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Formulation, Evaluation and Characterization of Hydrochlorothiazide Niosomes

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Abstract

One of the many different carriers for getting a drug molecule to its site of action is a niosome, also known as a nonionic surfactant vesicle. Hydrophilic and hydrophobic medicines can both be trapped by them. The primary purpose of the medication hydrochlorothiazide, an angiotensin II type 1 receptor (AT1) antagonist, is to treat high blood pressure. Using cholesterol and nonionic surfactants (span 60) at varying concentrations, niosomes containing hydrochlorothiazide were created by the thin film hydration method. FTIR investigations, in vitro release studies, vesicular diameter, drug content, repeatability, shape and size distribution microphotography, and entrapment efficiency were all assessed for each niosome formulation.According to the findings, entrapment efficiency rises with surfactant concentration in all developed niosomal formulations. Low SD was found for the drug content, which ranged from 90.060.57 to 96.150.42. It was discovered that niosomes ranged in size from 0.280±0.098µm to 0.299±0.044µm and had a spherical shape. The medicine and formulation additives did not interact, according to the IR spectral analysis. Membrane diffusion cells were used to study the in vitro dissolution parameters. The findings indicate that formulation F6 exhibits a more controlled release action compared to the other formulation, with a 'n' value of 0.917, indicating that zero order kinetics were used to release the medication.

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INTRODUCTION

Microscopic non-ionic surfactant vesicles known as niosomes are produced by hydrating synthetic non-ionic surfactant, either with or without cholesterol. These resemble liposomes. Amphiphilic as well as lipophilic medicines are actively transported by both Niosomes and liposomes. The phospholipids that make up the liposomal bilayer are generated by liposomal systems, whereas non-ionic surfactants form the niosomal bilayer. Niosomes are created when

Table 1 Formulation table

Formulation code	Hydro-chlorothiazide (mg)	Cholesterol (mg)	Span-60 (mg)	Chloroform (ml)	Methanol (ml)	Phosphate buffer pH 7.4 (ml)
F1	10	10	5	10	10	10
F2	10	10	10	10	10	10
F3	10	10	15	10	10	10
F4	10	10	20	10	10	10
F5	10	10	25	10	10	10
F6	10	10	30	10	10	10
F7	10	10	35	10	10	10
F8	10	10	40	10	10	10

non-ionic surfactants self-assemble in aqueous fluids [1]. Depending on the preparation technique, they can take on spherical, unilamellar, bilayered, multilamellar, or polyhedral forms, or they can take on an inverse structure when the solvent is non-aqueous. The surfactant's orientation in the niosome is such that its hydrophilic ends face outward and its hydrophobic ends face each other, forming a surfactant bilayer. The niosomes vary in size from 10 to 1000 nm. The stabilisation of niosomal vesicles generated by the non-ionic surfactant is achieved with the addition of cholesterol and a small amount of anionic surfactant, such as dicetyl phosphate. Since phospholipids are more readily hydrolyzed due to the ester link and are less expensive than niosomes, it is argued that niosomes are superior than liposomes due to the greater chemical stability of surfactants. A novel drug delivery method is demonstrated by niosomes. Niosomal formulation can be administered transdermally, intramuscularly, intravenously, or orally [2].

MATERIALS AND METHODS

Hydrochlorothiazide is the gift sample from Hetro lab Pvt Ltd, Hydrabad, and the other polymer mixtures such as Chloroform, Methanol from Rankem chemicals,secunderadad, Span – 60, Sodium chloride and Potassium dihydrogen phosphates is from S.D. Fine Chem. Ltd. Mumbai.

METHODS

Preformulation study

Drug and excipients interaction (FTIR) study

FTIR spectra obtained (Bruker Pvt. Ltd, Germany) were used to determine the compatibility between the pure medication and surfactants, cholesterol. The KBr press was used to create the potassium bromide pellets [3]. The solid powder sample was ground with 100 times the quantity of KBr in a mortar to make the pellets. The powder was finely milled and added to a stainless steel die. About 10t/in2 of pressure was applied to the powder as it was squeezed between polished steel anvils in the die. On a pellet, a thin layer of the liquid sample is created for liquid samples. The wave numbers of 8000 cm-1 to 500 cm-1 were covered by the spectrum recordings [4].

Formulation of niosomes:

In a flask with a round bottom, the weighed amount of cholesterol and Span-60 was dissolved in a solution of methanol and chloroform (1:1). The flask was subsequently spun in a thermostatically controlled water bath at 37°C for 20 minutes at 100 revolutions per minute using a rotary flask evaporator [5]. Under reduced pressure (10–15 mmHg), the flask was spun at a height of 1.5 cm above the water bath until the entire organic phase evaporated and a slimy layer was left on the round-bottom flask wall. The weighed amount of drug was dissolved in 10 ml phosphate buffer pH 7.4 and the aquose phase was added to thin dry organig film formed in the flask. After the niosomal suspension had produced, it was put in an appropriate container and heated to a temperature of 30 degrees Celsius using a bath sonicator [6]. Then the dispersion was allow standing for 2 hrs at room temperature to form the niosomes. Then niosomes are stored in refrigerator.

Characterization of noisome:

Measurement of angle of repose:

Using the funnel method, the angle of repose of dry niosome powder was determined. The powdered niosomes were added to a funnel that was adjusted such that its exit aperture was 10 cm above a level black surface [7]. After the powder flowed out of the funnel and formed a cone on the surface, the diameter of the cone's base and its height were measured to determine the angle of repose.

Equation for calculating angle of repose is as follows:

θ = tan-1 (h/r)

Drug content:

100 millilitres of water were used to dissolve the weighed quantity of hydrochlorothiazide niosomes, which is equal to 100 milligrammes of eprosartan [8]. After filtering and further diluting the solution, a concentration of 10 μg/ml was achieved. Using distilled water as a blank, the absorbance of the solutions was measured at 272 nm using a double beam UV-visible spectrophotometer, as well as the percentage of drug present in the sample was computed.

Entrapment efficiency:

The following formula can be used to determine the entrapment efficiency.

$$\% \, Entrapment \, efficiency = \frac{\text{Actual drug loaded}}{\text{Theoritical drug loaded}} \times 100$$

Vesicular size and shape:

Particle size analysis was carried out using an optical microscope (compound microscope) with a calibrated eyepiece micrometer [9].

Calibration of eye piece micrometer:

For calibration, a conventional stage micrometre was employed. On stage, each division value is 10µ. There are one hundred divisions in the eye piece micrometre. The standard stage micrometre was calibrated to determine the measure of each division. The eye piece micrometre was used to determine particle size after calibration. Niosomes were suspended in a saline buffer with a pH of 7.4. A suspension drop was placed on a slide and examined under a microscope. Using an eye piece micrometre, about 200 niosomes were measured one at a time. Their size distribution range and mean diameter were computed, as well as an average was taken.

Microphotography:

Niosomal suspensions are examined under an optical microscope to check on the vesicle's shape and lamellar makeup. Microphotographs were captured using an 8 megapixel Nikon D-500 camera [10].

SEM

One crucial component is the size of the niosomes' particles. SEM was used to examine the size distribution and surface appearance of niosomes. Niosomal powder was applied on aluminium stubs using a double-sided tape that was attached to them [11]. The aluminium stub was put into an XL 30 ESEM with EDAX, Philips, Netherlands, vacuum chamber for a scanning electron microscope. A gaseous secondary electron detector (working pressure of 0.8 torr, acceleration voltage-30.00 KV) XL 30 (Philips, Netherlands) was used to observe the morphological characteristics of the samples.

***In vitro* release studies**

Using the membrane diffusion technique, the release of hydrochlorothiazide from niosomal formulations was ascertained. The niosomal formulation, which was equal to 10 mg of LP, was transformed into niosomal suspension as well as placed in a glass tube with a 2.5 cm diameter and an 8 cm effective length. The tube served as a donor compartment and was previously coated with a soaking osmosis cellulose membrane. As a receptor compartment, the glass tube was put in a beaker with 100 ml of saline buffer pH 7.4. The entire assembly was adjusted so that the diffusion medium's surface was only touched (1-2 mm deep) by the bottom end of the tube carrying the suspension [12]. The receptor medium was stirred using a magnetic stirrer at a speed of 100 rpm while maintaining a temperature of 37±1{C. The same volume of medium was replaced after each periodic pullout of aliquots containing five millilitres of sample. A double beam UV-VIS spectrophotometer was used to analyse the samples at a wavelength of 272 nm. Saline buffer 7.4 was used as a blank for this analysis [13].

Table 2 Interpretations of FTIR

Functional Groups	Hydro chloro thiazide	Cholesterol	Span – 60	Hydro chlorothiazide + Cholestrol	Hydro chlorothiazide + Span – 60	Hydro chlorothiazide + Cholestrol + Span – 60
O-H (stretch, free)	3735.48	3392.20	3408.45	3367.22	3408.51	3408.45
Alkyl C-H Stretch	2868.62	1710.43	2922.35	2929.38	2922.62	2922.69
C=O stretch	1714.21	1710.43	1462.66	1458.61	1739.51	1739.20
CH_3 bend	1338.58	1371.91	1377.24	1377.29	1377.21	1377.45
C-H bend (meta)	885.16	883.45	872.80	840.52	882.42	876.32

Sterility test:

Being sterile means that there are no living bacteria present. The notion of sterility for a pharmaceutical product must be defined in terms of its intended use, as the requirements that ensure perfect sterility are typically too stringent for active components. The gramme staining method on agar medium can be used to perform the sterility test [14].

Release kinetics

The following models were used to perform a mathematical analysis of the release data in order to look into potential drug release mechanisms from the manufactured niosomes:

Zero order- Q=Ko t 25

First order- Log Q= Log Qo-K1 t/2.30326.

Higuchi- Qt = KH t ½ 26.

Korsmeyer - Peppas- Qt/Qα = K tn27.

Where,

Q is the amount of drug release at a time (t) and K is the rate constant.

Stability studies:

For three months, the stability tests for the optimal niosome formulation were conducted in accordance with ICH guidelines. Three groups of formulated niosomes were created. One group was maintained at 4°±2°C under refrigeration. The second group was maintained at 25°±2°C, room temperature [15].

RESULTS AND DISCUSSION

Preformulation Study:

Drug and excipients interaction (FTIR) study:

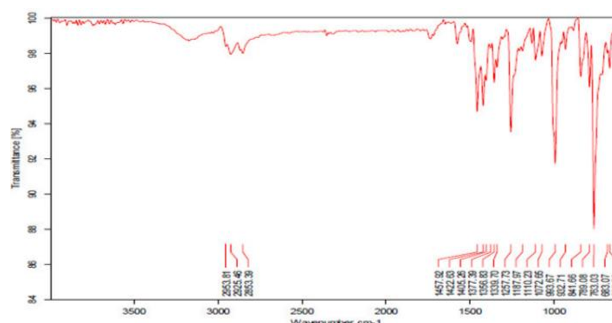

Figure 1 FTIR Spectrum of Hydrochlorothiazide

FTIR spectrum of LP, cholesterol, span 60, 0 and niosomal formulations are shown in figures 5-10. FTIR spectrum of Hydrochlorothiazide showed characteristics absorption bands in the IR region, 3735.48cm-1 (O-H(stretch, free)); 3171.36cm-1 (N-H stretch); 1338.58cm-1 (CH_3 bend); 885.16cm-1 (C-H bend). Span 60 in pure form shows the presence of hydroxyl absorption at 3416 cm-1, strong aromatic CH=CH stretching at 2920cm-1 and a strong C=O of carboxylic ester is notice at 1739cm-1. Cholesterol shows the presence of hydroxyl absorption at 3423cm-1, strong aromatic CH=CH stretching at 2868.62 cm-1 and a strong C=O of carboxylic ester at 1710.43cm-1. Similarly, cholesterol as expected shows the presence of hydroxyl absorption at 3392.20cm–1. The FTIR spectrum of niosomal formulation shows C=O stretch at 1739.20 cm-1; C-H bend at 835.17 cm-1; CH_3 bend at 1377.45 cm-1; O-H (stretch, free) at 3408.45 cm-1. From the spectra of Hydrochlorothiazide, physical mixture of Hydrochlorothiazide and excipients, Hydrochlorothiazide niosomes was observed that all characteristic peaks of Hydrochlorothiazide were present in the combination spectrum, thus

indicating compatibility of the Hydrochlorothiazide and excipients. IR Spectra are shown in **Figure 1Figure 2Figure 3Figure 4Figure 5Figure 6**.

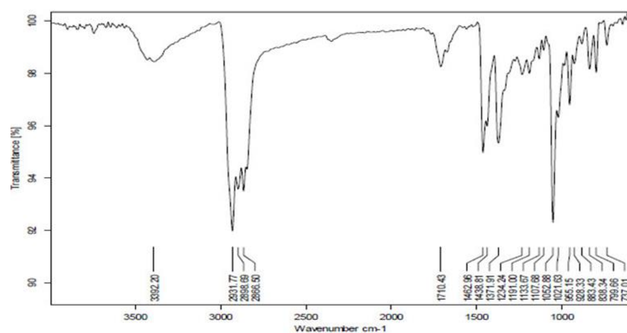

Figure 2 FTIR Spectrum of Cholesterol

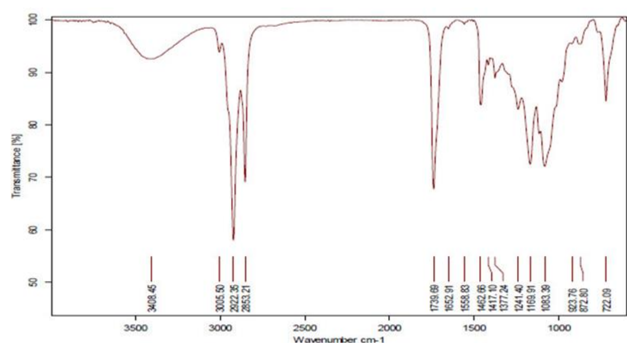

Figure 3 FTIR Spectrum of Span – 60

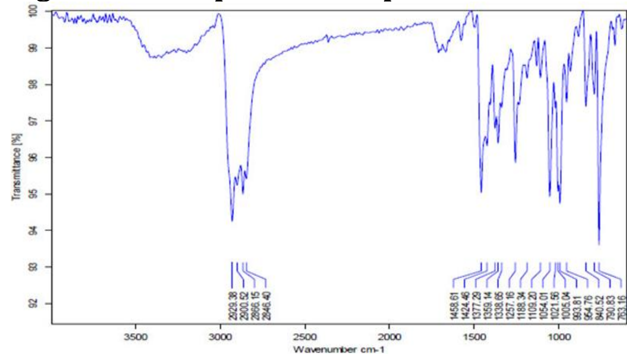

Figure 4 FTIR Spectrum of Hydrochlorothiazide + Cholestrol

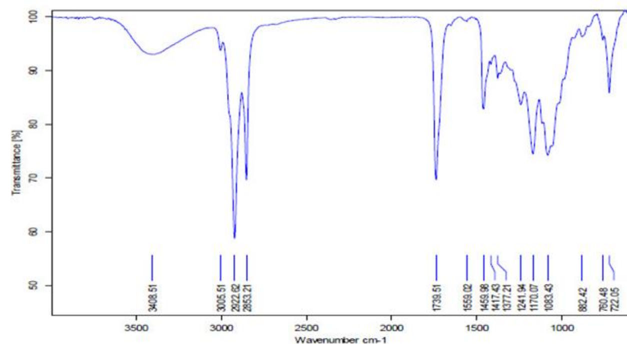

Figure 5 FTIR Spectrum of Hydrochlorothiazide + Span – 60

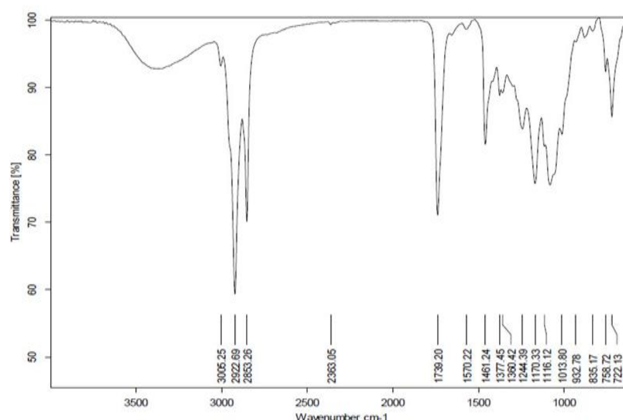

Figure 6 FTIR Spectrum of Hydrochlorothiazide + Cholestrol + Span – 60

Characterization of noisome:

Angle of repose:

Table 3 displays the measured angle of repose of the powdered dry niosomes using the funnel method. Among dry niosomes, the angle of repose ranged from 27°84′±0.19 to 28°14′±0.34.

Entrapment efficiency:

Table 11 displays the entrapment efficiency of niosomes prepared at different surfactant concentrations (Span 60). For each of the eight formulations, the drug entrapped ranged from 48.34±0.16, 53.04±0.56, 56.95±0.49, 56.38±0.85, 59.37±0.59, 61.28±0.72, 62.05±0.39, and 64.46±0.29, respectively. As surfactant concentration rises, it also increases its entrapment efficiency.

Drug content:

The amount of drug in each niosomal formulation was ascertained. Three determinations on average were taken into account. The range of the drug content was determined to be 90.06±0.57 to 96.15±0.42.

Vesicular size, shape:

Following their conversion to niosomal suspension, the size of the niosomes was assessed using an optical microscope equipped with a micrometre for calibration of the eyepiece. A diameter measurement was taken of around 200 niosomes per batch, and tables 4 computed the average value. Table displays the distribution of sizes. Niosomes have a spherical shape, as seen by the SEM pictures of formulation F6 (**Figure 8**).

Table 3 Angle of repose ,% encapsulation and %Drug content of formulation F1 to F8

Formulation code	Angle of repose(θ)*±SD	Percentage Entrapment* ±S.D	Percentage Drug content* ±S.D
F1	27°84′±0.19	48.34±0.16	90.06±0.57
F2	29°22′±0.35	53.04±0.56	91.96±o.37
F3	25°92′±0.15	56.95±0.49	92.48±0.62
F4	26°12′±0.28	56.38±0.85	92.39±0.29
F5	28°52′±0.62	59.37±0.59	95.15±0.59
F6	26°34′±0.26	61.28±0.72	97.25±0.52
F7	29°15′±0.48	62.05±0.39	94.43±0.28
F8	28°14′±0.34	64.46±0.29	96.15±0.42

Table 4 Particle size of niosomes

Formulation code	Mean Particle size*±S.D in (nm)	Mean Particle size*±S.D in (μm)
F1	288±0.98	0.280±0.098
F2	285±6.26	0.285±0.625
F3	260±3.18	0.256±0.214
F4	268±0.28	0.273±0.025
F5	250±5.14	0.248±0.053
F6	282±4.46	0.283±0.045
F7	260±4.55	0.315±0.026
F8	295±4.25	0.299±0.044

*Average of three readings

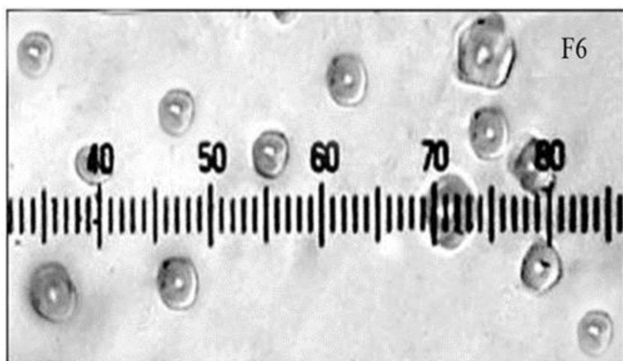

Figure 7 Image of formulation F6 Optical microscopy

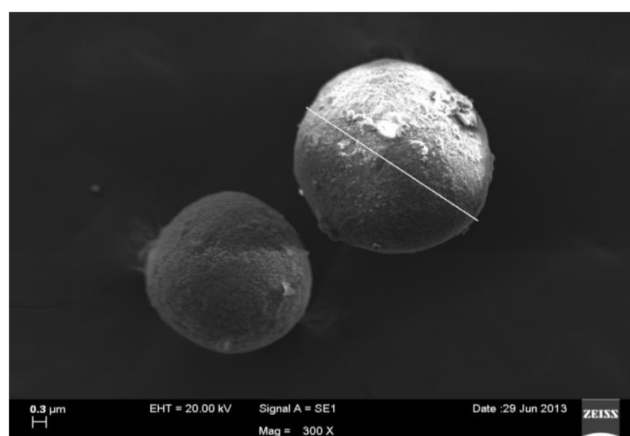

Figure 8 SEM image of formulation F6

In vitro Drug Release Studies:

In vitro drug release tests were conducted on the several hydrochlorothiazide niosomal formulations that were developed. The results are displayed in Table 6 and the dissolution kinetic profiles are provided in Figures 10-53. The drug release percentages for the niosomal formulations F1 (95.03 at 7 hours), F2 (96.02 at 7 hours), F3 (93.75 at 8 hours), F4 (93.64 at 8 hours), F5 (90.58 at 9 hours), F6 (92.65 at 10 hours), F7 (92.47 at 9 hours), and F8 (95.53 at 8 hours) are as follows.

Because of the formulations' first niosome bursting, 17% to 30% of the medication is released in the first few hours of use in every formulation. Nonetheless, the medication was retained by the stable niosomes for up to 12 hours of continuous action, resulting in a steady release of the drug after 3 hours. In comparison to other formulations, the niosomal formulation F6 exhibits better controlled releasing. The zero order, first order, Korsemayer Peppas, and Higuchi Matrix kinetic models were chosen. Tables 25 displayed the regression coefficient values for each of these models. Peppas, with a "n" value between 0.768 and 0.917, was determined to be the best-fit model in every instance. The 'n'

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value of formulation F6 was 0.917 and suggesting that the drug was released by Zero order kinetics.

Table 5 Invitro diffusion profile for API (Hydrochlorothiazide)

Time in hrs	Absorbance In 272 nm	Cumulative % drug release
1	0.125	20.34
2	0.242	40.12
3	0.365	55.52
4	0.475	75.45
5	0.592	92.43

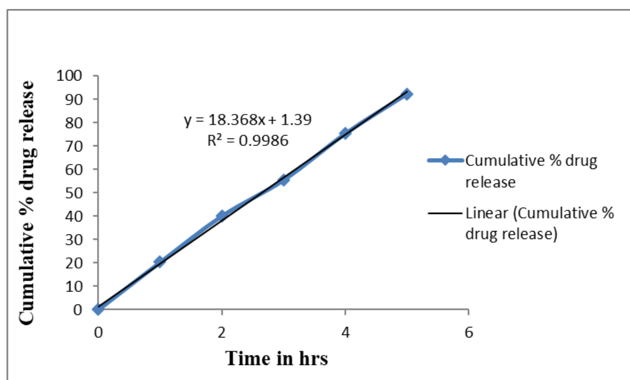

Figure 9 Invitro diffusion profile for API (Hydrochlorothiazide)

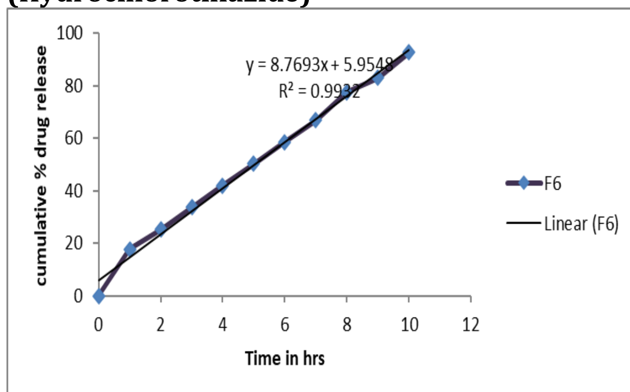

Figure 10 Zero order order kinetic for F6 formulation

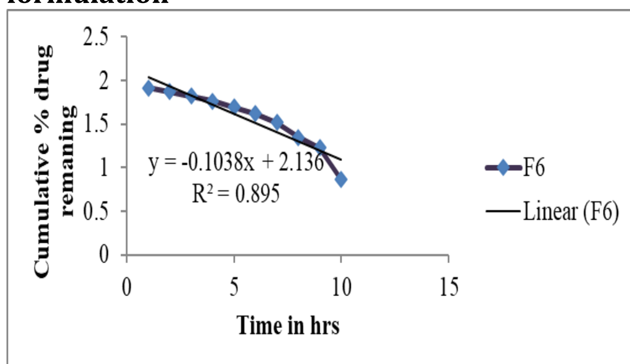

Figure 11 First order order kinetic for F6 formulation

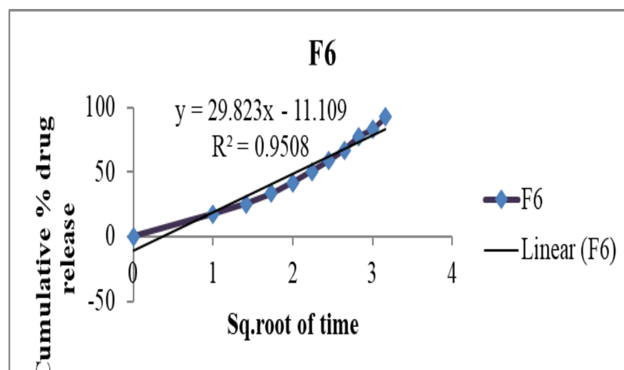

Figure 12 Higuchi kinetic model module for F6 formulation

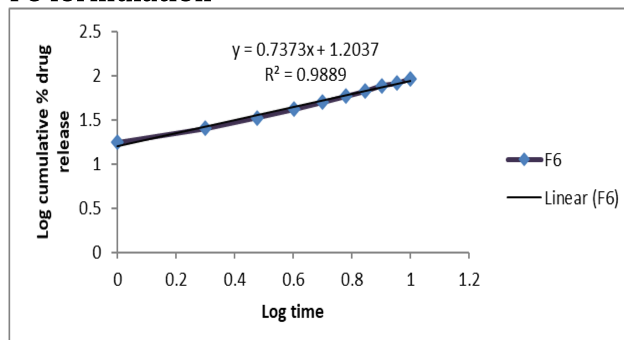

Figure 13 Korsmeyer-Peppas model module for F6 formulation

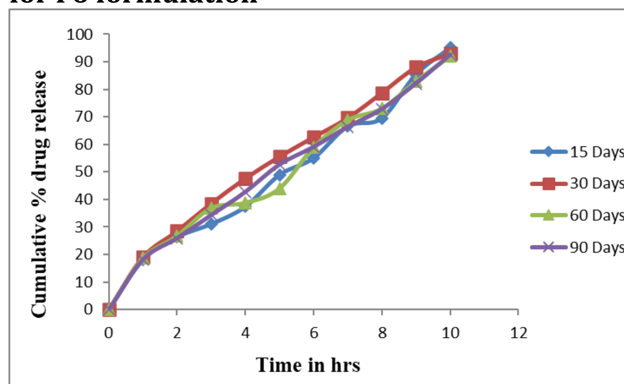

Figure 14 Invitro studies of formulation F6 stored at refrigeration condition

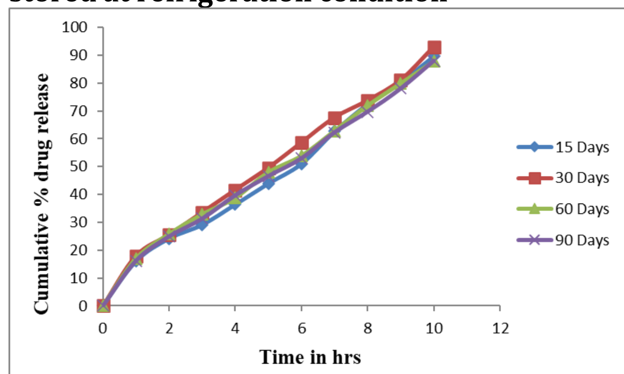

Figure 15 Invitro studies of formulation F6 stored at room temperature

Table 6 Invitro drug release kinetic for F6 formulation

Time in hrs	square root of time	log time	cumulative percentage drug release	cumulative percentage drug remaining	log cumulative percentage drug release	log cumulative percentage drug remaining
1	1	0	17.73	82.27	1.248709	1.9152
2	1.414	0.30103	25.36	74.64	1.404149	1.87297
3	1.732	0.477121	33.64	66.36	1.526856	1.82191
4	2	0.60206	41.92	58.08	1.622421	1.76403
5	2.236	0.69897	50.293	49.707	1.701508	1.69642
6	2.449	0.778151	58.62	41.38	1.768046	1.61679
7	2.645	0.845098	66.91	33.09	1.825491	1.5197
8	2.828	0.90309	77.63	22.37	1.89003	1.34967
9	3	0.954243	83.06	16.94	1.919392	1.22891
10	3.162	1	92.65	7.35	1.966845	0.86629

Table 7 Pharmacokinetic parameters for formulation F1 to F8

Formulation code	Zero order (R^2)	First order (R^2)	Higuchi model (R^2)	Korsmeyer-Peppas model (R^2)	N
F1	0.9847	0.7731	0.9623	0.9881	0.781
F2	0.9642	0.8427	0.9843	0.9932	0.794
F3	0.9853	0.8582	0.9587	0.9832	0.768
F4	0.9923	0.8763	0.9517	0.9948	0.876
F5	0.9865	0.9311	0.9687	0.9985	0.895
F6	0.9932	0.895	0.9508	0.9889	0.917
F7	0.9807	0.885	0.9649	0.9786	0.892
F8	0.9869	0.8341	0.9611	0.989	0.793

Table 8 Sterility test for formulation F1 to F8

Formulation code	Gram + ^{ve} bacteria	Gram - ^{ve} bacteria
F1	Negative	Negative
F2	Negative	Negative
F3	Negative	Negative
F4	Negative	Negative
F5	Negative	Negative
F6	Negative	Negative
F7	Negative	Negative
F8	Negative	Negative

Table 9 Stability analysis of formulation F6 under various circumstances

Time period	4°C ± 1°C		25°C ± 5°C		30°C ± 2°C and 60% RH ± 5% RH	
	% Drug content	Sterility of product	% Drug content	Sterility of product	% Drug content	Sterility of product
15 Days	96.22±0.80	Sterile	96.30±0.56	Sterile	96.85±0.78	Sterile
30 Days	96.03±0.36	Sterile	94.91±0.73	Sterile	95.98±0.76	Sterile
60 Days	95.58±0.43	Sterile	94.05±0.42	Sterile	94.71±0.76	Sterile
90 Days	95.08±0.85	Sterile	95.43±0.68	Sterile	94.02±0.68	Sterile

Table 10 Invitro studies of formulation F6 stored at refrigeration condition

Time in hrs	Cumulative percentage drug release			
	15 Days	30 Days	60 Days	90 Days
1	18.14	19.08	18.65	18.23
2	26.46	28.56	26.86	25.96
3	31.13	38.58	36.95	34.35
4	37.45	47.66	38.83	42.75
5	48.97	55.59	44.06	52.66
6	55.08	62.67	58.95	59.04
7	66.65	69.64	68.89	66.32
8	69.54	78.75	73.08	72.76
9	85.48	88.05	82.96	82.08
10	95.08	92.97	92.04	92.45

Table 11 Invitro studies of formulation F6 stored at room temperature

Time in hrs	Cumulative percentage drug release			
	15 Days	30 Days	60 Days	90 Days
1	16.04	17.95	17.04	16.22
2	24.22	25.54	25.85	24.94
3	29.14	33.56	32.95	31.34
4	36.44	41.65	38.85	39.72
5	43.96	49.58	48.02	46.62
6	51.05	58.64	53.93	53.02
7	62.68	67.62	62.92	62.32
8	72.52	73.72	72.02	69.74
9	80.44	81.05	79.95	78.06
10	89.68	92.97	87.84	88.06

Table 12 Invitro studies of formulation F6 stored at Accelerated condition

Time in hrs	Cumulative percentage drug release			
	15 Days	30 Days	60 Days	90 Days
1	16.65	17.04	14.97	16.04
2	26.14	24.87	24.52	24.96
3	34.05	33.84	31.17	34.05
4	42.82	41.07	39.43	43.16
5	48.52	48.42	48.84	52.64
6	56.65	55.54	53.43	56.31
7	67.84	63.63	62.33	64.23
8	75.62	70.52	69.17	71.05
9	84.08	79.14	81.12	78.32
10	91.65	88.04	89.12	88.04

Sterility test:

All samples passed sterility test, it indicates absence of microorganisms in noisome formulation.

Stability studies:

According to ICH guidelines, stability studies are conducted for the optimal formulation (F6) for a period of three months in three distinct storage conditions. The formulation are analyzed for the drug content, invitro drug release studies and sterility studies. After a 3 months studies it revolves that there is no change in sterility of formulation, but in vitro drug release studies, there was a small variation in the percentage of drug content, but it remained within the acceptable range. (Table 9) Durg content percentages under various stability conditions.

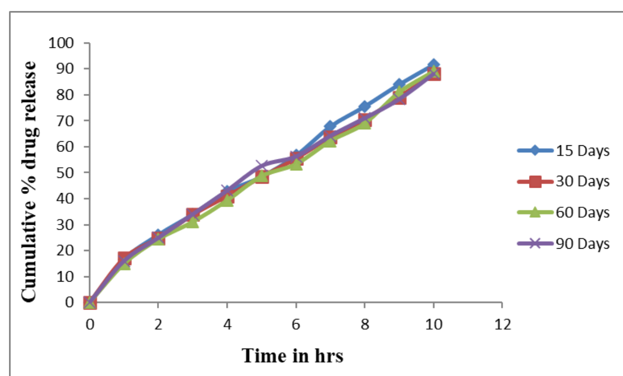

Figure 16 Invitro studies of formulation F6 stored at Accelerated condition

CONCLUSION

The thin-film hydration method makes it easy to generate niosomal formulations by utilising cholesterol at varying concentrations and nonionic surfactants (span 60). Through the use of the funnel method, it was discovered that all of the niosomal powders were free flowing, with angles of repose ranging from 27.84±0.19 to 28.14±0.34. If the concentration of span 60 is increased, the entrapment efficiency of niosomal formulations also increases. The findings were repeatable, and the drug content of the niosomal formulations ranged from 90.06±0.57 to 96.15±0.42 with a small standard deviation. All of the batches' average niosome vesicular sizes fell between 0.280±0.098μm and 0.299±0.044μm. The spherical shape of the niosomes was revealed by the SEM images of niosomal formulations F6. Drug release from vesicles is reliant on span 60 concentrations. Phase transition temperature is the primary cause of it. With a "n" value ranging from 0.768 to 0.917, Peppas was determined to be the best-fitting model across all formulations.With a "n" value of 0.917, formulation F6 has a more controlled released action than the other formulations, indicating that zero order kinetics were used to release the drug.

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REFERENCES

[1] Giuseppe Derosa, Pietro D Ragonesi, Amedeo Mugellini, Leonardina Ciccarelli, and Roberto Fogari. Effects of telmisartan compared with eprosartan on blood pressure control, glucose metabolism and lipid profile in hypertensive, type 2 diabetic patients: a randomized, double-blind, placebo-controlled 12-month study. Hypertension Research, 27(7):457-64, 2004.

[2] R Fogari, A Zoppi, I Ferrari, A Mugellini, P Preti, P Lazzari, and G Derosa. Comparative effects of telmisartan and eprosartan on insulin sensitivity in the treatment of overweight hypertensive patients. Harmone and Metabolic Research, 41(12):893-8, 2009.

[3] Greg L Plosker. Eprosartan: a review of its use in hypertension. Drugs, 69(17):2477-99, 2009.

[4] Domenic A Sica, Barry Carter, William Cushman, Lee Hamm. Thiazide and loop diuretics. Journal of Clinical Hypertension, 13(9):639-43, 2011.

[5] Vijaya M Musini, Mark Nazer, Ken Bassett, and James M Wright. Blood pressure-lowering efficacy of monotherapy with thiazide diuretics for primary hypertension. The chochrane Database of Systematic Reviews, (5):CD003824, 2014.

[6] Karim Masud Kazi, Asim Sattwa Mandal, Nikhil Biswas, Arijit Guha, Sugata Chatterjee, Mamata Behera, and Ketousetuo Kuotsu. Niosome: A future of targeted drug delivery systems. Journal of Advanced Pharmaceutical Technology and Research, 1(4):374-80, 2010.

[7] Adnan Azeem, Md Khalid Anwer, and Sushama Talegaonkar. Niosomes in sustained and targeted drug delivery: some recent advances. Journal of Drug Targeting, 17(9):671-89, 2009.

[8] N B Mahale, P D Thakkar, R G Mali, D R Walunj, and S R Chaudhari. Niosomes: novel sustained release nonionic stable vesicular systems--an overview. Advances in Colloid and Interface Science, 183-184:46-54, 2012.

[9] Yasmeena Thabet, Mahmoud Elsabahy, and Noura G Eissa. Methods for preparation of niosomes: A focus on thin-film hydration method. Methods, 9-15, 2022.

[10] Bwalya A. Witika, Kokoette E. Bassey, and Patrick H. Demana, Xavier Siwe-Noundou, and Madan S. Poka. Current Advances in Specialised Niosomal Drug Delivery: Manufacture, Characterization and Drug Delivery Applications. International Journal of Molecular Sciences, 23(17): 9668, 2022.

[11] Ashutosh Lohumi. A Novel Drug Delivery System: Niosomes Review. Journal of Drug Delivery and Therapeutics, 2(5): 129-135, 2012.

[12] Kauslya Arumugam, Borawake Payal D, Shinde Jitendra V, and Chavan Rajashree S. Niosomes: A Novel Carrier Drug Delivery System. Journal of Drug Delivery and Therapeutics, 11(1):162-170, 2021.

[13] Ravindra Bhana, Ajay Verma, and Sanjay Jain. Development and Characterization of Ethosomes Bearing Losartan Potassium for Transdermal Drug Delivery. International Journal of Pharmacy and Pharmaceutical Sciences, 5(1): 35-40, 2012.

[14] Sakthivel M, Kannan K, Manavalan R, and Senthamarai R. Formulation and in vivo Evaluation of Niosomes containing Oxcarbazepine. Journal of Pharmaceutical Sciences and Research, 5(1): 8-11, 2013.

[15] P Arunothayanun, M S Bernard, D Q Craig, I F Uchegbu, and A T Florence. The effect of processing variables on the physical characteristics of nonionic surfactant vesicles (niosomes) formed from hexadecyl diglycerol ether. International Journal of Pharmaceutics, 201(1):7-14,2000.

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