International Journal of Research in Pharmacology & Pharmacotherapeutics (IJRPP)

IJRPP |Vol.14 | Issue 3 | Jul - Sept -2025

www.ijrpp.com

ISSN: 2278-2648

DOI : https://doi.org/10.61096/ijrpp.v14.iss3.2025.376-381

Research

Niosomal Gel loaded with Aceclofenac: A controlled drug delivery system

K. Neelima Devi[1], M.L.N.T. Amaleswari[1], Vikas Kandapu*[2], Karnam Keerthana[2], Kammari Sai Charan[2], Kata Sanjay[2], Kathi Mahathi[2]

Assistant Professor, Malla Reddy college of Pharmacy, Maisammaguda, Hyderabad, Telangana. 500014.
Student, Malla Reddy college of Pharmacy, Maisammaguda, Hyderabad, Telangana. 500014.

*Author for Correspondence: Vikas Kandapu
Email: vikaskandapu@gmail.com

Published on: 18 July 2025

Published by:
Futuristic Publications

Abstract

The problem with BCS Class 3 & 4 drugs is their permeability. Though easily soluble and compatible with body fluids, topical application of these drugs struggle to get through skin layers effectively, making the solubility part not so useful. Recent studies have made this easy by the use of nano medicine technology such as liposomes, solid nano particles, polymeric micelles etc., These drug delivery systems help the drugs to permeate through the skin and the rest is taken care of, by the drug's own solubility; in case of class 3 & solubility enhancers in case of class 4. Thus Class 3 & 4 drugs have found a way to effectively deliver the drugs into the body. However, a problem to acknowledge is of Class 2 drugs, which have good permeability but low solubility. This odd combination can be used favourably as a controlled drug delivery system using another nano medicine technology i.e. niosomes. These allows drug's slow penetration through skin and also slow release of drug, less enough to be soluble in body fluids. In short, the formulation would give us a controlled or delayed drug delivery system. We used this formulation to make a Aceclofenac loaded niosomal gel. We've prepared niosomes by ether injection method. Aceclofenac, a very well-known anti-inflammatory agent, is known to have a good pain-killing action with a short half-life (about 4 hours) prompting the subjects to take multiple dosages in a day. So, this drug as a niosomal gel would allow slow release and slow permeation of drug allowing prolonged action of the drug. This effectively lets the subject to administer the formulation in lesser frequency for a prolonged action, increasing the compatibility and patient compliance.

Keywords: Aceclofenac, Niosomes, Ether injection method, Controlled drug delivery system, Delayed drug delivery, Drug permeation.

INTRODUCTION

Niosomes, commonly known as non-ionic surfactant vesicles, are tiny lamellar formations created by blending non-ionic surfactants from the alkyl or dialkyl polyglycerol ether group with cholesterol, followed by their hydration in aqueous solutions. These vesicular systems, similar to liposomes, can act as transporters for medications that have both amphiphilic and lipophilic characteristics. The technique for creating niosomes relies on liposome technology. The fundamental manufacturing method stays unchanged, as the lipid phase is combined with the aqueous phase. The lipid phase might consist of a single surfactant or a mixture of surfactant and cholesterol. Niosomes effectively tackle problems associated with drug insolubility, instability, low bioavailability, and quick degradation. Various methods have been developed to create niosomes from the materials mentioned earlier, depending on their clinical relevance, lamellarity, and particle size.[1]

Several techniques have been devised to synthesize niosomes from the substances listed in the previous section based on their clinical applicability, lamellarity, and particle size. [2,3,4]
These methods include

1. Ether injection method
2. Bubble method
3. Manual shaking method
4. Micro-fluidization method
5. Sonication method
6. Thin film hydration method
7. Multiple membrane extrusion method
8. Transmembrane pH gradient method
9. Reverse phase evaporation method [2,3,4,6]

Ether injection method: [2,3,4,5,7]

- In this method, the cholesterol and non-ionic surfactant are first dissolved in ether and then slowly injected through a needle into the aqueous phase containing a drug or natural molecule, all while stirring at temperatures above 60 °C in a heated water bath.
- Since ether has a low boiling point, as soon as the mixture touches the hot aqueous phase, it evaporates and lets spontaneous vesicle formation i.e. niosomes.
- The method is continued until all the ether mixture is finished.
- Later the mixture is allowed to cool and then subjected to sonication for 5-10 minutes for more finer niosomes.
- To load the drug, it shall be dissolved in appropriate solvent, either aqueous phase or ether phase. Aceclofenac is poorly soluble in water and hence added in ether.

Ether injection methods was selected among all available choices based on the availability of chemicals, equipment. Ether injection method is considered relatively simple and efficient though known to give out lesser entrapment efficiency. The faster output of technique allowed us for quick evaluation so as to select a better formula.

MATERIALS

For preparation of niosomes by ether injection method, chemicals used are:

- Cholesterol
- Span 60
- Phosphate Saline Buffer (pH 7.4)
- Diethyl ether
- Aceclofenac

For preparation of niosomal gel from the niosomal suspension prepare, following chemicals are used:

- Carbopol 940
- Distilled water
- Triethanolamine

Methodology

For preparation of niosomes by ether injection method.

1. Accurate amount of cholesterol, span 60 and drug were weighed.
2. One by one, these are transferred into a beaker containing required amount of diethyl ether.
3. The mixture is stirred until all ingredients are dissolved.
4. A beaker containing required amount of PBS buffer is preheated up to 70° C.
5. The PBS buffer is subjected to magnetic stirring at a constant pace until vortexing is observed.
6. When vortex appears, the diethyl ether mixture is loaded in syringe and added in the hot PBS, drop by drop at a uniform rate.
7. After finishing adding all the ether mixture, set the final mixture aside for cooling.
8. The cooled mixture is then allowed to sonicate for 5 min for fine niosomes.

Table 1: Formulations of niosomal suspension

Formulation	Surfactant: Cholesterol	Drug added
F1	2:1	150mg
F2	1.5:1	100mg
F3	1:1	100mg

For preparation of niosomal gel, below steps were followed:

1. Accurately weigh required amount of Carbopol 940, to soak in appropriate amount of water overnight to make 1% Carbopol gel.
2. Weigh about 2gm of niosomal suspension and mix it with Carbopol gel accordingly.
3. Add triethanolamine drop by drop while stirring, until required consistency is achieved.
4. Transfer and store the gel in a container.

Fig 1: Niosomal Gel loaded with Aceclofenac

The niosomal gel thus prepared is subjected to various characterizing tests both physical and chemical.

Characterization of Niosomal gel

Entrapment efficiency [7,8]: - The entrapped drug was first separated by centrifugation method and supernatant liquid was collected, which is then subjected to UV spectroscopy to determine drug's concentration. Finally, the entrapment efficiency was calculated using following formula:

$$\text{E. E} = \frac{\text{Amount of entrapped drug}}{\text{Amount of total drug}} \times 100$$

Drug content in niosomes [7,8]: - Niosomal gel is diluted accordingly and subjected to longer sonication (40-60 min) to break the niosomal structure and release the drug. The resultant solution is diluted again as specified and drug concentration was analysed using UV spectrophoto -metry at 275 nm.

In-vitro Drug release studies [7,9]: - The gel was studied for its drug release properties by Franz Diffusion technique. Nitrocellulose membrane was placed between donor and receptor compartment with appropriate amount of gel on top of membrane. Receptor compartment is filled with about 50ml PBS. Temperature and rotation rate were set and procedure is started. Sample of 5ml was withdrawn every 30 min and same amount of fresh buffer was fed into receptor compartment. The withdrawn samples are then analysed using UV spectrophotometer.

In-vitro anti-inflammatory assay [10]: -To test the gel's anti-inflammatory activity, egg albumin denaturation assay was performed. 1% egg albumin solution is prepared, along with various dilutions of niosomal gel. Each test solution contains, 2.8ml of buffer, 2ml of test dilution of various concentrations and 0.2ml of egg albumin solution. These solutions are incubated at 36° C for about 30 min. Then they are all heated for 15 min at 70° C to induce denaturation. Once cooled, they are all checked for absorbance at 280nm in UV spectrophotometer along with a control (i.e. no drug content added) with distilled water as the blank. The percentage inhibition of denaturation is calculated by the formula:

$$\% \textbf{ inhibition} = \frac{\textbf{Abs of control} - \textbf{Abs of test}}{\textbf{Abs of control}} \times \textbf{100}$$

The inhibition of denaturation indicates anti-inflammatory action. More inhibition percentage indicates more anti-inflammatory activity.

RESULTS AND DISCUSSION

Physical Parameters:

1. **Colour: -** The niosomal gel colour was found to be translucent.
2. **Texture: - T**he formulated niosomal gel appeared smooth, with no lumps or grittiness, indicating a well-formed dispersion.
3. **Odour:** The gel formulation was odourless.
4. **Homogeneity:** Visual inspection of gel revealed a uniform dispersion without any visible particles or phase separation.
5. **Viscosity: -** Viscosity of the gel was measured by using Brookfield viscometer. The Viscosity of the gel is found to be 2643 cps.
6. **pH: -** Sample of gel was diluted accordingly and was measured for pH using a standard pH meter. The pH of the gel was found to be 6.9.
7. **Spreadability: -** Spreadability of gel was measured by glass slide method, and was found to be 4.9 g.cm/sec.
8. **Washability: -** The washability test results showed that the hydrogel formulation was readily removable with water, suggesting its suitability for applications where ease of removal is desired.

Entrapment efficiency

Entrapment efficiency was calculated and found to be 40%, and is desirable considering the fact that the ether injection was supposed to give poor to moderately loaded niosomes.

Drug Content

Drug content in niosomes was calculated and found to be around 80%, from the entrapped efficiency of each niosome and drug content in the overall suspension.

In-vitro drug release studies

Calibration curve of Aceclofenac is drawn from the standard calibration concentration values used by Rajput et.al and the equation required is obtained. From the obtained equation, the next steps of the calculation of drug release were carried out using the observations from Franz diffusion data.

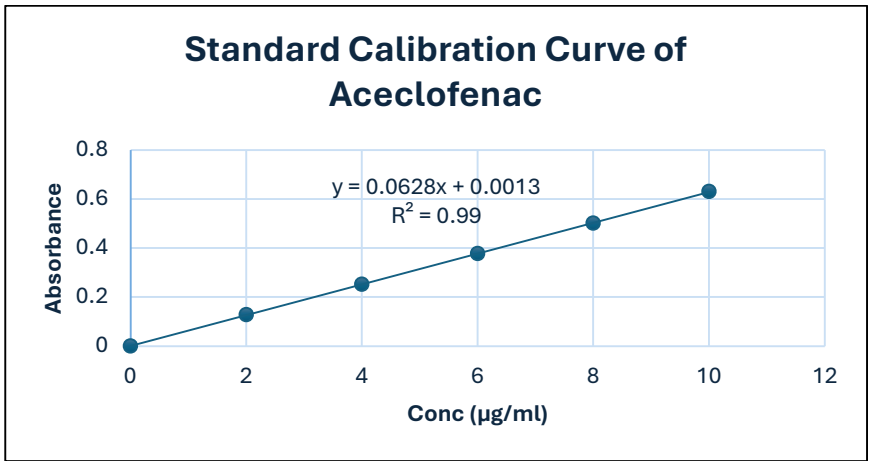

Fig 2: Standard Calibration Curve of Aceclofenac [11]

Table 2: Data of Franz diffusion of Aceclofenac niosomal gel

Time (Hrs)	Absorbance	Conc.	Cumulative mt per cm^2
0.5	0.047	0.72	0.041
1.0	0.147	2.32	0.172
1.5	0.223	3.53	0.371
2.0	0.259	4.10	0.603
2.5	0.282	4.46	0.855
3.0	0.294	4.66	1.119
3.5	0.352	5.58	1.434
4.0	0.356	5.64	1.753
4.5	0.405	6.42	2.117
5.0	0.429	6.81	2.501
5.5	0.532	8.45	2.979

The diffusion studies carried out indicated that the gel permeated through the nitrocellulose membrane over the 5 hours period implying that with increase in time the drug slowly permeates through the skin leading to a favourable controlled drug delivery setup. A Graph drawn against Time and Cumulative amount permitted per cm^2, shows the direct relationship between the data.

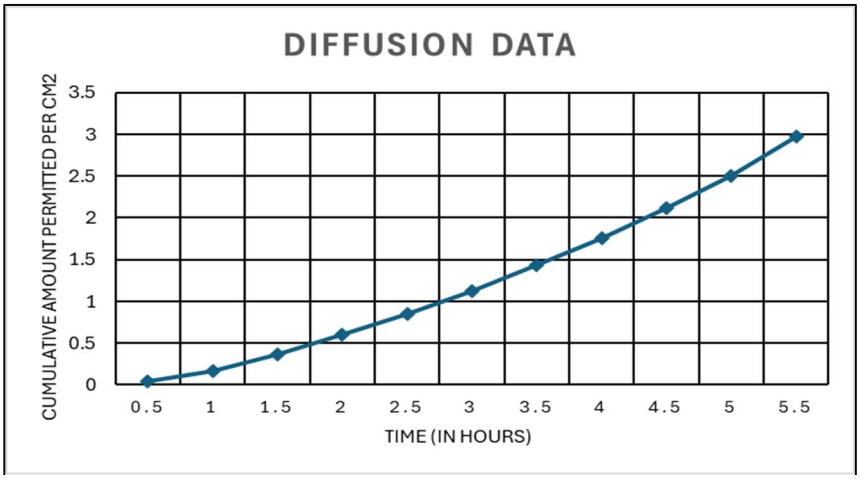

Fig 3: Diffusion studies of Aceclofenac Niosomal gel

Egg albumin denaturation Assay

Table 3: Data of anti-inflammatory assay

Concentration	% inhibition
Control	0
1	16.0%
2	42.8%
3	61.9%
4	80.0%

The assay results were calculated and the percentage inhibition of albumin denaturation data obtained suggested that the drug inhibited the protein denaturation significantly. This inhibition of denaturation has been observed to have increased with increase in the drug's concentration. This effectively displays the anti-inflammatory potential of the formulation.

CONCLUSION

The gel thus formulated has shown satisfactory results in terms of physical properties such as viscosity, spreadability, pH etc., The niosomal gel loaded with Aceclofenac has also shown a good anti-inflammatory property and confirms the entrapped drug is indeed releasing and showing the activity. The Franz diffusion data suggests that the gel has a good diffusion property. Not only that, but the gel diffusion data shows that it is at least 2 times slower than any ideal gel, suggesting that the gel achieved to delay the drug delivery, even with a good penetration. This effectively satisfies the need of the study to develop a niosomal gel loaded with Aceclofenac for anti-inflammatory activity with a delayed drug delivery. With the data and statistical evidence presented, we conclude that the gel has given positive results to all the tests done so far and is an example that niosomes can practically be helpful in delaying drug delivery or controlled drug delivery.

REFERENCES

1. Biju SS et.al. Vesicular system: an overview. Ind J Pharm sci. 2006; 68: 141-153.
2. Yasamineh S et.al. A state-of-the-art review on the recent advances of niosomes as a targeted drug delivery system. Int. J. Pharm. 2022, 624, 121878.
3. Izhar, M.P et.al. Drug Delivery through Niosomes: A Comprehensive Review with Therapeutic Applications. J. Clust. Sci. 2023, 34, 2257 2273.
4. Durga Bhavani G et.al. Recent advances of non-ionic surfactant-based nano-vesicles (niosomes and proniosomes): A brief review of these in enhancing transdermal delivery of drug. Future J. Pharm. Sci. 2020, 6, 100.
5. Moghtaderi M et.al. Niosomes: A novel targeted drug delivery system for cancer. Med. Oncol. 2022, 39, 240.
6. Saeid Mezail Mawazi et.al. Niosome Preparation Techniques and Structure: An Illustrated Review
7. Abbaraju Krishna Sailaja et.al. Formulation and Evaluation of Etoricoxib Niosomes by Thin Film Hydration Technique and Ether Injection Method
8. Shailendra Kumar Singh et.al. Niosomes: A Controlled and Novel Drug Delivery System.
9. Ali Moammeri et.al. Current advances in niosomes applications for drug delivery and cancer treatment
10. Hewa Dikkumburage Tharindu Madhuranga et.al.In vitro Anti-Inflammatory Egg Albumin Denaturation Assay: An Enhanced Approach
11. Jayesh M. Rajput et.al. Studies on formulation and evaluation of Aceclofenac matrix drug delivery system using a natural gum found in Satpuda region of north Maharashtra