Formulation and Characterization of Novel Non-Ionic Surfactant Based Aceclofenac Gel as a Potential Drug Delivery System

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Authors’ contributions
This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Aceclofenac is considered to the first line drug in the symptomatic treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. The successful treatment of arthritis depend on the maintenance of effective drug concentration level in the body, for which a constant and uniform supply of drug is desired. The short biological half-life (about 4 hrs) and dosing frequency more than once a day as well as (70-80%) of dose is excreted by renal transport make aceclofenac an ideal candidate for formulation of niosomal gel.

Methodology: The niosomal gel of aceclofenac in order to sustain the release of aceclofenac topically, decreases the side effect of GI disturbance by maintaining the concentration of the drug in the blood and decrease the renal excretion as well as frequency of dosing. Niosomal gel was prepared by coacervation phase separation method. Preformulation studies, structural analysis, in-vitro drug release study, mechanism of drug release kinetic and data analysis (zero order, first order and higuchi’s model), percentage entrapment efficiency and stability study were performed (n=3). Anti-Inflammatory study was performed for final optimized formulation.

Result and conclusion: It is revealed from preformulation studies that materials obtained for study did not show any incompatibility. Particle size was determined in the range of 9.46±1.055 to

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1. INTRODUCTION

The drug delivery systems such as liposomes and niosomes which are vesicular carriers have the distinct advantage over the other dosage form due to behaviour of vesicle as drug containing reservoir [1,2]. The affinity of target site or drug release rate can be adjusted by some modification in vesicle composition or surface. Niosomes lead desired interaction with human skin during topical administration by modifying horny layer characteristic, consequently, it results in reduction in transdermal water loss and smoothen the skin-by-skin lipid replenishment [3]. Niosomes are essentially non-ionic surfactant based vesicles in which an aqueous solution of solute(s) is entirely enclosed by a membrane resulted from the organization of surfactant macromolecules as a bilayer [4]. Niosomes, a unique novel drug delivery system, are non-ionic surfactant based liposome prepared by cholesterol or their hydrating mixture. The positive role of niosomes is to impede its clearance from the circulation which improves the therapeutic performance of the API [5].

The main aim of pharmacotherapeutics is the attainment of effective drug concentration at the intended site of action for sufficient period of time to elicit a pharmacological response [6,7]. Although the topical and localized applications are still an acceptable and preferred way to achieve therapeutic level of drug at the site of action in different drug delivery system. Such dosage forms are no longer sufficient to combat various diseases like due to poor bioavailability, which is a result of efficient mechanism protecting the body from harmful materials and agents. These protective mechanisms result in the rapid removal of harmful materials and agents. The rational for the development of various particulate systems for sustained drug delivery is based on possible entrapment of the particles. An attractive feature of utilizing nanoparticles (liposomes/niosomes) for ocular drug delivery system is that it can be easily administered in liquid dosage forms, with patient’s compliance, with modulated drug release profile and high drug pay load [8-11]. Liposomes and niosomes (vesicular drug delivery system) are microscopic phospholipids bilayer vesicles made up of natural phospholipoids and cholesterol membrane i.e. biocompatible lipid core and an amphiphillic surfactant as an outer shell [12,13]. These act as drug carriers due to their bio compatibility and versatility. The trans-dermal route is widely used as it is convenient, safe and offers numerous astonishing by advantages over conventional ones that includes evading GI incompatibility, variable GI absorption, passing first pass metabolism, enhanced bioavailability, decreased frequency of administration, improved patient compliance and rapid cessation of drug input and can maintain a suitable plasma concentration [14-17].

Aceclofenac is considered to the first-line drug in the symptomatic treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. The successful treatment of arthritis depends on the maintenance of effective drug concentration level in the body, for which a constant and uniform supply of drug is desired [15,18].

![Fig. 1. Structure of Aceclofenac](image)

(C_{10}H_{13}Cl_3NO_2, Mol. Wt. = 354.185)
2. MATERIALS AND METHODOLOGY

2.1 Materials

Aceclofenac was obtained as a gift sample from Welcure Pharmaceuticals, Indore. Cholesterol was purchased from Sunchem India Pvt. Ltd., lecithin, span 20, span 60, span 80, methanol were purchased from Sigma-Aldrich ®.

2.2 Methodology

Identification of procured drug was made by following methodology.

2.2.1 FTIR

The identification of drug sample was done by IR spectroscopy and spectrum was compared with the standard IR as per the Indian Pharmacopoeia (IP).

2.2.2 Melting point

The melting point of the aceclofenac was determined by capillary method. Small amount of drug sample was taken in a capillary tube and the capillary tube was placed in a melting point apparatus. Drug in the capillary tube was melted with increments of time and the temperature was shown on the digital meter. This process was repeated three times and the average of the reading was taken [19].

2.2.3 Solubility studies

Solubility of aceclofenac was determined by saturation solubility method. Equivalent amount of drug was added to the test-tubes containing 10 ml of solvent to obtain saturated solution of drug. Resultant dispersion was filtered through the whatman filter paper (Grade 5 – Size 25 mm to 320 mm) and dissolved drug was analysed spectrophotometrically at 275 nm (1700 Shimadzu UV spectrophotometer).

2.2.4 Partition co-efficient determination

Accurately weighed drug was dissolved in 10 ml of phosphate buffer saline and 10 ml of n-octanol in separating funnel. This mixture was shaken for 30 seconds in 10 minutes interval for 1 hour and left it for 24 hours. The two layers were separated out and resultant aqueous phase was diluted 100 times with phosphate buffer saline [20]. The partition coefficient was determined by following formula:

\[
\text{Partition coefficient} = \frac{\text{Concentration of drug in organic phase}}{\text{Concentration of drug in aqueous phase}} \times 100
\]

2.3 Preparation of Niosomal Gel

Niosome was prepared by a coacervation phase separation method. Precisely weighed amounts of surfactant, lecithin, cholesterol and drug were taken in a clean and dry wide mouth glass vial of 5.0 ml capacity and alcohol (0.5 ml) was added to it. After heating at moderate temperature, all the ingredients were mixed well with a glass rod, the open end of the glass bottle was covered with a lid to prevent the loss of solvent from it and warmed over water bath at 60-70°C for about 5 mins until the surfactant mixture was dissolved completely. Further, the aqueous phase (0.1% glycerol solution) was added and heated on a water bath till a clear solution was obtained which was incorporated into niosomal gel on cooling [16,21-22].

2.4 Particle Size Analysis

The particle size analysis was performed using optical microscopy. The niosomal gel (100 mg) was dispersed in 10 ml of PBS (pH 7.4) and was shaken for 5 min. A drop of the suspension was mounted on the slide and observed under the optical microscope at 100X magnification thrice. Mean of reading was taken and their size distribution range, mean diameter was calculated [23].

2.5 Encapsulation Efficiency

Percent encapsulation efficiency (EE) was determined by centrifugal method. The niosomal gel (100 mg) was converted to niosomal dispersion by adding 10 ml PBS (pH 7.4) with gentle heating, which was centrifuged at 18,000 rpm for 40 min at 50°C in order to separate unentrapped drug. The supernatant was taken and diluted with PBS [24-25]. The drug concentration in the resulting solution was assayed spectrophotometrically at 275 nm.

\[
\% \text{Entrapment Efficiency} = \frac{\text{Entrapped drug (mg)}}{\text{Total drug (mg)}} \times 100
\]
2.6 In-Vitro Release Study

The release of aceclofenac from niosomal formulations were determined by using membrane diffusion technique. 100 mg of niosomal gel was converted to niosomal suspension by adding 10 ml of PBS pH 7.4. This suspension was taken in a Franz diffusion cell. Cellulose membrane was used to separate donor and receptor compartment. The temperature was maintained at 37±10°C and the medium was agitated with constant stirring using magnetic stirrer. At predetermined time intervals, aliquots (5 ml) were withdrawn and replaced with fresh buffer [26].

2.7 Drug Release Kinetic Data Analysis

The drug release kinetic data obtained from various formulations were studied further for their fitness of data in different kinetic models like zero order, first order and Higuchi’s kinetic model [27-28].

2.8 Stability Studies

A physical stability test was carried out to investigate the leaching of drug from niosomes during storage. The niosomal samples were sealed in glass vials and stored at two different temperature conditions, i.e., Refrigeration temperature (4-8°C) and room temperature (40°C) for one month and the samples were taken after a particular time interval [29]. The drug leakage from the formulations was analysed by determining its encapsulation efficiency in the same manner as described previously.

2.9 Anti-Inflammatory Activity

The anti-inflammatory activity of aceclofenac loaded niosomal gel formulations was evaluated by the carrageenan-induced rat hind paw edema method. Anti-inflammatory activity of the aceclofenac loaded niosomal gel was compared with marketed gel of diclofenac (Voveron Emulgel). The studies were conducted on albino rats of either sex, weighing between 150-200g. The rats were divided into two groups; Group 1 (Standard group): animals were treated with diclofenac gel BP (Voveron Emulgel); Group 2 (Test group): animals were treated with aceclofenac loaded Niosomal gel.

Inflammation was produced in the rats by injecting 0.1 ml of 1% w/v carrageenan suspension, in to the plantar surface of the rat's left hind paw and after 1 hour, formulations were applied topically on the inflamed paw of rats by gently rubbing with index finger and the thickness of the paw was measured with the help of vernier calliper. The thickness of the paw was measured at 1 hour time intervals till 5 hours after carrageenan injection [30]. The percentage inhibition of inflammation was calculated by the following formula.

\[
\text{Percentage Inhibition} = \left( \frac{\text{Control paw edema} - \text{Test paw edema}}{\text{Control paw edema}} \right) \times 100
\]

3. RESULT AND DISCUSSION

The successful treatment of arthritis depends on the maintenance of effective drug concentration level in the body, for which a constant and uniform drug release is desired. The short biological half-life (about 4 hrs) and dosing frequency more than once a day, as well as 70-80 % of dose is excreted by renal transport, makes aceclofenac an ideal candidate for formulation of Niosomal gel. Cholesterol act as a “vesicular cement” used to improve the stability of vesicles. Higher into a Cholesterol content led to significant increase in entrapment efficiency (%) due to increase in rigidity and the permeability of drug through the membrane decreases and hence, improves the entrapment efficiency. But after certain limit, further increase in cholesterol concentration results in significant decrease in entrapment efficiency.

3.1 Determination of FT-IR

The infrared spectrum of aceclofenac was found to be concordant with the reference IR spectrum of aceclofenac given in IP 2010. The IR spectrum of drug aceclofenac shown in Fig. 1 (a). In FTIR spectrum of pure aceclofenac drug, the principle peaks were found at 3404.20 cm⁻¹ attribute to secondary N-H rocking, at 2936.77 cm⁻¹ attributes to aliphatic C-H stretching vibrations, signal at 1636.28 cm⁻¹ showed C-O stretching to carbonyl group, at 1463.22 cm⁻¹ attributes to C-C stretching of aromatic ring, at 737.20 cm⁻¹ because of C-Cl stretching.

The FTIR spectrum of aceclofenac has been compared with FTIR spectrum of physical mixture of aceclofenac and other excipients used in the formulation and no interference was as shown in Fig. 2.
3.2 Determination by Melting Point

The melting point of Aceclofenac was found in the range of 149-155°C.

3.3 Solubility Studies

Solubility study of aceclofenac was conducted in different solvents at room temperature which revealed that the drug is soluble in methanol, ethanol, while insoluble in purified water.

3.4 Determination of Partition Coefficient

Partition coefficient value of aceclofenac revealed that the drug is lipophilic in nature as it is found to be 1.82 in n-octanol/Phosphate buffer saline (PBS-pH 7.4) system. The more the partition coefficient the greater is the lipid solubility.

3.5 Preparation of Niosomal Gel

Niosomal gel can be prepared by the use of coacervation phase separation method, the hydrated niosomes found in the range of 9.46-12.91μm. Vesicle size was found to be smallest in F6 due to the presence of span 80. Increasing hydrophobicity of the surfactant monomer led to a smaller vesicle. The particle size of F2 was found to be the largest due to the presence of span 20. It is reported that surfactants with larger alkyl chains generally give larger vesicles. Composition of niosomal gel is given in Table 1.

3.6 Determination of Microscopy of Niosomes

The particle size of niosomes was measured using an optical microscope with calibrated...
eyepiece micrometer. The photomicrograph of drug loaded hydrated reveal that the niosomes are multilamellar vesicles having spherical shape and no aggregation or agglomeration was observed. The photomicrograph of the preparation obtained from the microscope by using a digital camera is shown in Fig. 3.

Table 1. Composition of Niosomal gel system

| Sr. No. | Formulation Code | Surfactant Type | Ratio (mg) | Cholesterol (mg) | Lecithin (mg) | Alcohol (ml) | Water (ml) |
|---------|-----------------|----------------|------------|----------------|--------------|--------------|------------|
| 1       | F1              | S60:S20        | 5:5        | 100            | 100          | 0.5          | 1.0        |
| 2       | F2              | S60:S20        | 8:2        | 100            | 100          | 0.5          | 1.0        |
| 3       | F3              | S60:S20        | 2:8        | 100            | 100          | 0.5          | 1.0        |
| 4       | F4              | S60:S80        | 5:5        | 100            | 100          | 0.5          | 1.0        |
| 5       | F5              | S60:S80        | 8:2        | 100            | 100          | 0.5          | 1.0        |
| 6       | F6              | S60:S80        | 2:8        | 100            | 100          | 0.5          | 1.0        |

*Drug concentration used was 100 mg in each formulation.

Fig. 3. Photomicrograph of drug loaded Niosomes

3.7 Surface Morphology of Niosomes

Fig. 4. Scanning Electron Microscope of Niosomes
3.8 Determination of Entrapment Efficiency

The entrapment efficiency of all Niosomal formulations is reported in Table 2. The entrapment efficiency was found to be higher with the formulation F2 (78.55%) due to the larger alkyl chains of span 20. The entrapment efficiency of span 80 formulations F6 (63.49%) was found less in comparison to span 20 due to the presence of unsaturated alkyl chain. Introduction of a double bond into the paraffin chain causes a marked enhancement in the permeability in niosomes. This might be the reason for the lower entrapment of the span 80 system.

3.9 In-Vitro Release Study

The comparative dissolution profile of all the niosomal preparations is depicted. The highest % cumulative release was found in F2 (88.35%) and lowest drug release is in F6 (70.55%). High HLB value results in reduction of surface free energy which allows forming vesicles of larger size. High HLB value of span 60 and span 20, results reduction in surface free energy which allows forming vesicles of larger size hence large area exposed to the dissolution medium and skin as follows in Tables 3 and 4.

3.10 In-Vitro Drug Release Kinetic Data Analysis

Mathematical models are commonly used to predict the release mechanism and to compare release profile. To analyze the mechanism for the release and release rate kinetics, the data obtained were fitted into Zero order, First order and Higuchi’s model. In this by comparing the R² value obtained, the best fit model was selected.

For all the formulations (F1 to F6), the cumulative per cent drug release vs time (zero order), the cumulative per cent drug release vs square root of time (Higuchi plot), and log cumulative per cent drug remaining vs time (first order) were plotted and in each case, R² value was calculated from the graph and reported. In F1 and F2 formulations, the best fitting linear parameter model was zero order and their correlation coefficient was found to be 0.996 and 0.985 and from F3 to F6 the best fit model was First order as given in Table 5. The comparison of zero order release, first order release and Higuchi’s order release shown in Fig. 4.

This indicates that the drug release was in the controlled manner from the vesicles. The Higuchi’s plot concluded that the drug was released from niosomes by a diffusion-controlled mechanism.

Table 2. Particle size analysis and entrapment efficiency

| Formulation code | Particle size ± SD* (µm) | %Entrapment efficiency ± SD* |
|------------------|--------------------------|-----------------------------|
| F1               | 12.176±1.942             | 73.20±0.722                 |
| F2               | 12.913±3.587             | 78.55±0.425                 |
| F3               | 11.596±2.342             | 72.87±0.126                 |
| F4               | 10.086±1.777             | 67.26±0.266                 |
| F5               | 11.016±2.003             | 70.23±0.290                 |
| F6               | 09.46±1.055              | 63.49±0.265                 |

Fig. 4 (a). Comparison of Zero order release of all formulations
3.11 Determination of Stability

Physical stability of niosomal formulations were studied for a period of one month. The encapsulation efficiency was determined for all niosomal formulations stored at different temperatures. There was less decrease in the %EE of all the niosomal formulations at refrigerated conditions while at room temperature %EE decreases 10-15% within the period of one month due to the melting point of the surfactant and the lipid present in the formulations. Therefore, the niosomal preparation which was stored at refrigerated condition (4-8°C), was quite stable compared to formulation stored at room temperature. The data is tabulated in Table 6.

3.12 Determination of Anti-inflammatory Activity

Anti-inflammatory activity (detailed in methodology) of F2 formulation was carried out and compared with commercial reference product (Voveran Emulgel) during the entire 5 hours duration of the study. The maximum percentage inhibition of anti-inflammatory activity was analysed (Table 7). The percentage inhibition of inflammation was calculated by the following formula and the results are shown in Table 7.

\[
\text{Percentage Inhibition} = \left( \frac{\text{Control paw edema} - \text{Test paw edema}}{\text{Control paw edema}} \right) \times 100
\]

The percentage inhibition of marketed product was achieved at 3 hours (21.22%) while the maximum percentage inhibition of Niosomal formulation F2 was observed at 5 hours (20.88%). This shows that the percentage inhibition of paw edema produced by reference products were statistically higher as compared to the aceclofenac-loaded Niosomal gel. The study shows that the aceclofenac loaded Niosomal gel possesses fair anti-inflammatory activity but it is not as good as the commercial product.
Table 3. *In-vitro* drug release

| Time (hrs) | Absorbance | Concentration (μg/ml) | % Cumulative drug release |
|-----------|------------|-----------------------|--------------------------|
|           | F1         | F2                    | F3                       | F4           | F5   | F6   |
| 0         | 0          | 0                     | 0                        | 0            | 0    | 0    |
| 1         | 0.071      | 0.052                 | 0.068                    | 0.071        | 0.072| 0.059|
| 2         | 0.065      | 0.060                 | 0.142                    | 0.120        | 0.125| 0.097|
| 3         | 0.069      | 0.069                 | 0.183                    | 0.154        | 0.175| 0.136|
| 4         | 0.072      | 0.070                 | 0.223                    | 0.187        | 0.224| 0.168|
| 5         | 0.074      | 0.156                 | 0.263                    | 0.226        | 0.263| 0.198|
| 6         | 0.123      | 0.269                 | 0.309                    | 0.259        | 0.296| 0.227|

Table 4. *In-vitro* drug release kinetics

| Time (hrs) | %Cumulative drug release Vs time (Zero order model) | Log %Cumulative drug remaining to be released Vs time (First order model) | % Cumulative drug release Vs square root of time (Higuchi model) |
|-----------|---------------------------------------------------|------------------------------------------------------------------------|---------------------------------------------------------------|
|           | F1    | F2    | F3    | F4    | F5    | F6    | F1    | F2    | F3    | F4    | F5    | F6    | F1    | F2    | F3    | F4    | F5    | F6    |
| 0         | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.081 | 0.014 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| 1         | 6.114 | 6.600 | 5.763 | 5.624 | 5.861 | 5.069 | 0.232 | 0.036 | 0.041 | 0.041 | 0.043 | 0.041 | 0.246 | 0.190 | 0.237 | 0.246 | 0.249 | 0.211 |
| 2         | 3.065 | 3.280 | 2.773 | 2.74   | 2.853 | 2.479 | 0.115 | 0.018 | 0.039 | 0.034 | 0.034 | 0.031 | 0.335 | 0.285 | 0.488 | 0.449 | 0.461 | 0.376 |
| 3         | 2.040 | 2.183 | 1.808 | 1.79   | 1.850 | 1.614 | 0.077 | 0.013 | 0.033 | 0.029 | 0.032 | 0.028 | 0.412 | 0.371 | 0.730 | 0.650 | 0.694 | 0.560 |
| 4         | 1.527 | 1.636 | 1.327 | 1.321 | 1.350 | 1.187 | 0.058 | 0.010 | 0.031 | 0.026 | 0.030 | 0.026 | 0.482 | 0.443 | 0.979 | 0.856 | 0.946 | 0.750 |
| 5         | 1.221 | 1.259 | 1.038 | 1.033 | 1.060 | 0.932 | 0.046 | 0.017 | 0.029 | 0.025 | 0.028 | 0.024 | 0.545 | 0.618 | 1.237 | 1.079 | 1.208 | 0.948 |
| 6         | 0.993 | 0.993 | 0.842 | 0.845 | 0.867 | 0.762 | 0.044 | 0.024 | 0.028 | 0.024 | 0.026 | 0.023 | 0.660 | 0.902 | 1.515 | 1.310 | 1.473 | 1.153 |
Table 5. Drug release kinetic studies of Niosomal gel

| Formulation codes | Zero order model | First order model | Higuchi’s model | Conclusion |
|-------------------|------------------|------------------|-----------------|------------|
|                   | Slope     | R²               | Slope          | R²         |           |
| F1                | 3.442     | 0.996            | -0.083         | 0.965      | 17.85     | 0.910     | Zero order kinetics |
| F2                | 3.726     | 0.985            | -0.085         | 0.969      | 19.37     | 0.900     | Zero order kinetics |
| F3                | 3.205     | 0.720            | -0.080         | 0.985      | 19.03     | 0.863     | First order kinetics |
| F4                | 2.843     | 0.726            | -0.080         | 0.985      | 16.89     | 0.870     | First order kinetics |
| F5                | 3.019     | 0.711            | -0.081         | 0.982      | 17.97     | 0.857     | First order kinetics |
| F6                | 2.759     | 0.719            | -0.079         | 0.983      | 16.40     | 0.864     | First order kinetics |

Table 6. Data of stability analysis at two different conditions

| Formulation codes | Conditions                | %EE at 0 day | %EE at 10 days | %EE at 20 days | %EE at 30 days |
|-------------------|---------------------------|-------------|---------------|---------------|---------------|
| F1                | Refrigerated temperature  | 72.04       | 71.09         | 69.25         | 68.30         |
|                   | Room temperature          | 72.96       | 70.17         | 68.30         | 65.54         |
| F2                | Refrigerated temperature  | 79.05       | 78.16         | 77.29         | 75.54         |
|                   | Room temperature          | 78.16       | 75.54         | 72.93         | 71.21         |
| F3                | Refrigerated temperature  | 72.44       | 71.47         | 69.49         | 68.52         |
|                   | Room temperature          | 73.44       | 70.50         | 68.52         | 65.58         |
| F4                | Refrigerated temperature  | 68.76       | 67.77         | 65.75         | 64.76         |
|                   | Room temperature          | 68.76       | 66.78         | 63.76         | 61.74         |
| F5                | Refrigerated temperature  | 70.98       | 69.04         | 68.09         | 66.15         |
|                   | Room temperature          | 70.00       | 67.10         | 65.19         | 63.25         |
| F6                | Refrigerated temperature  | 64.22       | 63.11         | 60.87         | 59.77         |
|                   | Room temperature          | 63.11       | 57.52         | 53.07         | 50.83         |

Table 7. Percentage inhibition of anti-inflammatory activity in different groups

| Sr. No. | Time (hr) | % Inhibition in Standard group | % Inhibition in Test group |
|---------|-----------|--------------------------------|---------------------------|
| 1       | 1         | 17.83%                         | 11.89%                    |
| 2       | 2         | 21.05%                         | 16.31%                    |
| 3       | 3         | 21.22%                         | 17.80%                    |
| 4       | 4         | 19.41%                         | 20.58%                    |
| 5       | 5         | 18.35%                         | 20.88%                    |

The exact mechanism of penetration of drug loaded vesicles through the skin are not yet explored, but the penetration will depends on the nature and type of the drug used, vesicles formed and hydration temperature. The lipids used in the preparation of niosomes, act as carrier that will form depot at the site of action and hence sustains the action. The rate-limiting step in transdermal drug delivery is the lipid (ceramides) part of stratum corneum, which packed tightly as bilayer by hydrogen bonding. The hydrogen bonding will strengthen and stabilize the lipid bilayer and as a result will impart the barrier property of stratum corneum. Liposomes will hydrate to niosomes when applied to skin. On to the skin surface, the niosomes formed adsorbs, fuses and loosens the ceramides by competitively breaking the hydrogen bond network leading to high thermodynamic activity at the interface. This will increase the concentration gradient and hence increases the diffusion pressure for the driving of drug through the stratum corneum.

4. CONCLUSION

An attempt has been made to prepare the niosomal gel of aceclofenac by a coacervation-phase separation method in order to sustain the release of aceclofenac topically, which can reduce the side effect of GI disturbance by maintaining the concentration of the drug in the blood and decrease the renal excretion as well.
as frequency of dosing. It would be faster and more economical to alter beneficially the properties of the existing drugs than developing the new drug entities. The transdermal route is widely used as it is convenient, safe and offers numerous astonishing by advantages over conventional ones that includes evading GI incompatibility, variable GI absorption, passing first pass metabolism, enhanced bioavailability, decreased frequency of administration, improved patient compliance and rapid cessation of drug input and can maintain a suitable plasma concentration. Finally, anti-inflammatory activity of the final formulation was compared with commercial reference product (Voveran Emulgel) gel, and concluded that aceclofenac loaded niosomal gel possesses fair anti-inflammatory activity but it is not as good anti-inflammatory as the commercial product of diclofenac.

DISCLAIMER
The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT
It is not applicable.

ETHICAL APPROVAL
The studies were carried out as per the guidelines designed by Institutional Animal Ethics Committee (Reg. No. 1323/AC/10/CPCSEA).

COMPETING INTERESTS
Authors have declared that no competing interests exist.

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