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Formulation, Evaluation, and Characterization of Indapamide Niosomes

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Abstract

Niosomes, also known as nonionic surfactant vesicles, are one of the many carriers used to carry drug molecules to their target sites. They can hold both hydrophilic and hydrophobic medicines. Indapamide is an angiotensin II type 1 receptor (AT1) antagonist medication primarily used to treat high blood pressure. Niosomes containing Indapamide were created utilizing the thin film hydration process with various cholesterol concentrations and nonionic surfactants (span 60). All noisome formulations were assessed for entrapment efficiency, drug content, reproducibility, vesicular diameter, shape and size distribution microphotography, FTIR analysis, and in vitro release experiments. The results indicate that in all of the created niosomal formulations, as the surfactant content increases, the entrapment efficiency also increases. The drug content ranged between 90.06±0.57 and 96.15±0.42, with a low standard deviation. Niosomes range in size from 0.280±0.098µm to 0.299±0.044µm and have a spherical shape. The IR spectrum analysis indicated no interaction between the medication and the formulation ingredients. Membrane diffusion cells were used to study the in vitro dissolution parameters. The results demonstrate that formulation F6 had a better-controlled release action than other formulations, with an 'n' value of 0.917, indicating that the medication was released using zero-order kinetics.

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INTRODUCTION

Microscopic nonionic surfactant vesicles known as niosomes are produced by hydrating synthetic nonionic surfactant, either with or without cholesterol. They are inside the liposome. Both Niosomes and liposomes actively transport amphiphilic and lipophilic medicines. Liposomal systems generate the phospholipids that comprise the liposomal bilayer, whereas nonionic surfactants form the liposomal bilayer. Niosomes are created when nonionic surfactants self-

assemble in aqueous fluids. Depending on the preparation technique, they can take on spherical, unilamellar, bilayered, multilamellar, or polyhedral forms or take on an inverse structure when the solvent is non-aqueous [1]. The surfactant's orientation in the noisome 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 stabilization of niosomal vesicles generated by the nonionic surfactant is achieved by adding cholesterol and a small number of anionic surfactants, such as diacetyl 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 to liposomes due to surfactants' more excellent chemical stability. Niosomes demonstrate a novel drug delivery method. Niosomal formulation can be administered transdermally, intramuscularly, intravenously, or orally [2].

MATERIALS AND METHODS:

MATERIALS:

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

METHODS:

Preformulation study

Drug and excipients interaction (FTIR) study

FTIR spectra made it possible to determine whether the pure drug and the surfactants, cholesterol, were compatible (Bruker Pvt. Ltd, Germany). Potassium bromide pellets were made using a KBr press. The solid powder sample was mashed in a mortar using 100 times the amount of KBr to prepare the pellets [3]. A stainless steel die was filled with the finely ground powder. At roughly 10t/in2 pressure, the powder was compressed in the die between polished steel anvils. A thin layer of the liquid sample is created on the pellet for liquid samples. The wave number range covered by the recorded spectra was 8000 cm-1 to 500 cm -1 [4].

Formulation of Niosomes

The weighed amounts of cholesterol and Span-60 were dissolved in a 1:1 mixture of methanol and chloroform in a round-bottom flask. Afterward, the flask was placed in a thermostatically controlled water bath at 37°C and spun for 20 minutes at 100 rpm in a rotary flask evaporator. After all of the organic phase had evaporated and a slimy film had formed on the wall of the round-bottom flask, the flask was rotated at a height of 1.5 cm above the water bath while operating at a reduced pressure of 10–15 mmHg [5]. The medication was weighed and dissolved in 10 milliliters of PH 7.4 phosphate buffer. The aqueous phase was then added to the thin, dry organic film that had developed in the flask. After the liposomal suspension had been produced, it was put in an appropriate container and heated to a temperature of 30 degrees Celsius using a bath sonicator [Table 1]. After that, the dispersion was let to stand at room temperature for two hours to create niosomes. Niosomes are then kept in a refrigerator [6].

Characterization of noisome

Measurement of angle of repose

Table 1 Formulation table

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

The funnel method determined the angle of repose of dry noisome powder. The powdered niosomes were added to an adjusted funnel such that its exit aperture was 10 cm above a level black surface. 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 [7]. The equation for calculating the angle of repose is as follows:

θ = tan-1 (h/r)

Drug content

One hundred milliliters of water were used to dissolve the weighed quantity of Indapamide niosomes, equal to 100 mg of Eprosartan. After filtering and further diluting the solution, a ten µg/ml concentration was achieved [8]. Using distilled water as a blank, the absorbance of the solutions was measured at 285 nm using a double-beam UV-visible spectrophotometer, and the percentage of drug present in the sample was computed.

Entrapment efficiency

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

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

Vesicular size and shape:

A particle size examination was performed using an optical microscope (compound microscope) with a calibrated ocular micrometer [9].

Microphotography:

An optical microscope examines niosomal suspensions to examine the vesicles' lamellar structure and form. Microphotographs were captured using an 8-megapixel Nikon D-500 camera [10].

SEM

A key aspect is the size of the liposome particles. SEM was used to examine the size distribution and surface appearance of niosomes. Niosomal powder was applied to aluminum stubs using a double-sided tape. The aluminum stub was put into an XL 30 ESEM with EDAX, Philips, Netherlands, vacuum chamber for a scanning electron microscope. Using a gaseous secondary electron detector (working pressure of 0.8 torr, acceleration voltage of 30.00 KV) XL 30, the morphological characteristics of the samples were studied [11].

***In vitro* drug release studies [12]**

The membrane diffusion method was used to measure Indapamide release from niosomal formulations. The 10 mg of LP that made up the niosomal formulation was transformed into niosomal suspension and placed in a glass tube measuring 2.5 cm in diameter and 8 cm in length. The tube was coated with a soaking osmosis cellulose membrane as a donor compartment. The glass tube was put into the receptor compartment, and a beaker was filled with 100 ml of saline buffer pH 7.4. Everything was adjusted such that the tube containing the suspension barely touched (1-2 mm deep) the diffusion medium's surface. C. Periodically, aliquots containing five milliliters of the sample were removed, and the same medium volume was reintroduced. Saline buffer 7.4 was used as a blank when analyzing the samples at 285 nm in a double-beam UV-VIS spectrophotometer. °The magnetic stirrer was used to agitate the receptor media at a speed of 100 rpm while maintaining a temperature of 37±1.

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 gram staining method on agar medium can be used to perform the sterility test [13].

Release Order Kinetics [14]

The following models were used to perform a mathematical analysis of the release date 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.

Stability studies:

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

RESULTS AND DISCUSSION

Preformulation Study:

Drug and excipients interaction (FTIR) study:

FTIR spectrum of LP, cholesterol, span 60, 0, and niosomal formulations are shown in figures 5-10. FTIR spectrum of Indapamide 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). When Span 60 is pure, it exhibits aromatic solid CH=CH stretching at 2920 cm-1, hydroxyl absorption at 3416 cm-1, and a solid carboxylic ester C=O at 1739 cm-1. Strong aromatic CH=CH stretching at 2868.62 cm-1, hydroxyl absorption at 3423 cm-1, and a solid carboxylic ester C=O at 1710.43 cm-1 are all present in cholesterol. Similarly, cholesterol exhibits hydroxyl absorption at 3392.20 cm−1, as would be expected. 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. Based on the Indapamide spectra and the physical mixture of Indapamide and excipients, it was noted that all of the Indapamide's characteristic peaks were present in the combination spectrum, showing that the Indapamide and excipients were compatible. Table 2 & Figures 1 display IR spectra.

Table 2 Interpretations of FTIR

Functional Groups	Indapamide	Cholesterol	Span – 60	Indapamide + Cholestrol + Span – 60
O-H (stretch, free)	3735.48	3392.20	3408.45	3408.45
Alkyl C-H Stretch	2868.62	1710.43	2922.35	2922.69
C=O stretch	1714.21	1710.43	1462.66	1739.20
CH_3 bend	1338.58	1371.91	1377.24	1377.45
C-H bend (meta)	885.16	883.45	872.80	876.32

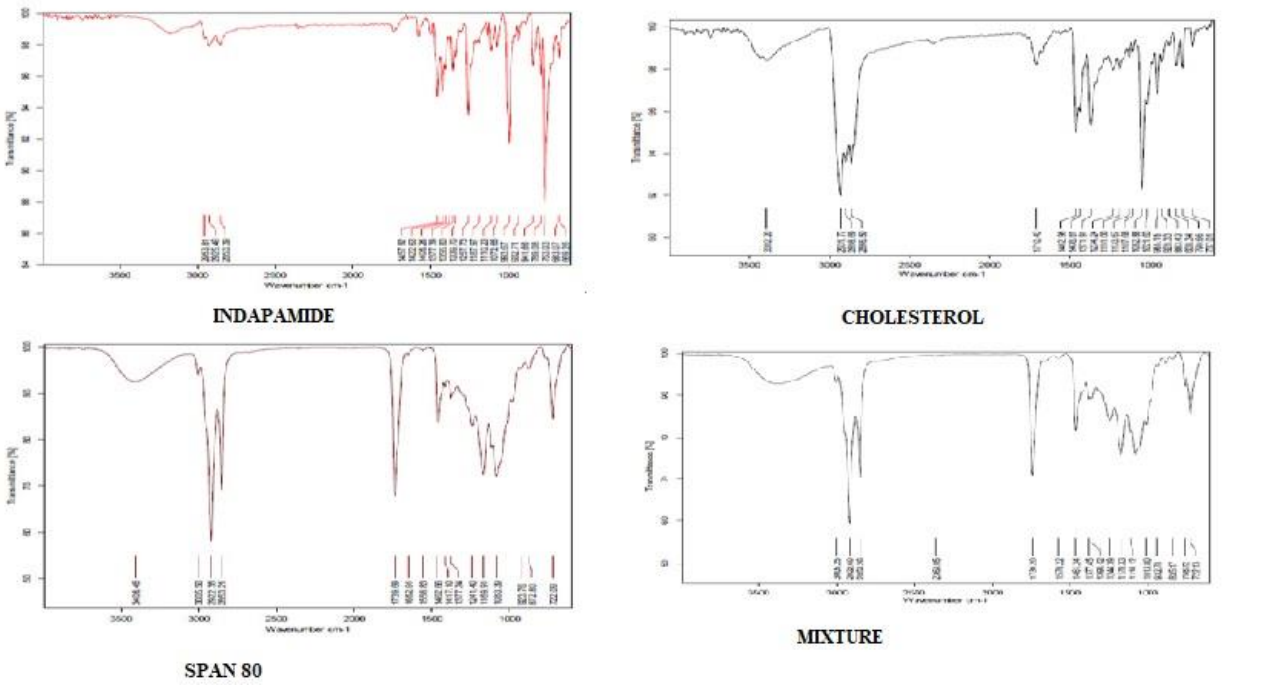

Figure 1 FTIR Spectrum Drug, Polymer and Mixture of compounds

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	26°84′±0.18	46.34±0.17	91.06±0.56
F2	28°22′±0.34	52.04±0.55	92.96±o.36
F3	24°92′±0.14	55.95±0.48	93.48±0.61
F4	25°12′±0.27	54.38±0.84	93.39±0.28
F5	27°52′±0.61	58.37±0.58	94.15±0.58
F6	25°34′±0.25	62.28±0.71	96.25±0.51
F7	27°15′±0.47	61.05±0.38	95.43±0.27
F8	28°14′±0.33	63.46±0.28	97.15±0.41

*Average of three readings

Characterization of noisome:

The angle of repose:

Table 3 displays the angle of repose of dry noisome powder as determined by the funnel method. Dry niosomes had an angle of repose ranging from 26°84′±0.18 to 27°15′±0.47.

Entrapment efficiency:

Table 3 displays the entrapment efficiency of niosomes prepared at different surfactant concentrations (Span 60). The drug entrapped in the range of 46.34±0.17, 52.04±0.55, 55.95±0.48, 54.38±0.84, 58.37±0.58, 62.28±0.71, 61.05±0.38, and 63.46±0.28 for F1, F2, F3, F4, F5, F6, F7, and F8, successively. With a rise in surfactant concentration, the entrapment efficiency rises.

Drug content:

The amount of drug in each niosomal formulation was ascertained. Three determinations, on average, were taken into account [Table 3]. It was discovered that the drug content ranged from 91.06±0.56 to 97.15±0.41.

Vesicular size shape:

After the niosomes were transformed into niosomal suspension, their size was assessed using an optical microscope equipped with a micrometer to calibrate the eyepiece. Approximately 200 niosomes per batch were measured for diameter separately; the average was computed and shown in Table 4. The table displays the size dispersion. The spherical shape of niosomes is seen by the SEM pictures of formulation F6 (figure 8).

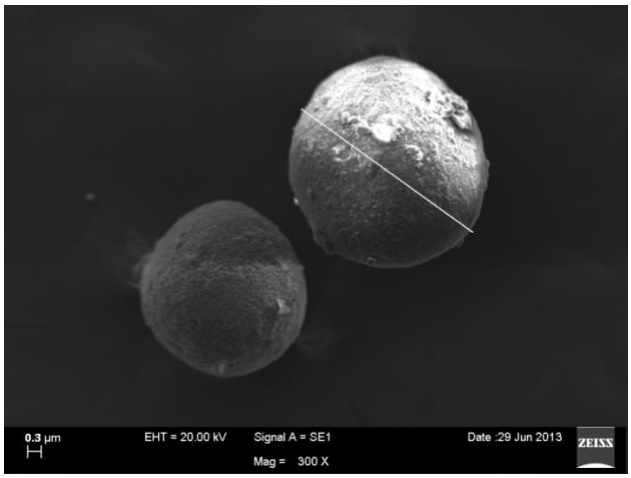

Figure 2 SEM image of formulation F6

Table 4 Particle size of niosomes

Formulation code	Mean Particle size* ± S.D in (nm)	Mean Particle size* ± S.D in (μm)
F1	285±0.97	0.282±0.097
F2	289±6.25	0.286±0.624
F3	262±3.19	0.257±0.215
F4	264±0.27	0.274±0.026
F5	255±5.15	0.249±0.054
F6	285±4.45	0.284±0.046
F7	265±4.56	0.316±0.027
F8	297±4.27	0.298±0.042

*An Average of three readings

In vitro Drug Release Studies:

In vitro drug release tests were performed on the various Indapamide niosomal formulations, and the results are displayed in Table 5, with dissolution kinetic profiles provided in Figures 3-7. The percentage drug release from niosomal formulations F1 and F2 is 91.06 at 7 hours, 92.96 at 7 hours, 93.48 at 8 hours, 93.39 at 8 hours,

90.58 at 9 hours, 92.65 at 10 hours, 92.47 at 9 hours, and 95.53 at 8 hours.

Table 5 In vitro diffusion profile of API (Indapamide)

Time in hrs	Absorbance In 285 nm	Cumulative % drug rel
1	0.124	21.33
2	0.241	41.13
3	0.364	56.53
4	0.472	74.46
5	0.588	91.42

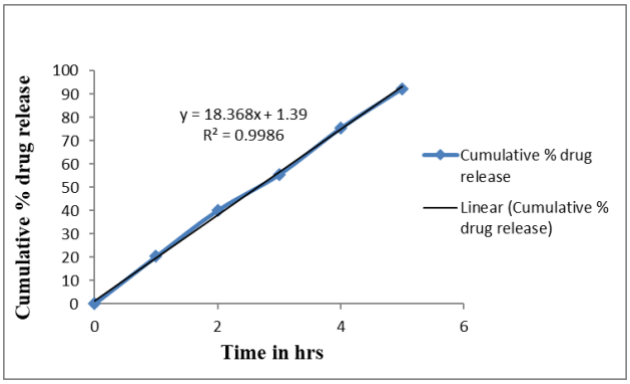

Figure 3 In vitro diffusion profile for API (Indapamide)

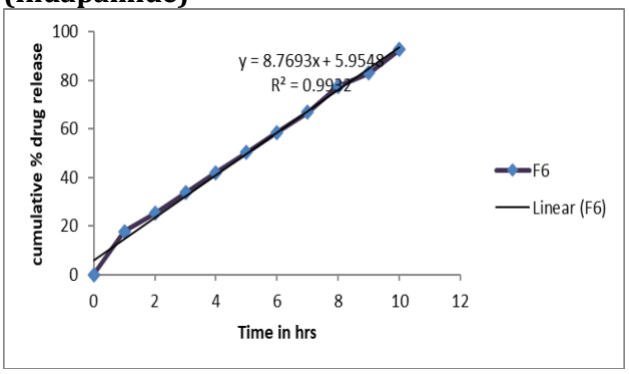

Figure 4 Zero order order kinetic for F6 formulation

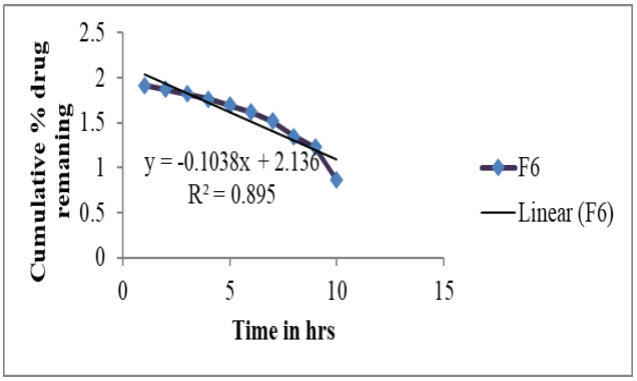

Figure 5 First order order kinetic for F6 formulation

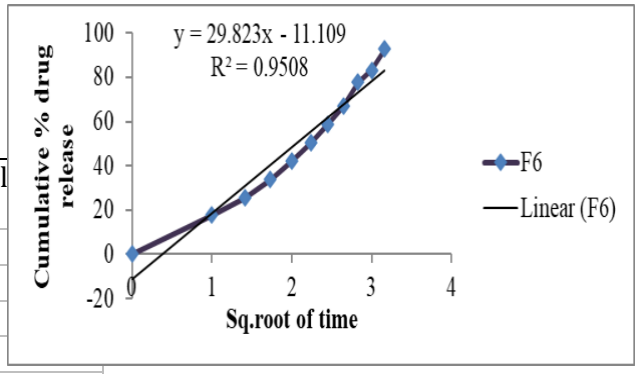

Figure 6 Higuchi kinetic model module for F6 formulation

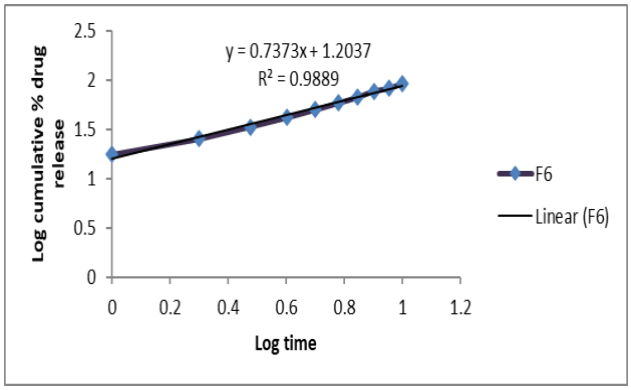

Figure 7 Korsmeyer-Peppas model module for F6 formulation

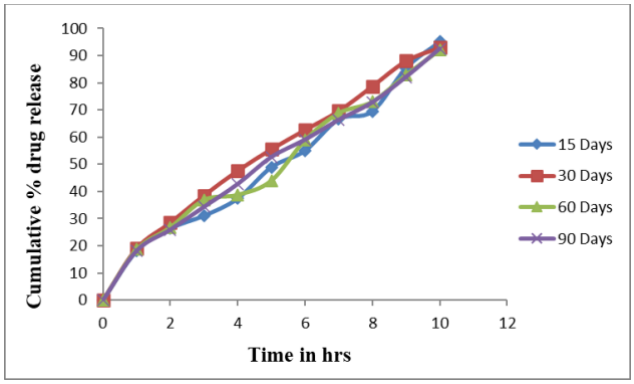

Figure 8 Invitro studies of formulation F6 stored at refrigeration condition

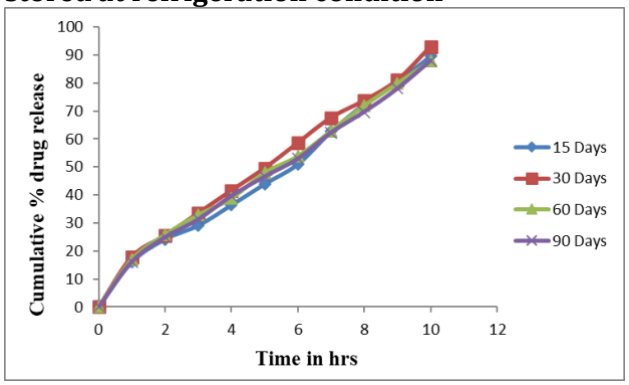

Figure 9 Invitro studies of formulation F6 stored at room temperature

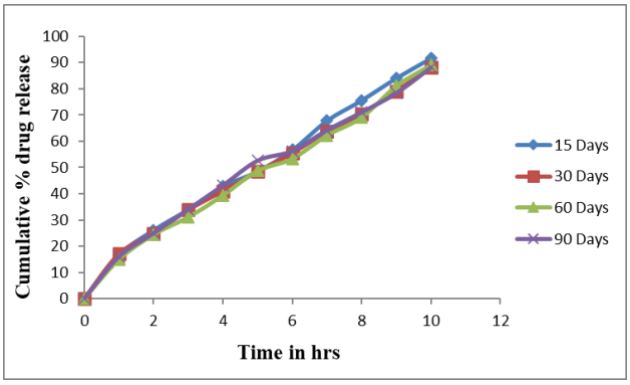

Figure 10 In-vitro studies of formulation F6 stored at Accelerated condition

kinetic models used were zero order, first order, Higuchi matrix, and Korsemayer Peppas. Table 5 shows the regression coefficient values for each of these models. In all situations, the best-suited model was peppas, with 'n' values ranging from 0.768 to 0.917. The 'n' value of formulation F6 was 0.917, indicating that the medication was released using zero-order kinetics.

Sterility test

All samples passed the sterility test, indicating the noisome formulation's absence of microorganisms.

Table 6 In vitro drug release kinetic for F6 formulation

Time in hrs	square root of time	log time	cumulative percentage drug release	cumulative percentage of drug remaining	log cumulative percentage drug release	log cumulative percentage of 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

In all formulations, 17% to 30% of the drug is released within the first hour due to the early bursting of defective niosomes. However, after 3 hours, the release was consistent because the stable niosomes retained the drug, and the release time was extended to 12 hours with sustained effect. The niosomal formulation F6 has a more regulated release than other formulations. The

Stability studies

Stability studies are conducted for the optimal formulation (F6) by ICH guidelines in three distinct storage conditions for three months. The formulation is evaluated for drug content, in vitro drug release studies, and sterility tests. After three months of testing, it was discovered that there was no change in formulation sterility.

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 study for formulation F6 in different conditions

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	95.21±0.79	Sterile	95.31±0.55	Sterile	96.86±0.79	Sterile
30 Days	95.02±0.35	Sterile	93.92±0.72	Sterile	95.99±0.77	Sterile
60 Days	95.58±0.42	Sterile	93.06±0.43	Sterile	94.72±0.77	Sterile
90 Days	95.07±0.84	Sterile	95.44±0.67	Sterile	94.03±0.69	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	19.15	18.09	17.64	19.23
2	27.47	27.57	25.85	26.96
3	32.14	37.59	35.94	32.35
4	38.46	46.67	37.82	41.75
5	49.96	54.58	43.07	51.66
6	56.09	63.66	57.94	58.04
7	67.64	68.63	67.88	65.32
8	68.53	79.74	72.09	71.76
9	84.47	89.04	81.97	81.08
10	94.07	91.98	91.05	91.44

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	15.05	16.94	18.03	17.21
2	23.21	24.53	24.84	25.93
3	28.15	32.57	33.94	31.33
4	35.43	42.66	39.84	38.71
5	42.95	48.59	49.03	47.61
6	52.06	57.65	54.94	52.03
7	61.67	66.63	63.93	61.31
8	71.53	72.73	73.03	68.73
9	79.43	82.06	78.96	77.05
10	88.67	91.98	88.85	87.05

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	17.66	18.05	15.98	17.05
2	27.15	25.88	25.53	25.97
3	35.06	34.85	32.18	35.06
4	43.83	42.08	38.44	44.17
5	49.53	49.43	49.85	53.65
6	57.66	56.55	54.44	57.32
7	68.85	64.64	63.34	65.24
8	76.63	71.53	68.18	72.04
9	85.09	78.15	82.13	79.31
10	92.66	89.05	88.13	89.05

Still, there was a tiny variation in drug content percentage and in vitro drug release tests, both of which were within acceptable limits (Table 9) percentage of drug content in various stability conditions.

CONCLUSION

Niosomal composition entrapment efficiency rises as the concentration of Span 60 increases. The drug content in all niosomal formulations ranged from 91.06±0.56 to 97.15±0.42, with minimal standard deviation and repeatable results. The average vesicular size of niosomes in all batches was between 0.285±0.098µm and 0.297±0.044µm. Niosomal formulations can be easily made utilizing the thin film hydration process with nonionic surfactants (span 60) and cholesterol at varying concentrations. The funnel method revealed that all niosomal powders were free-flowing, with angles of repose ranging from 26□84±0.18 to 28. The SEM pictures of niosomal formulations F6 revealed that the niosomes were spherical. Drug release from vesicles is dependent on Span 60 concentrations. It is primarily due to the effect of phase transition temperature. Peppas were shown to be the best-fit model in all formulations, with 'n' values ranging from 0.768 to 0.917. The formulation F6 had a better controlled released action than the other formulations, with an 'n' value of 0.917, indicating that the drug was released using zero-order kinetics.

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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-masked, 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. Hormone 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, and Lee Hamm. Thiazide and loop diuretics. Journal of Clinical Hypertension, 13(9):639-43, 2011.

[5] Vijaya M Musini, Mark Nazer, Ken Bassett, James M Wright. Blood pressure-lowering efficacy of monotherapy with thiazide diuretics for primary hypertension. The

Cochrane Database of Systematic Reviews, (5): CD003824, 2014.

[6] Karim Masud Kazi, Asim Sattwa Mandal, Nikhil Biswas, Arijit Guha, Sugata Chatterjee, Mamata Behera, 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, 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, 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.