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Preparation and Evaluation of Dexamethasone Incorporated Niosomal suspension for Oral Drug Delivery

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ABSTRACT: OBJECTIVE: The objective of this work was to prepare Multilamellar Niosomal vesicles of Dexamethasone by Hand shaking method for Oral Drug Delivery. **Material and method:** Dexamethasone incorporated Niosomes prepared by Hand Shaking Method using Span 60, Tween 20 and Tween 80. Dexamethasone is a steroid medication having anti-inflammatory and immunosuppressant activity. A major problem of this drug is its low water solubility which results into poor bioavailability after oral administration of Drug. Prepared Niosomal suspension was evaluated its Drug Content, vesicle shape, % Entrapment Efficiency, Zeta Potential, Invitro Drug Release, Release Kinetics and Stability. **Results:** The selected formulation (F4) was showed highest entrapment efficiency of Dexamethasone. After encapsulation in Niosomal vesicles with Span 60, Tween 20 and Tween 80 showed significant reduction in Invitro drug release in 8 hours compared drug Solution. The data collected from the release study were placed into release kinetic model which are Higuchi equation, First order, Korsmeyer-Peppas equations, Zero Oder and Hixson-Crowell model. The best fit with higher correlation (R2 > 0.98) was found with the Zero order equation with the R2 value of 0.995. Stability study of niosomal formulation was done for 1 month at room temperature and refrigerated condition. Storage under refrigerated condition showed greater stability. But in both the storage conditions drug content was found to be within the specification of 95-105% throughout the study period of 1 month. **Conclusion:** Niosomal formulation could be a promising delivery system for Dexamethasone with improved bioavailability and prolonged drug release profiles.

KEYWORDS: Niosome, Scanning Electron Microscopy, Zeta potential, Oral Delivery, Stability

I. INTRODUCTION

Niosomes are a novel bilayer Non ionic Surfactant Vesicles. Niosomal vesicles are manly composed aqueous media, synthetic surfactants and cholesterol. [1], [2] Niosomal vesicles deliver Drug as a rate controlling membrane. Niosomal Vesicles can act as drug reservoirs system. [3] Niosomes are store house of drug and release drug in controlled and sustained manner. [4] Non ionic surfactants are comprised of polar and non-polar segments, possessing high interfacial activity upon hydration form bilayer. [5] The first non-ionic surfactant vesicles came from the cosmetic applications devised by L'Oreal. Niosome are obtained on hydration of synthetic non-ionic surfactants, with or without cholesterol incorporation or their lipids. [6] Niosomes can deliver both hydrophobic and hydrophilic drugs. [7] It increase skin penetration of drugs and act as local depot for sustained Drug Delivery of dermally active compounds. [8] Niosomes can enhance the drug adsorption on or adhesion to the skin surface creating high thermodynamic activity with subsequent drug transfer. [9] Dexamethasone are commonly used Corticosteroids in inflammatory condition, skin disorders and rheumatism. Dexamethasone prevents release of inflammation causes substances in the body Dexamethasone is a steroid medication having anti-inflammatory and immunosuppressant activity. A major problem of this drug is its low water solubility which results into poor

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bioavailability after oral administration of Drug. [10], [11]

II. MATERIAL AND METHOD

Dexamethasone Was Obtained Gift Sample From Alpa Laboratory Indore (M.P.). Span 60 Purchased from Sisco Research Lab. Mumbai, Tween 20 and Tween 80 Purchased from LOBA Chemie, Mumbai, Chloroform And Methanol of Analytical Grade Was Used.

Preparation Of Niosomal Suspension

Hand Shaking Method was used for the preparation of Dexamethasone Containing Niosomes. The Cholesterol and different concentration of Surfactants Tween 80, Span 60 and Tween 20 was dissolved in Chloroform: Methanol (1:1) in Round Bottom Flask [Table 1]. Organic Solvent was removed by hand shaking on a Water Bath at 40°C to Form a thin film on the wall of flask. Thin film dry then hydrated with drug containing Phosphate buffer solution (7.4) and sonicated for 5 min. in bath sonicator then niosome dispersion transferred into container and stored at 4°c. [12]

Table 1: Composition of Niosomal Suspension

Formulations	Drug (mg)	Cholesterol (mg)	Surfactant (mg)	Methanol: chloroform
Tween 80(F1)	50	50	25	1:1
Tween 80(F2)	50	50	50	1:1
Tween 80(F3)	50	50	75	1:1
Span 60(F4)	50	50	25	1:1
Span 60(F5)	50	50	50	1:1
Span 60(F6)	50	50	75	1:1
Tween 20(F7)	50	50	25	1:1
Tween 20(F8)	50	50	50	1:1
Tween 20(F9)	50	50	75	1:1

EVALUATION PARAMETERS

IR-spectra

Fourier-transform infrared spectroscopy was performed using by KBr disc method. Samples were scanned over the range of 4,000.00 to 650.00 cm^{-1}. Infrared spectroscopic analysis was done for pure drug with IR grade KBr in the ratio of 1:100. Discs prepared by applying 15000lb of pressure in a hydraulic press and discs were scanned in an inert atmosphere over a wave number range of 4000-650cm^{-1}. [13]

Drug-Excipients Compatibility Study

Incompatibility studies were done by a stress at different temperatures such as freezer (10°C-20°C), Cold (2°C-8°C) and room temperature, using refrigerator with 1:1 ratio of Drug and polymers. The study was carried out for one month (1st. 7th, 15th, 21st and 30th day) and observed for the physical changes such as colour, liquefaction etc. The cholesterol, pure drug and physical mixture of cholesterol and the drug were mixed separately with IR grade KBr in the ratio of 1:100 and analysed for interaction. Discs prepared by applying 15000lb of pressure in a hydraulic press and discs were scanned in an inert atmosphere over a wave number range of 4000-650cm^{-1}. [14]

Shape of Niosomes

Niosomes suspension (Small amount) taken in slide and cover slip placed on the specimen stub. Niosomal dispersion was spread on an aluminium stub and allowed to dry at room temperature then is sputter coated with gold for 40 seconds by using Ion-Sputter. The image was

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captured with the help of Scanning Electron Microscope. [14]

Entrapment efficiency

5 mg dexamethasone containing niosome suspension are centrifuged at 5,000 rpm for 1.5 hrs at 4ºC using a refrigerated centrifuge then separate free drug from niosomes suspension. Free drug concentration was analysed after further dilution of supernatant layer at 240 nm using UV-Visible Spectrophotometer (Shimadzu UV-1800, Japan) against blank solution. Following formula was used for the percentage of drug entrapment calculation. [15]

$$\% \textbf{ Entrapment Efficiency} = \frac{\textbf{Total Drug} - \textbf{Free Drug}}{\textbf{Total Drug}} \textbf{ X 100}$$

Drug content

1 ml of niosomal suspension (1 ml) was dissolved into a 100 ml of volumetric flask in phosphate buffer pH (7.4) and shaken well for the complete lysis of the vesicles. The solution in the volumetric flask was then made up to 100 ml with phosphate buffer (pH 7.4) and filtered. 0.2 ml of filtered solution was pipette out and was transferred into 10 ml volumetric flask and made up to the volume with phosphate buffer (pH 7.4). The solution was analyzed for drug content by using UV spectrophotometer (Shimadzu UV-1800) at 240 nm against blank solution. [16] The percentage of drug content was calculated by using the following formula:

$$\% \textbf{ Drug Content} = \frac{\textbf{Sample Absorbance}}{\textbf{Standard Absorbance}} \textbf{ X } \frac{\textbf{Standard Absorbance}}{\textbf{Sample Absorbance}} \textbf{ X 100}$$

Determination of Zeta Potential

The zeta potential of the F4 niosomal formulation was determined by using Zeta size (Malvern Instruments) at 25ºC. Niosomal suspension was diluted 100 times with double-distilled water and voltage was set at 100 V and an electrode of instrument was place in suspension for the measurement of zeta potential. [17]

In vitro Drug release

The release of Dexamethasone from niosomal formulations was determined by membrane diffusion technique. The niosomal formulation equivalent to 5 mg of Dexamethasone was placed in a glass tube of diameter 2.5 cm with an effective length of 8 cm which was tied with previously soaked Dialysis membrane, which acts as a donor compartment. The glass tube was placed in a beaker containing 100 ml of phosphate buffer (pH 7.4), acting as a receptor compartment. The whole assembly was fixed in such a way that the lower end of tube containing suspension was just touching (1-2 mm depth) the surface of diffusion medium. The temperature of receptor medium was maintained at 37 ± 5ºC and was agitated at the speed of 100 rpm using magnetic stirrer. Aliquots of 3ml sample were withdrawn periodically and after each withdrawal same volume of medium was replaced. The collected samples were analyzed at 240 nm in UV spectrophotometer (Shimadzu UV-1800, Japan) using phosphate buffer (pH 7.4) as blank. [18], [19], [20]

Drug release kinetic studies

It was used to investigate the possible mechanisms of Dexamethasone released from the prepared Niosomal dispersion, the release data were analyzed mathematically according to different kinetic models such as, zero order kinetics, first order kinetics, Higuchi's model, Korsmeyer-peppas model and Hixson Crowell model. [16]

Stability Study

Niosomal dispersions were stored in a sealed glass vials and subjected to stability study in triplicate. The vials were kept at two different storage conditions, i.e., 4±1°C with ambient humidity and room temperature, and the samples were withdrawn after 1 month, analyzed for drug content. [21], [22]

III. RESULT & DISCUSSION

IR-spectra

From the FTIR spectra interpretation the following results were obtained. The FTIR of pure Dexamethasone show intense band at 3390 and 1268 cm−1 were due to the stretching vibration of O–H and C–F bonds, respectively; the stretching vibration at 1706, 1662, and 1621 cm−1 were due to –C=O and double bond framework conjugated to –C=O bonds. It was used to ensure that no chemical interaction occurred between the drug and excipients [Figure 1, 2].

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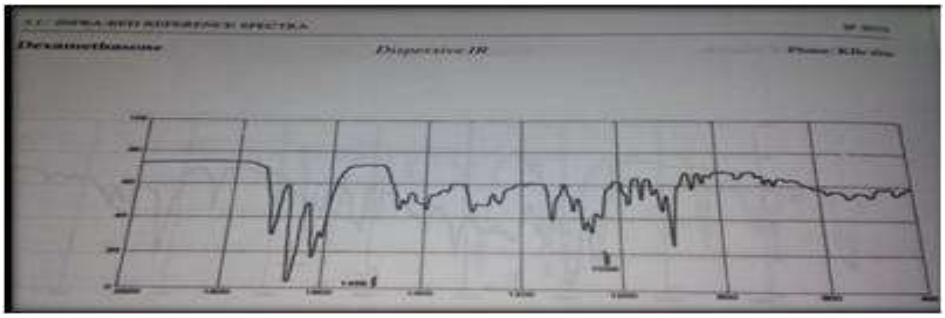

Figure 1: IR Spectrum of Dexamethasone (standard)

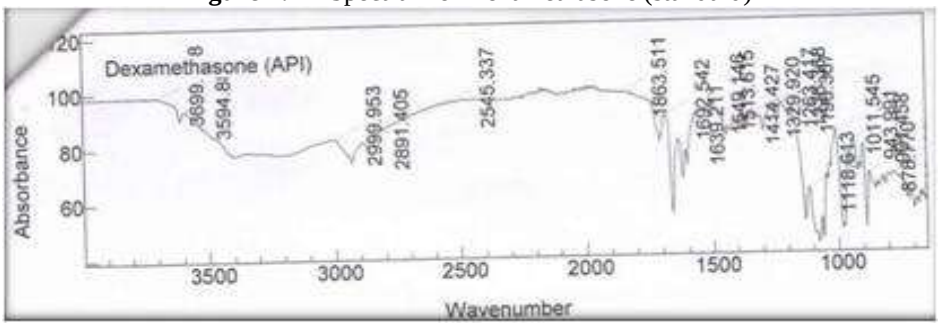

Figure 2: IR Spectrum of Dexamethasone (Sample)

Drug Excipient Compatibility Study

After one month (1st. 7th, 15th, 21st and 30th day) physical changes such as colour, liquefaction etc No observed. It indicates interaction was not found between Drug and Excipients [Table 2]. Chemical changes determined by IR analysis.

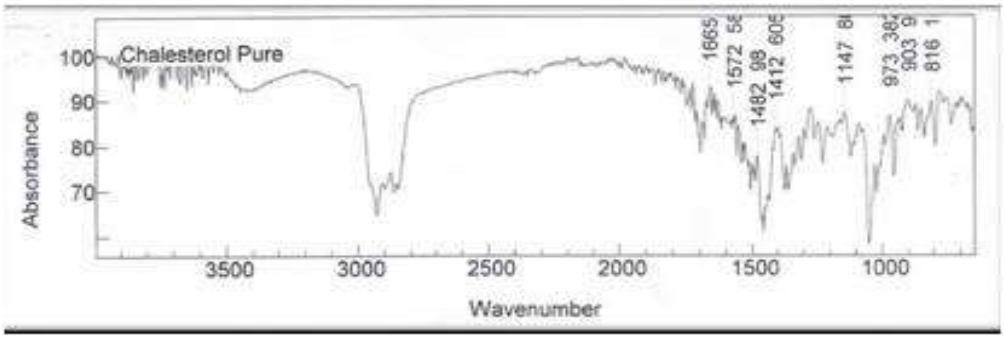

Figure 3: IR Spectrum of Cholesterol (pure)

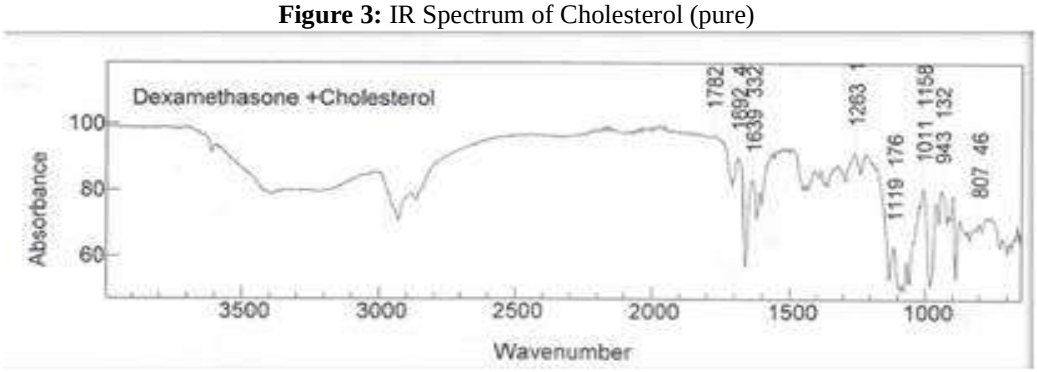

Figure 4: IR Spectrum of Dexamethasone + Cholesterol

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Table 2: Drug Excipient Compatibility Study (Physical Changes)

Sn.	API+ Excipient (1:1)	Conditions	Sample Intervals Days (Physical Changes)				
			1	7	15	21	30
1.	API+ Chol.	2°c-8°c	NOC	NOC	NOC	NOC	NOC
		10°-20°c	NOC	NOC	NOC	NOC	NOC
		RT	NOC	NOC	NOC	NOC	NOC
2.	API+ Span 60	2°c-8°c	NOC	NOC	NOC	NOC	NOC
		10°-20°c	NOC	NOC	NOC	NOC	NOC
		RT	NOC	NOC	NOC	NOC	NOC
3.	API+ Carbopol 940	2°c-8°c	NOC	NOC	NOC	NOC	NOC
		10°-20°c	NOC	NOC	NOC	NOC	NOC
		RT	NOC	NOC	NOC	NOC	NOC

NOC - No Observed Changes

From the above interpretation it is understood that there is no chemical interaction between Dexamethasone and excipients which were used in the Niosomes preparation [Figure 3, 4].

Shape of Niosomes

Scanning electron microscopy for the selected formulation F4 was carried out. The results were shown in the following SEM photographs [Figure 5].

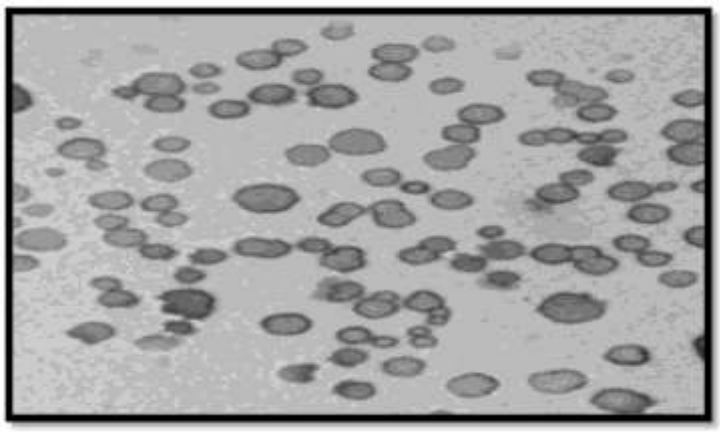

Figure 5: Niosome (SEM image)

Entrapment efficiency

Formulation (F4) containing Span 60 was showed highest Entrapment Efficiency at 84.455±0.473 %. Result showed increase concentration of surfactant leads to decrease in entrapment efficiency of the formulation while cholesterol content was constant [Figure 6].

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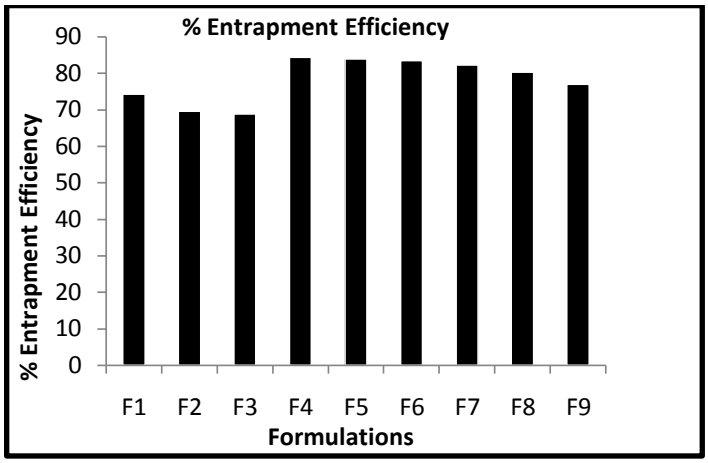

Figure 6: Entrapment efficiency Plot of various niosomal formulations

Drug content

Drug content was found in the range between 95.50±1.458 to 98.81±0.664 percent. Among the formulations (F4) showed maximum drug content 98.81±0.664%. Drug content of all the formulations are within the acceptable range which shows the proper mixing of the drug with the excipients [Figure 7].

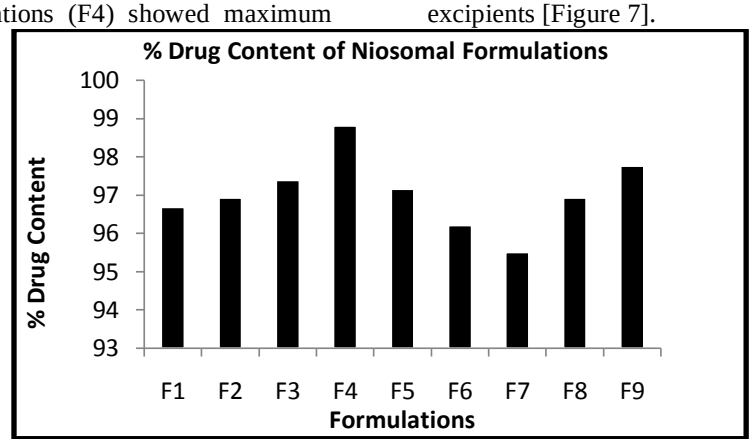

Figure 7: Drug Content Plot of various niosomal formulations

Zeta Potential Analysis

Formulation (F4) was subjected to zeta potential analysis had a zeta value of -23.0 mV, which is a measure of net charge of niosomal suspension [Figure 8]. Zeta potential magnitude gives an indication of stability. The higher charge on the surface of vesicle produces a repulsive force between the vesicles which made them stable. Large positive or negative charges can lead to rapid blood clearance.

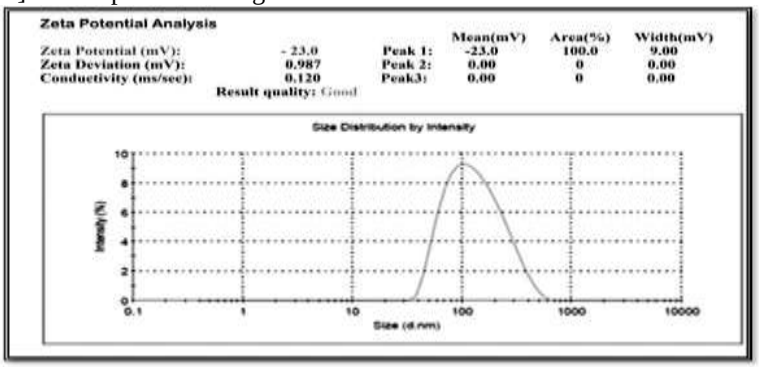

Figure 8: Zeta Potential Analysis

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In vitro Drug release

Changes in release of Niosomal Suspension were observed upon changing the type of surfactant used in the bilayer. In niosomal Suspension experimental studies showed that the rate of drug release depends on the % of drug entrapment. All formulations of niosome showed significant slower release than dexamethasone solution showed a release of about 98.86715 % within 4 hours. This confirms that a sink condition for Dexamethasone release was accomplished and the dialysis bag used in the dissolution procedure does not limit Dexamethasone release. Dexamethasone Niosomal formulations with Span 60, Tween 20 and Tween 80 show significant reduction in Invitro drug release in 8 hours compared with pure drug in solution [Figure 9].

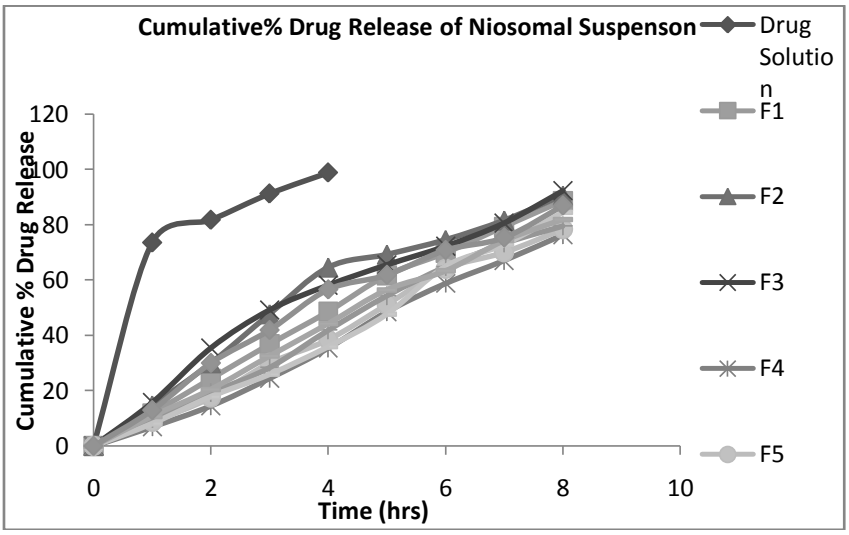

Figure 9: Release Profile of Niosomal Suspension

Drug release kinetics

The best fit with higher correlation was found with the Zero order with the R^2 value of 0.995. Niosomal suspension Formulation follows Zero Oder Release Kinetics [Figure 10].

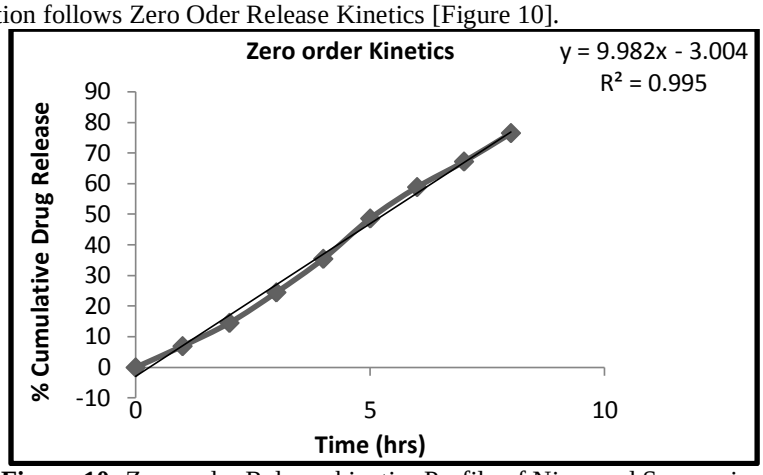

Figure 10: Zero order Release kinetics Profile of Niosomal Suspension

Stability Study

The stability of niosomes was carried out for 1 month. There is no evident for aggregation, fusion or disruption of the vesicles during the study period of 1 months and it was found that the prepared formulations were able to retain their multilamellar nature. Thus it was found that storage under refrigerated condition showed greater stability. But in both the storage conditions drug content was found to be within the specification of 95-105% throughout the study period of 1 month [Figure 10]. After 1 month Colour was not Change at room temperature [Table 3].

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Table 3: Effect of Storage Temperature on niosomal Suspension (F4)

Parameters	Initial	4^0C	Room Temp.
Colour	Milky White	Milky White	Milky White
%Drug Content	98.81±0.664	97.76±0.664	96.91±0.664

Mean± S.D., n=3

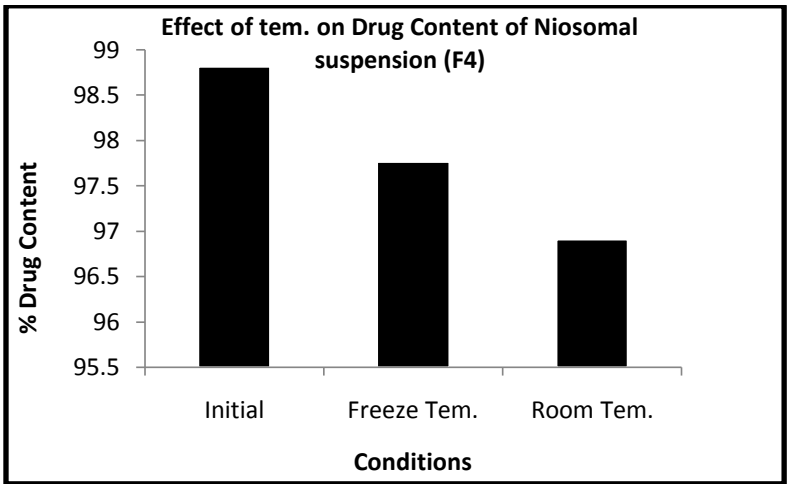

Figure 11: Drug Content after 1 month of Niosomal Suspension (F4)

IV. CONCLUSION

Niosomal dispersions of Dexamethasone were prepared by Hand shaking method using Span 60, Tween 20 and Tween 80 as surfactants in different ratios. Results may be concluded that formulation F4 was showing high Entrapment Efficiency of Dexamethasone. Result showed that the concentration of surfactant Increased leads to entrapment efficiency decrease while constant cholesterol content. Dexamethasone after encapsulation in Niosomal vesicles with Span 60, Tween 20 and Tween 80 showed significant reduction in Invitro drug release in 8 hours compared with Niosomal suspension Formulations. Dexamethasone Niosomal formulations with Span 60, Tween 20 and Tween 80 show significant reduction in Invitro drug release in 8 hours compared with pure drug in solution. Niosomal formulation could be a promising delivery system for Dexamethasone with improved bioavailability and prolonged drug release profiles.

REFERENCES

[1]. Gadhiya P, Shukla, Modi D, Bharadia P. Niosomes in Targeted Drug Delivery – A Review. IJPRS. 2012 May; 1(2):59-72.

[2]. Madhav NVS, Saini A. Niosomes: A Novel Drug Delivery System. IJRPC 2011, 1(3): 498 -511.

[3]. Dehghan MH, Hussain MA. Development and Evaluation of Niosomal Delivery System for Aceclofenac. IJPT 2010 Dec; 2(4): 1028-45.

[4]. Sankhyan A, Pawar P. Recent Trends in Niosome as Vesicular Drug Delivery System. Journal of Applied Pharmaceutical Science 2012; 02 (06): 20-32.

[5]. Akhilesh D, Bini KB, Kamath JV. Review on Span-60 Based Non-Ionic Surfactant vesicles (Niosomes) as Novel Drug Delivery. International Journal of Research in Pharmaceutical and Biomedical Sciences 2012 Mar; 3(1): 6-12.

[6]. Das MK, Palei NN. Sorbiton ester Niosomes for Topical Delivery of Rofecoxib. Indian Exp.Bio. 2011 Jun; 49: 438-45. 7. Vyas J, Vyas P, Sawant K. Int J Pharm Sci, 2011, 3(1), 123-26.

[7]. Muzzalupo R, Tavano L, Cassano R, Trombino S, Ferrarelli T, Picci N. A new approach for the evaluation of niosomes as effective transdermal drug delivery systems. European Journal of Pharmaceutics and Biopharmaceutics. 2011 Jan; 79: 28–35.

[8]. Mujoriya RZ, Bodla RB. Design and Development of Niosomal Delivery System for Ketoprofen. Advances in Life Science and Technology 2012; 3: 1-13.
[9]. Salimi A, Nezhad MS, Moghimipour E. In-vitro Permeation of Dexamethasone Microemulsion through Rat Skin. Sch. Acad. J. Pharm. 2015; 4(1): 30-34.
[10]. Chandra A, Sharma PK, Irchhiaya R. Microemulsionbased hydrogel formulation for transdermal delivery of dexamethasone. AJP 2009; 3(1): 30-36.
[11]. Parthibarajan R , Kumar S. P, Gowri Shankar N.L, Balakishan L, Srinivas B, Bhagya Laxmi V, et al. Design and Invitro Evaluation of Voriconazole Niosomes. Int J Pharm Sci.2013Apr; 5(3): 604-11.
[12]. Rasool BKA, Azeez OS, Lootah HA, Abusharbain IM, Abu-Alhaj HA, Nessa F. Extended Release Niosomal Hydrogel for Ocular Targeting of Piroxicam: In vitro and Ex vivo Evaluation. British Journal of Pharmaceutical Research 2014; 4(21): 2494-2510.
[13]. Sabarikumar K, Varatharajan V, Ilavarasan P, Shaik S.M. Bioavailability Enhancement of Aceclofenac Niosomes Containing Surfactants and Cholesterol . IJBPR. 2012; 3(3): 354-59.
[14]. Marwa A, Omaima S, Hanaa EL-G, Mohammed AS. Preparation and In-Vitro Evaluation of Diclofenac Sodium Niosomal Formulations. IJPSR, 2013; 4(5): 1757-65.
[15]. Valli GP, Vignesh M. Formulation of Niosomal Suspension with Enhanced Oral Bioavailability of Diclofenac Sodium. Journal of Global Trends in Pharmaceutical Sciences 2012 Apr; 3(2): 656-71.
[16]. Mahajan HS, Shah NN, Nerkar PP, Kulkarni A. Niosomes encapsulated with Gatiflaxacin for ocular drug delivery. Recent Advances in Pharmaceutical Science Research 2012; 1(1): 28-39.
[17]. Devaraj GN, Parakh SR Devraj R, Apte D, Rao BR, Rambhau D. Release Studies on Niosomes Containing Fatty Alcohols as Bilayer Stabilizers Instead of Cholesterol. Journal of Colloid and Interface Science 2002; 251**:** 360–65.
[18]. Jadon PS, Gajbhiye V, Jadon RS, Gajbhiye KR, Ganesh N. Enhanced Oral Bioavailability of Griseofulvin via Niosomes. AAPS Pharm. Sci. Tech. 2009 Dec; 10(4): 1186-92.
[19]. Srikanth K, Nappinnai M, Gupta V.R.M. Formulation and Evaluation of Topical Meloxicam Niosomal Gel. IJB. 2010; 1(1): 7-13.
[20]. Ramalingam N, Natesan G, Dhandayuthapani B, Perumal P, Balasundaram J, Natesan S. Design and characterization of Ofloxacin niosomes. Pak. J. Pharm. Sci., 2013 Nov; 26No.6:1089-96.
[21]. El-Ridy MS, Yehia SA, Mahfouz Abd-El-Megeid K, Mostafa DM, Nasr EA, Marwa HA. Niosomal encapsulation of Ethambutol hydrochloride for increasing its efficacy and safety. Drug Deliv 2013: 1-16.