storage condition		30 °C ± 2 °C / 65% RH ± 5% RH			
Time interval (days)	0	30	60		90
Homogeneity	+++	+++	+++		+++
Grittiness	+++	+++	+++		+++
PH	7.0	7.0	7.0		7.0
Drug content uniformity (%)	75	87.5	86.25		90
Skin irritation	No	No	No		No
+++ Excellent, ++Good, +satisfactory, -poor, --fail.					
In-vitro drug release (%)	0 h	0	0	0	0
	1 h	2.37	2.35	4.7	1.17
	2h	27.07	28.9	35.95	31.25
	3 h	47.62	42.425	51.97	50.7
	4 h	76.82	67.97	57.75	70.55
	5 h	84.3	77.6	63.62	81.4
	6 h	78.97	92.1	86.05	95.97
	7 h	88.77	91.6	84.05	86.15
No. of observation -03					

There was not much more variation in the properties of niosomal gel NG2 under stability study as the formulation retained all the properties when stored at specified storage conditions over a period of time, indicating that the niosomal gels were very much stable.

CONCLUSION: Novel vesicular drug delivery system has been used recently for the therapeutic effectiveness of transdermal drug delivery. According to the experiments that have been performed during the research , it is concluded that Montelukast sodium niosomal gel were successfully formulated by using niosomal prepared by thin hydration method by using span 60 and cholesterol in the ratio 1:1 and loaded in 2% carbopol was found to be best and promising. The niosomal gel formulation could be a useful dosage form to reduce the unwanted and undesirable side effect associated with oral route, niosomal gel may be considered as a best vesicular carrier for the effective delivery of Montelukast sodium via skin. The methodology applied for the preparation is simple and is also industrially feasible for lab as well as industrial scale. The niosomal gel formulation has immense potential and can be studied for its clinical implications in the future.

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