IJPSR (2016), Vol. 7, Issue 1 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 23 June, 2015; received in revised form, 22 August, 2015; accepted, 19 October, 2015; published 01 January, 2016

DEVELOPMENT AND CHARACTERIZATION OF TENOXICAM ENCAPSULATED NIOSOMES FOR ENHANCED TRANSDERMAL DELIVERY

J. Shaji* and A. Shah

Department of Pharmaceutics, Prin. K. M. Kundnani College of Pharmacy, Cuffe Parade, Mumbai-400005, Maharashtra, India.

Keywords:

Tenoxicam, transdermal delivery, niosomes, permeation studies, *in-vivo* study.

Correspondence to Author:
Dr. Jessy Shaji

Department of Pharmaceutics, Prin. K. M. Kundnani College of Pharmacy, Cuffe Parade, Mumbai-400005, India.

Email: jshaji@rediffmail.com

ABSTRACT: Objective: The aim of this current research is to study a novel carrier, niosome, for its enhanced transdermal delivery of tenoxicam. **Methods:** Niosomes are self assembled vesicles composed primarily of synthetic surfactants, cholesterol & edge activator (surfactant). Niosomes were prepared by Organic solvent injection technique and characterized by particle size, entrapment efficiency, transmission electron microscopy (TEM), *ex-vivo* skin corrosive test, *in-vitro* dissolution, *ex-vivo* permeation studies and *in-vivo* study. **Results:** Vesicle size and % EE of the optimized niosomal formulation was found to be 79.46 ± 55 nm and 88.8 ± 4.5% respectively. Zeta potential of the optimized niosomal formulation was found to be -39.6 ± 7.43 mv. The *ex-vivo* study showed transdermal flux of niosomal gel to be 43.09± 0.106µg/cm2/h which was 2.9 fold higher than that obtained after application of plain drug gel whose flux was 15.05±0.09 µg/cm2/h). **Conclusions:** Data obtained from this experimental work concludes niosomal formulation is safe, very effective and promising drug carrier for transdermal delivery of drug.

INTRODUCTION: Researchers n recently year found vesicular structures [1] such as liposomes, niosomes, transferosomes, etc acting as best carriers for the administration of drugs across the skin. Liposomes exhibit certain disadvantages as, their components such as phospholipids are chemically unstable because of their predisposition to oxidative degradation, they require special storage and handling and purity of natural phospholipids is variable.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.7(1).307-15

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.7(1).307-15

Apart from these disadvantages, researchers proved that the liposomes are incapable of penetrating into the deeper layers of the skin [2]. Transferosomes also have different disadvantages like expensive, tedious manufacturing processess and chemical instability [3]. Niosomes are globular submicroscopic structures and are prepared using nonionic surfactants such as Tweens, Spans etc. [4].

Niosomes has different advantages like:

- They are osmotically active and stable, and they increase the stability of entrapped drug.
- Handling and storage of surfactants requires no special conditions.

- They improve oral bioavailability of poorly absorbed drugs and enhance skin penetration of drugs.

- They can be made to reach the site of action by oral, parenteral as well as topical routes.

- The surfactants are biodegradable, biocompatible and non-immunogenic.

- They improve the therapeutic performance of the drug molecules by delayed clearance from the circulation, protecting the drug from biological environment and restricting effects to target cells.

Niosomal dispersion in an aqueous phase can be emulsified in a non-aqueous phase to regulate the delivery rate of drug and administer normal vesicle in external non-aqueous phase. Tenoxicam is a non-steroidal anti-inflammatory agent (NSAIDs), has been widely used in the treatment of rheumatoid arthritis, osteoarthritis. These vesicular structures acts as carriers for drugs and helps to overcome the barrier properties of the skin. The present study involves the preparation and characterization of tenoxicam entrapped niosomes and the excipients used in preparation of niosomes.

MATERIALS AND METHODS:

Materials:

Commercial grade Tenoxicam (TX) was a gift sample obtained from Ramdev chemicals, Mumbai. Span-60, Cholesterol, Sodium deoxycholate (SDC) purchased from S.D Fine Chemicals, India. Albino Wistar rats were obtained from Bharat Serum and Vaccines Pvt. Ltd. (Mumbai, India).

Methods:

Differential calorimetry analysis (DSC)

Tenoxicam-excipients interaction study was done by DSC (Seiko Exstar SII DSC 6220). TX, SDC and Cholesterol, physical mixture as well as the optimized formulation were subjected to DSC analysis. The instrument was calibrated with indium standard. Accurately weighed samples were placed in open, flat bottom, aluminum sample pans. Thermograms were obtained by heating the sample at a constant rate of 100C/minute. A dry purge of nitrogen gas at the rate of 20ml/min was used for all the runs. Samples were heated from 35C –400C. From the the Scans obtained. The melting point and the peak maxima were observed in the DSC graphs.

Formulation of niosomes:

The surfactants, lipid and drug were first dissolved in a suitable organic solvent. The prepared organic phase was then added drop wise into the aqueous phase. Surfactant: cholesterol ratio of 1:1 along with tenoxicam and Sodium deoxycholate were dissolved in chloroform:methanol in the ratio of 2:1. Thus the dissolved organic solution containing drug were injected dropwise through 24 gauge needle into preheated PBS PH 7.4, which was magneticaly stirred (Mechanical stirrer, Remi, Mumbai) and maintained at 65ºC. Stirring was continued until all chloroform & methanol evaporated to get drug loaded niosome. Vaporization of chloroform & methanol leads to the formation of single layered vesicles. [5, 6] These were further size reduced by ultra sound cavitation using probe sonicator (Oscar, Japan) to form small unilamellar vesicles.

Characterization of Niosomes:

Visualization by transmission electron microscopy (TEM):

Shape and morphology of the Niosomes was investigated using transmission electron microscopy. Niosomes were negatively stained with 2% w/v aqueous solution of phosphotungstic acid on a carbon-coated copper grid. The grid was examined under transmission electron microscope (Philips CM 200) with resolution of 2.4A° at an accelerating voltage of 200 kV.

Determination of entrapment efficiency:

Entrapment efficiency of Niosomes was determined by ultracentrifugation method [6]. Niosomes were separated by ultracentrifugation at 15,000 rpm for 60 minutes at a temperature of 4ºC. The sediment and supernatant liquid were separated, the amount of drug in the sediment was determined by rupturing the vesicles using methanol and the amount of drug was quantified spectrophotometrically at 369 nm. Entrapment efficiency was determined by the following equation;

$$\% \text{ Entrapment efficiency} = \frac{\text{Amount of Tenoxicam entrapped}}{\text{Total Tenoxicam added}} \times 100$$

Standard curves for TNX's and specificity of the UV method was studied [7]. The experiments were performed in triplicate to verify the reproducibility of the results. A SD in the range of ±0.2 was observed in case of all the three TNX's.

Determination of vesicle size and zeta potential:
The vesicle size and distribution were determined by dynamic light scattering method using Malvern zetasizer (Malvern Instruments Ltd.). Measurements were carried out at an angle of 90° at 25°C.

Preparation of niosomal gel:
0.75%Carbopol Ultrez 10 was soaked in minimum amount of water for 24 hr. Suspension was then added to the swollen polymer under stirring. Stirring was maintained at 700 rpm in a closed vessel and the temperature was maintained at 30°C until homogeneous Niosomal gel was obtained. The pH was then adjusted to neutral using triethanolamine and stirred slowly till a clear gel was obtained.

Characterization of TELs gel:
Assay: 1g of gel equivalent to 5mg of tenoxicam was weighed and dissolved in 100ml methanol. The drug content was determined using UV spectrophotometer at 369nm.

Spreadability: 1gm gel was placed within a circle of 1cm diameter pre-marked on a glass plate over which a second glass plate was placed. A weight of 500gm was allowed to rest on the upper glass plate for 5min. The increase in the diameter due to spreading of the gel was noted.

pH: The pH was determined using a digital pen pH meter, standardized using pH 4.0 and 7.0 standard buffers.

Viscosity:
Brookfield CAP 2000 viscometer was used to determine the viscosity of tenoxicam loaded niosomal gel using spindle no 32 at 25ºC.

***In vitro* release studies:**
The release of tenoxicam from the niosomes was examined under sink conditions. One milliliter samples of niosomes were placed in dialysis bags and suspended in 1000 ml of phosphate buffer saline PBS, pH 7.4 at 37 °C under gentle magnetic stirring at 100 rpm. At predetermined time intervals, 1 ml samples were withdrawn and the drug content in the supernatant was determined by UV method [8].

***Ex-vivo skin* permeation study:**
Porcine ear skin obtained from a slaughter house was used as a permeation membrane for the skin study because of its similarity to human skin in lipid content and permeability. The skin sample was mounted between the donor and receptor compartments of the diffusion cell. The receptor compartment was filled with 2 ml of niosomal suspension or 1 gm of niosomal gel equivalent to 7.5mg of tenoxicam. The receptor chamber was filled with PBS pH 7.4 and stirred with a magnetic bar at 100 rpm and the temperature was maintained at 32 ± 1°C. 1 ml of aliquot from the receptor compartment was withdrawn at predetermined time intervals and was replaced with equal volume of fresh PBS. The concentration of the drug in the samples was analyzed spectrometrically by UV, and the cumulative amount of drug was plotted as function of time.

Permeation data analysis:
The flux J, μg cm^{-2} hr^{-1} was calculated from the slope of linear portion of the plot divided by the skin surface area [10]. The steady state permeability coefficient (Kp) of the drug through porcine skin was calculated by using the following equation:

$$Kp = J/Co$$

Where; J is the flux and Co is the concentration of tenoxicam in the gel. The penetration enhancing activity of the enhancer may be calculated in terms of enhancement ratio (ER), using the following equation:

ER = Drug permeability coefficient of the Treated
Drug permeability coefficient Control

Skin deposition studies:
At the end of 24 hrs of the permeation experiment, the surface of the skin was washed five times with 30% methanol to remove excess of tenoxicam from the surface of the skin. The skin was cut into small

pieces which were further homogenized with 5 ml of 30% of methanol. The resulting solution was then centrifuged for 10 min at 5,000 rpm, the supernatant was then separated to determine the tenoxicam content by UV spectrophotometer at 369nm [11].

***Ex-vivo* skin corrosion studies**:

Corrosive potential of Niosomes gel was determined by Corrositex® test [12]. Corrosive substances destroy the epidermal proteins and cause color shift in the underlying chemical detection liquid. Corrosive potential of Niosomes gel was determined on porcine ear skin using 37% nitric acid and 0.9%w/v NaCl solutions as positive and negative controls respectively. Skin samples were prepared and clamped on Franz diffusion cell. 200µl of 37% nitric acid solution, 0.9% NaCl solution or Niosomes gel was deposited onto the epidermis of the porcine skin. After 15 min, the sample was removed and the epidermis was further washed with 2 ml of distilled water to remove the residual sample. 1ml of Sulforhodamine B (skin proteins labeling dye) was deposited onto the epidermis. After 15 min, 1ml the dye was removed and the epidermis was washed with 1 ml of distilled water. The experiment was conducted in triplicate. The absorbance of the washing water was measured with a spectrophotometer at 313 nm. The corrosive factor was calculated from the Eq. as shown below:

F= [Sample abs-0.9%NaCl solution Abs] / (0.9% NaCl solution Abs)

If F>0, then the sample is non-corrosive.
If F<0, then the sample is corrosive.

Vesicle skin interaction studies by light microscopy:

Skin irritancy and toxicity potential of the formulation upon in vivo application of the TDDS containing gel formulation, with and without drug was carried out by preliminary histopathological evaluation. After 24 h of application, skin was removed from the diffusion cell and stored in 10% formalin solution in ph 7.4 phosphate buffer saline followed by dehydration with alcohol. It was then treated with antimedia and embedded in paraffin for fixing. Sections of ~5 µm thickness were cut from each skin piece and stained with hematoxylin and eosin .These samples were then observed under light microscope (Leica, Germany) and compared with control sample for structural changes of epidermis [Jaiswal et al; 1999].

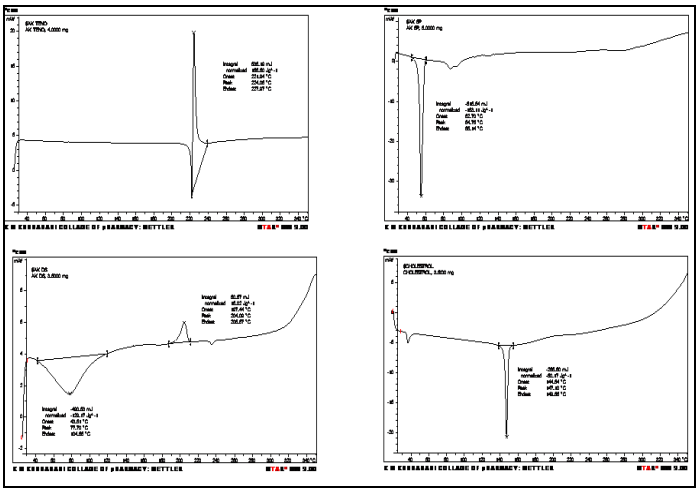
***In-vivo* anti inflammatory activity:**

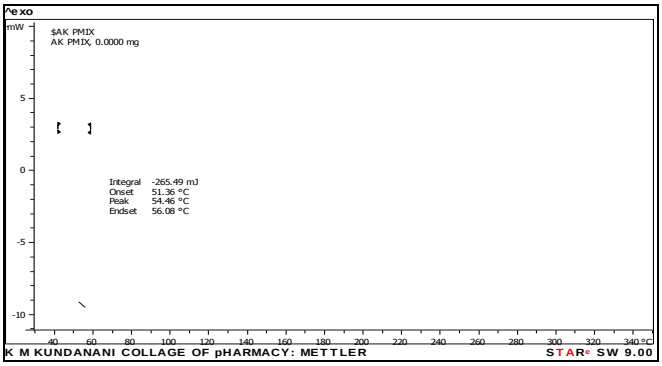
The anti-inflammatory activity of the gel was carried out by carrageenan induced paw edema method [13] (ethics committee protocol: 141505) to compare the activity of the marketed gel and the tenoxicam loaded Niosomes gel. After getting approval from ethical committee**,** male albino rats of Wister strain weighing 150-200gms was randomly divided into 3 groups of six rats each. Niosomesal gel and marketed gel were applied on the subplantar region of the left hind paw of first and second groups, respectively. Third group was untreated and served as control. 1 h post transdermal application, paw edema was induced by subplantar injection of 0.1 ml of a 1% w/v freshly prepared carrageenan in normal saline into the left hind paw of each rat. The paw volume up to the ankle joint was measured before and at different time intervals after the carragenan injection using graduated plethysmograph (INCO, India). Percentage reduction in edema was calculated using the following formula:

$$\% \text{ Inhibition of paw edema} = \frac{(Vt - V0)\text{ control} - (Vt - V0)\text{ treated}}{(Vt - V0)\text{ control}}$$

RESULTS AND DISCUSSIONS:

Differential calorimetry analysis (DSC): Drug & Excipient Interactions:





Thermograms of Fig 1.1=Tenoxicam
Fig 1.2=span60
Fig 1.3=sodium deoxycholate
Fig 1.4 =cholestrol
Fig 1.5 =mixture

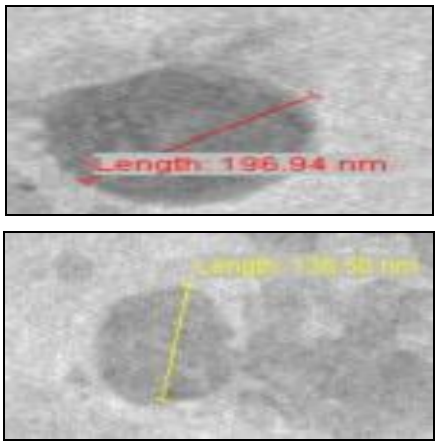


FIG. 1: TEM IMAGES OF NIOSOMES

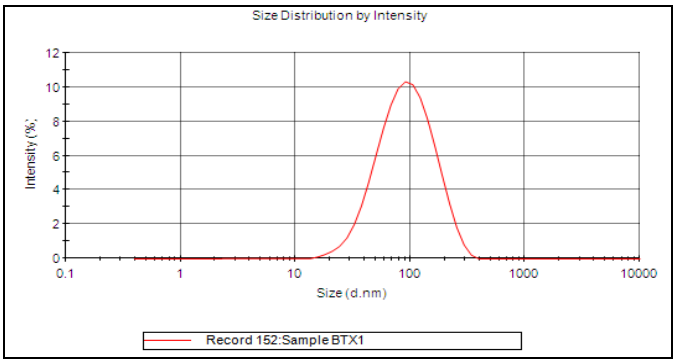


FIG. 2: PARTICLE SIZE OF OPTIMIZED FORMULATION (F-1) BATCH

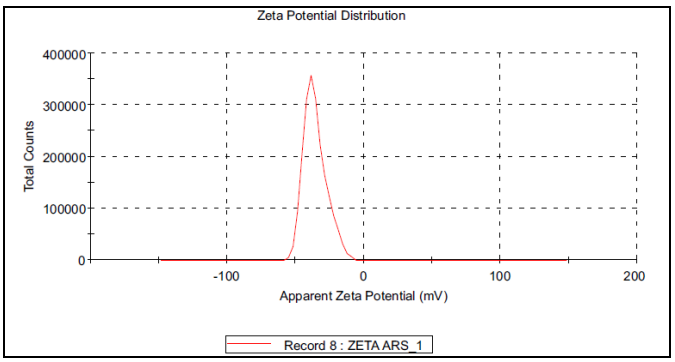


FIG. 3: ZETA POTENTIAL OF OPTIMIZED FORMULATION (F-1) BATCH

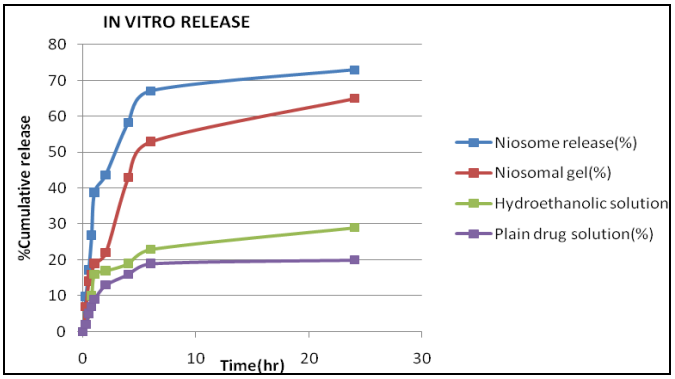


FIG. 4: *IN-VITRO* RELEASE OF TENOXICAM FROM (A) PLAIN DRUG SOLUTION (B) HYDROETHANOLIC DRUG SOLUTION (C) NIOSOMES DISPERSION (D) NIOSOMES GEL

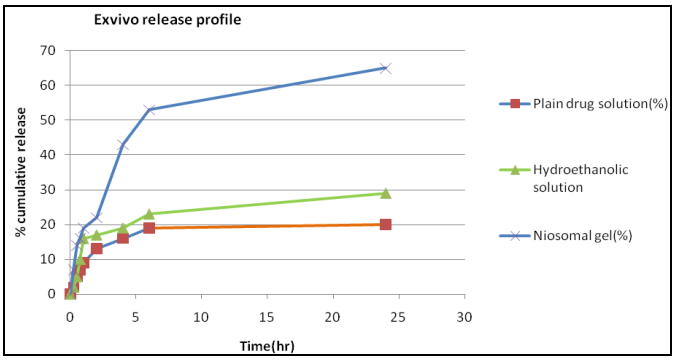


FIG. 5: E*X VIVO* RELEASE PRFILE OF TENOXICAM FROM (A) PLAIN DRUG SOLUTION (B) HYDROETHANOLIC DRUG SOLUTION (C) NIOSOMAL GEL

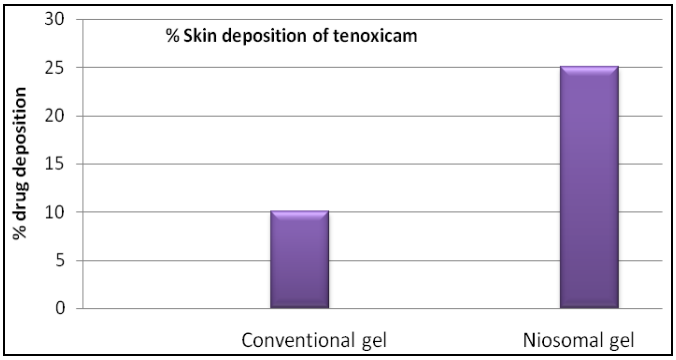


FIG. 6: % SKIN DEPOSITION OF TENOXICAM NIOSOMAL GEL AND CONVENTIONAL GEL

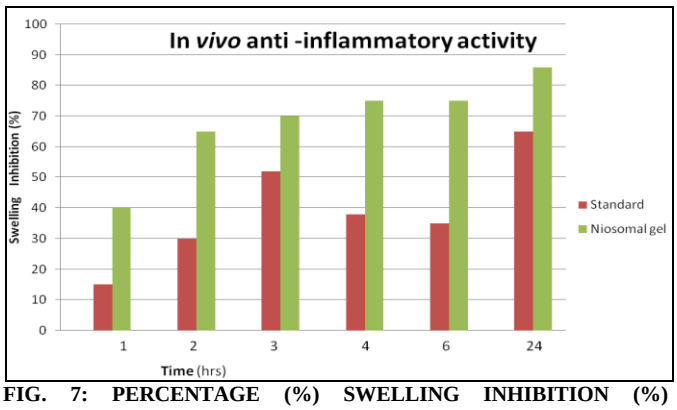


FIG. 7: PERCENTAGE (%) SWELLING INHIBITION (%) PRODUCED BY TENOXICAM LOADED NIOSOMAL GEL, AND STD MARKETED GEL IN CARRAGEENAN INDUCED RAT PAW

TABLE 1: COMPOSITION OF NIOSOMAL FORMULATIONS

Formultion code	Span 60(mg)	Sodium deoxy cholate (mg)	Chloroform :methanol (2:1)	Cholesterol (mg)	Drug (mg)
F1	18	0.8	10ml	20	7.5
F2	18	1.2	10ml	20	7.5
F3	20	1.2	10ml	20	7.5
F4	20	1.6	10ml	20	7.5
F5	16	1.6	10ml	20	7.5
F6	18	1.6	10ml	20	7.5
F7	16	0.8	10ml	20	7.5
F8	20	0.8	10ml	20	7.5
F9	16	1.2	10ml	20	7.5

TABLE 2: ENTRAPMENT EFFICIENCY AND PARTICLES SIZE OF NIOSOMALS FORMULATIONS

Formulation code	Size (nm)	% Entrapment efficiency
F-1	79.46	88.8
F-2	140.8	89.21
F-3	130.4	84.32
F-4	171	85.93
F-5	190	77.88
F-6	188.3	89.98
F-7	95.02	78.49
F-8	97.18	80.11
F-9	119.1	79.84

TABLE 3: TRANSDERMAL FLUX AND ER OF THE FORMULATION

Formulations	Flux (µg h^{-1} cm^{-2})	ER*
Niosomal gel	43.09	2.9
Plain drug solution	15.05	-

ER* Enhancement Ratio

TABLE 4: CORROSIVE FACTOR OF THE FORMULATIONS

Formulation	Corrosive Factor
37% Nitric acid solution (positive control)	-0.6547± 0.005
Niosomal gel	0.987 ± 0.004

Characterization of TELs gel:

Assay: All hydrogels have a mild acidic pH which is acceptable for topical preparations. The tenoxicam content of niosomal gel was found to be 96.96 % ± 0.17.

Spreadability:

The diameter of niosomal gel was found to be 5.533 ± 0.18 cm which indicates good spreadability.

pH: pH of niosomal gel was found to be 7 which was within the acceptable limits.

Viscosity: The viscosity of the tenoxicam loaded TELs gel was found to be 11500 cps respectively.

Percent drug entrapment:

PDE was expressed as a fraction of drug incorporated into niosomes relative to total amount of drug used. In the present study the observed percentage entrapment efficiency for all batches were in the range of 77%-91%. Percentage entrapment efficiency was significantly affected by the applied processing variables such as concentration of span 60 as well as cholesterol. It was clearly indicated that with increase in concentration of span 60 percentage entrapment efficiency was increased [14].

Visualization by transmission electron microscopy (TEM):

TEM image of tenoxicam loaded niosomes was shown in fig 3. The niosomes were spherical in shape. The vesicle size was in the range of 79-190 nm supplementing the results of particle size analysis.

Determination of vesicle size and zeta potential:

The mean vesicle size of drug loaded niosomes of the different batches ranged between 79-190 nm. The polydispersvity index (PDI) was in the range of 0.207 – 0.341 for drug loaded niosomes which indicates a narrow vesicle size distribution. The mean vesicle size and PDI of all the nine batches of factorial design is shown in **Table 1**. It was observed that the relative amount of span 60 and cholesterol was found to play an important role in the determination of the vesicle size. Vesicle size of drug loaded niosomal batches were found to decrease as concentration of span increases.

Zeta potential of niosomes showed negative values, which is due to sodium deoxycholate [6]. The charge on the noisome vesicles is an important parameter that can influence both vesicular properties such as

stability, as well as skin-vesicle interactions. The values of zeta potential showed prepared niosome have sufficient charge to inhibit aggregation of vesicles due to electric repulsion[14].

Drug release:

The *in vitro* and *ex vivo* release study were done by using 0.22µm nylon membrane and porcine skin respectively. The *ex vivo* diffusion data indicates that the released diminished to a great extent as compared to the *in vitro* release. This could be because of accumulation of drug in the skin layers. This result was probably due to the release retarding effect of the polymeric matrix of gelling agents.[15, 14] The release profile of the developed formulation is as shown in **Fig. 4** and **5**.

***In-vitro* Diffusion Studies**:

Encapsulation of tenoxicam into niosomes led to significant prolongation of its release across the artificial membrane in comparison with the hydroethanolic and plain drug solution. From the **Fig. 4**, it was observed that the sustained effect was in the order: Niosome dispersion > Niosomal gel > hydroethanolic drug solution > plain drug solution. Higher permeation of TELs gel might be due to combination of both span 60 and sodium deoxycholate. The release profile of tenoxicam loaded niosomes enriched gel indicated slow release as compared to noisome dispersion. This may be due to the fact that drug diffuses from the niosome carrier followed by diffusion from the gel matrix which results in sustained release effects.

***Ex-vivo* skin permeation analysis**:

Permeation of niosomes is much enhanced as compared to simple hydroethanolic drug solution. The order of permeation profile observed from **Fig. 5** is as follows: Niosomal gel > hydroethanolic drug solution > plain drug solution.

Higher flux and higher release was observed for niosomal gel in comparison to hydroethanolic and plain drug solution because of the synergistic mechanisms of span 60 & sodium deoxycholate vesicles, edge activator and skin lipids interaction, which promoted the passage of tenoxicam through porcine skin. The percent cumulative permeation in 24hr was found to be 65.593% for niosomal gel which was found to be higher than that of hydroethanolic and plain drug gel. As shown in **Table 3** enhancement ratio of the TELs gel was found to be 2.9 fold higher as compared to hydroethanolic solution and the transdermal flux of niosomal gel was found to be 2.9 fold higher than that obtained after application of plain drug gel.

Drug Deposition Studies:

Skin deposition studies were performed by using porcine skin. Results indicated that 25% of drug was accumulated in the skin layers from niosomal gel formulation & from that of conventional gel was found to be 10% as shown in **Fig 6**. Thus niosomal gel formulations enhanced the permeation of the drug into epidermal layer but did not enhance the penetration of the drug through the skin layers into the diffusion medium. [16]

***Ex-vivo* corrosive studies:**

The experiment was conducted in triplicate. The results are shown in **Table 4**. As observed, niosomal dispersion was found to be non-corrosive as compared to the positive control.

Pharmacodynamics Study:

Application of TELs gel and the marketed gel resulted in 85% and 65% inhibition of edema after inducing carrageenan for 24hrs as shown in **Fig. 8.** Fig shows there was increase in the percent swelling inhibition. There is a significant difference between the tested groups and the control as determined by a one way ANOVA with $P < 0.05$.

Vesicle skin interaction studies by light microscopy:

In control the uppermost layer namely epidermis, dermis and subcutaneous tissues were clearly seen, whereas in the treated skin with teno- niosomal gel after 24 h, widened and loose stratum corneum [5–6 distinct layers] with presence of empty spaces were seen in the dermis. It is also apparent that surfactant & cholesterol occlude the skin surface and thus can increase tissue hydration, thereby increasing drug permeation, justifying carrier's proposed mechanism of penetration into the skin and further fusing with the skin lipids into the epidermis and dermis Therefore it was concluded that the Niosomes is an enhanced carrier for the transdermal drug delivery of tenoxicam. In treated skin sample no other major epidermal or dermal

changes were visible. Cells also did not show any signs of degenerative changes or any other disintegration.

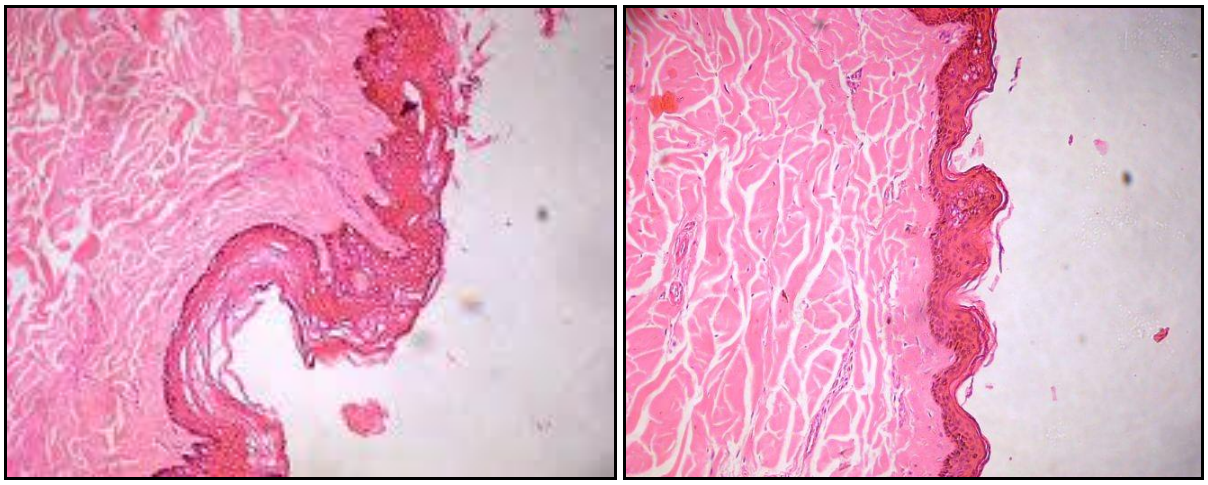


FIG.8: PHOTOMICROGRAPHS OF HISTOARCHITECTURAL STRUCTURE OF PORCINE EAR SKIN, A: Control; B: Skin treated with Teno- niosomal gel

CONCLUSION: The results obtained from this study indicates that the carrier niosomes are self assembled vesicles which are composed primarily of synthetic surfactants , cholesterol & edge activator, enhances the permeation of tenoxicam due to its better penetration as compared to hydroethanolic drug solution and plain drug solution. *In-vivo* studies showed better anti-inflammatory activity as compared to the marketed formulation. Thus, the developed niosomal formulation could be a potential carrier for niosomes and other similar drugs especially due to their simple production process and ease of scale-up.

REFERENCES:

1. Biju SS, Sushama Talegaonkar, Mishra PR, Khar RK.: Vesicular systems: An overview, Indian Journal Pharmaceutical Sciences 2009; 68: 141-153
2. Touitou E, Dayan N, Bergelson L Godin B, Eliaz M: Ethosomes: A novel vesicular system, Journal Control Release 2009; 65: 403-418.
3. Jain S, Jain P, Umamaheshwari RB and Jain NK: Transfersomes--a novel vesicular carrier for enhanced transdermal delivery: development, characterization, and performance evaluation. Indian Pharm 2013; 29(9): 1013-26.
4. Aggarwal D, Garg A, Kaur: Development of a Topical Niosomal Preparation of Acetazolamide: Preparation and Evaluation. Journal Pharmacy Pharmacology 2014; 56: 1509-1517
5. Satturwar PM, Fulzele SV, Nande VS, Khandare JN: Formulation and evaluation of ketoconazole niosomes. Indian Journal Pharmacy Sciences. 2012; 64:155–158.
6. Y. Hao, F. Zhao, N. Li, Y. Yang, K. Li: Studies on a high encapsulation of colchicine by a niosome system, International . Journal of Pharmacy. 244 (2012) 73.
7. S.K. Mehta, N. Jindal, G. Kaur: Quantitative investigation, stability and in vitro release studies of anti-TB drugs in Triton niosomes , Journal of Colloids Surface 87 (2011) 173.
8. B. Shi, C. Fang, Y. Pei: Stealth PEG-PHDCA niosomes: effects of chain length of PEG and particle size on niosomes surface properties, in vitro drug release, phagocytic uptake, in vivo pharmacokinetics and antitumor activity, Journal. Pharm. Sci. 95 (2010) 1873–1887.
9. Nayak AK, Mohanty B, Sen KK: Comparative Evaluation of *In-vitro* Diclofenac sodium Permeability across Excised Mouse Skin from Different Common Pharmaceutical Vehicles. International Journal Pharm Tech Res, 2010; 2(1): 920–930.
10. Prasanthi D, Lakshmi PK: Development of Ethosomes with Taguchi Robust Design-based Studies for Transdermal Deliver of Alfuzosin hydrochloride. International Current Pharmaceutical Journal, 2012; 1(11): 370-375.
11. Mura, S., Pirot, F., Manconi, M., Falson, F., Fadda, A.M., 2007: Liposomes and niosomes as potential carriers for dermal delivery of minoxidil. Journal Drug Target. 15, 101–108.
12. Padois K, Pirot F, Falson F. French patent 0952059, 2009.
13. Marianecci: Ammonium glycyrrhizinate-loaded niosomes as a potential nanotherapeutic system for anti-inflammatory activity in murine models ,Journal of Controlled Release 164 (2012) 17–25.
14. Desai et al. Development and Evaluation of Antifungal Topical Niosomal Gel Formulation. International Journal Pharm Pharm Sciences, Vol 3, Suppl 5, 224-231.
15. Mokhtar M, Ibrahim A: *In vitro* evaluation of Proniosomes as a Drug Carrier for Flurbiprofen. AAPS PharmSciTech. 2009: 782-790.

16. Shashiwala A, Misra A: Studies in Topical Application of niosomally entrapped nimesulide. Journal Pharma Pharmaceutical Sciences. 2002; 5: 220-225.

How to cite this article:
Shaji J and Shah A: Development and characterization of tenoxicam encapsulated niosomes for enhanced transdermal delivery. Int J Pharm Sci Res 2016; 7(1): 307-15.doi: 10.13040/IJPSR.0975-8232.7 (1).307-15.