International Journal of Applied Pharmaceutics

ISSN- 0975-7058 Vol 15, Issue 5, 2023

Original Article

FORMULATION AND EVALUATION OF NIOSOMAL GEL OF AZELAIC ACID FOR ANTIACNE ACTIVITY

VIVEK KASHYAP, ANJNA RANI*

Noida Institute of Engineering and Technology (Pharmacy Institute), 19 Knowledge Park-II, Institutional Area, Greater Noida-201306, Uttar Pradesh, India
*Corresponding author: Anjna Rani; *Email: anjna.sharma89@gmail.com

Received: 13 Jun 2023, Revised and Accepted: 14 Jul 2023

ABSTRACT

Objective: This study aimed to develop niosomes loaded with azelaic acid (AA) to administer in gel form. The primary objective was to achieve controlled and sustained release of the drug while minimizing potential side effects.

Methods: Niosomes were fabricated using a combination of various non-ionic surfactants and cholesterol through the application of thin film hydration technique. Furthermore, the processing parameters were optimized and drug excipient compatibility study was conducted using FTIR spectroscopy. The formulations were extensively characterized in terms of entrapment efficiency, particle size, shape, and *in vitro* release. Subsequently, the improved niosomal dispersions were employed to formulate gels, which underwent analysis to evaluate their visual properties, pH, and rheological behavior. Stability study was also conducted.

Results: Total 15 formulations were prepared, out of which 3 formulations F3, F9 and F15 were found to exhibit maximum entrapment efficiency. These formulation were having particle size 260.1 nm, 272.3 nm and 226.3 nm respectively. *In vitro* drug release was found to be maximum in F9 formulation. The release was found to be dose-dependent across all formulations, with regression values between 0.97 and 0.99, confirming first-order release kinetics. FTIR spectra indicated the absence of any drug-cholesterol-nonionic surfactant interaction in the formulation. The niosomal gel formulations exhibited optimal performance when stored within the temperature range of 4 to 8 °C.

Conclusion: This investigation demonstrates the utility of the thin film hydration technique in effectively incorporating poorly water-soluble medications such as azelaic Acid (AA) into niosomes, resulting in high entrapment efficiency. These findings suggest that niosomes containing AA, when topically applied as a gel, have the potential to be an efficacious treatment for acne.

Keywords: Azelaic acid, Niosomes, Thin film hydration, Topical gel, Sustained release, Entrapment efficiency

© 2023 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (https://creativecommons.org/licenses/by/4.0/)
DOI: https://dx.doi.org/10.22159/ijap.2023v15i5.48593. Journal homepage: https://innovareacademics.in/journals/index.php/ijap

INTRODUCTION

Acne, a prevalent skin condition affecting over 17 million individuals worldwide [1], is primarily caused by Propionibacterium acnes, a resident bacterium in the pilosebaceous unit, as well as the secretion of inflammatory mediators by the follicles and dermis [1]. During adolescence, acne commonly appears on the face, chest, and back due to an increase in sebaceous gland size triggered by elevated adrenal androgen levels [2]. The formation of inflammatory papules, pustules, and nodules can arise from micro-comedones, which occur when follicles become obstructed by sebum and desquamated epithelial cells. Acne is categorized into three main types: comedonal acne, mild inflammatory acne, and inflammatory acne. Comedonal acne represents the initial clinical stage, characterized by non-inflammatory comedones present in the central forehead, chin, nose, and paranasal areas [4, 5]. Acne commonly emerges during puberty or early adolescence and is attributed to excessive sebum production and abnormal epidermal desquamation. Mild inflammatory acne follows the initial non-inflammatory comedonal phase, characterized by the presence of a few comedones along with occasional papules or pustules [6]. Topical antibiotics, benzoyl peroxide, or a combination of both are effective in treating this type of acne, which predominantly affects women in their twenties. Inflammatory acne, the most prevalent form, manifests as comedones, papules, and pustules on the face and trunk. Treatment for inflammatory acne aims to prevent the escalation of underlying factors contributing to the condition. Research has shown that acne affects nearly 85% of individuals between the ages of 12 and 24, with a higher prevalence during adolescence. In a study by lucky *et al.*, the prevalence and severity of acne in adolescents were found to increase with the onset of puberty, and over 50% of boys aged 10-11 exhibited more than 10 comedones on their faces. Among young girls aged 8-12, the prevalence of acne ranged from 78% to 90%, with an increase observed with age. Acne also represents the most common skin disease among adults, as demonstrated by large-scale studies conducted in the United Kingdom, France, and the United States. Multiple pathogenic factors contribute to the development of acne, including hormonally-controlled sebum overproduction, follicular hyperkeratosis, microbial flora variation, immunological processes, and inflammation [7]. Seborrhea and increased keratinization of the follicular epithelium, promoting rapid Propionibacteria proliferation, have been associated with perifollicular inflammation [8]. Furthermore, inflammation resulting from and contributing to other pathogenetic factors plays a significant role [9]. Acne vulgaris affects tens of millions of individuals worldwide, and long-lasting inflammation can manifest in various forms, including comedones, papules, pustules, and nodules [10]. The colonization of sebaceous glands by Propionibacterium acnes (P. acnes) bacteria, leading to sebum overproduction, is a prominent cause of sebaceous gland inflammation. Topical medications such as retinoids, benzoyl peroxide, antibiotics, and azelaic acid are commonly used for acne treatment [11, 12]. Niosomes, a novel drug delivery system, have gained attention due to their potential benefits. Niosomes are composed of non-ionic surfactants, vesicles aimed at prolonging drug release time, improving stability, and enhancing bioavailability [4]. This study aimed to develop and evaluate niosomes loaded with azelaic acid (AA) for sustained drug release, aiming to alleviate the challenges associated with topical administration methods.

MATERIALS AND METHODS

Materials

Azelaic acid was obtained as a gift sample from East West Pharma, Haridwar (Uttarakhand). Cholesterol was purchased from SD Fine Pvt. Ltd, carbopol 940, sodium chloride, disodium hydrogen phosphate, potassium dihydrogen phosphate, chloroform, sorbiton monolaurate, sorbiton monopalmitate, sorbiton monostearate and methanol were purchased from Spak Orgochem Pvt. Ltd. All other ingredients used were of analytical grade.

Methods

Preparation of phosphate buffered saline (PBS) PH 7.4

The phosphate buffer saline solution contains 2.38 g of disodium hydrogen phosphate, 0.19 g of potassium dihydrogen phosphate, and 8.0 g of sodium chloride dissolved in distilled water.

Compatibility tests for drug excipients

FT-IR spectroscopy was used to obtain spectra of both pure drugs and drugs combined with excipients.

Standard curve for azelaic acid

Stock solution of azelaic acid was prepared. Phosphate-buffered saline (pH 7.4) was added to bring the volume back up to 100 ml after 10 ml was withdrawn using a pipette. This solution was divided into aliquots and subsequently diluted to get final concentrations of 2, 4, 6, 8, and 10 µg/ml. Absorbance at 225 nm was measured in a solution of pH 7.4 phosphate-buffered saline containing a trace of methanol using a UV-Visible Spectrophotometer (Shimadzu). Absorbance versus concentration was plotted to get the standard curve.

Formulation of azelaic acid niosomes

Niosomal formulations were developed via thin-film hydration method. Aloe vera gel was also incorporated in the formulation to reduce skin irritation produced by azelaic acid [11]. The drug, non-ionic surfactant (Span 20, 40, 60), and cholesterol were dissolved in a solvent combination (Chloroform: Methanol 2:1), and the resultant solution was clear (table 1). By evaporating the solution at 60 °C, 20-25 mm of mercury in a vacuum, and 100 revolutions per minute in a 1000 ml rotating flask, a uniformly thin dry layer may be created. Subsequently, this clear solution was subjected to evaporation at 60 °C under reduced pressure (20-25 mm of mercury) in a rotary evaporator to create a uniformly thin, dry layer. After the flask cooled down to room temperature, 20 ml of distilled water was added, and gentle agitation at 50 rpm raised the temperature to 60 °C. At this point, aloe vera gel was incorporated into the mixture to reduce the side effects associated with the use of azelaic acid. The rehydration process allowed for the formation of a niosomal suspension containing azelaic acid and aloe vera gel. Finally, the niosomal suspension was carefully sealed to maintain its integrity and stored in a refrigerated condition for further evaluation.

Table 1: Formulation code of niosome

Formulation code	Non-ionic surfactant	Drug+aloe vera gel: surfactant: cholesterol: (µ mole)
F1	SPAN 20	1:1:1
F2		1:2:1
F3		1:3:1
F4		1:4:1
F5		1:5:1
F6	SPAN 40	1:1:1
F7		1:2:1
F8		1:3:1
F9		1:4:1
F10		1:5:1
F11	SPAN 60	1:1:1
F12		1:2:1
F13		1:3:1
F14		1:4:1
F15		1:5:1

1 stand for 25 µmol

Optimization of process-related variables

The first parameter examines how hydration time impacts the characteristics of niosomal formulations. Centrifugation was performed to determine the entrapment efficiency and vesicle production after hydrating the formulations for 30, 60, and 90 min. The results showed that longer hydration durations lead to a higher degree of medication encapsulation, as evidenced by smaller vesicle sizes. Moving on to the second parameter, the influence of the evaporator flask's volume and rotating speed on the uniformity and consistency of the niosomal film was investigated. Niosomal compositions was spinned at 50, 100, and 150 rpm while visually evaluating their appearance. Our findings reveal that higher rotational speeds result in thinner and more uniform films, whereas lower speeds yield thicker and less uniform films. For the third parameter, the impact of sonication time on the niosomal formulations was studied. The formulations was subjected to ultrasonic vibrations for 1 to 5 min and determine the entrapment efficiency. Our study demonstrates that longer sonication periods lead to higher entrapment efficiency, indicating a greater level of drug encapsulation in the niosomes. Moving to the fourth parameter, the effects of osmotic stress on the niosomal formulations was studied. After incubating the formulations in hypertonic, isotonic, and hypotonic solutions, the vesicle size was measured. The results indicate a significant increase in vesicle size after exposure to hypertonic and hypotonic solutions, while the isotonic solution has no effect. This suggests that niosomes respond to tonicity variations by expanding or contracting.

Characterization of niosomes

Particle size analysis

A Malvern zeta sizer was used to measure the average vesicle size of the niosomes. The niosomal solution was diluted and placed in a cuvette with an appropriate blank.

Drug content analysis

Niosomes were lysed in 50% n-propanol to assess the concentration of the drug in the final formulation. Niosomal solution was prepared by adding a suitable amount of 50% n-propanol and vigorously shaking the mixture until the vesicles were completely lysed, at which point 1 ml was pipetted out. The absorbance of the diluted solution was determined using a UV-Visible Spectrophotometer at 225 nm. Adding 10% methanol to regular salt water yields a phosphate-buffered saline solution (pH 7.4). A combination of inert excipients was used as the inactive component of the niosomal suspension.

Estimation of entrapment efficiency

To evaluate the entrapment efficiency of the formulations, we first diluted a 1 ml solution to 10 ml with distilled water and then centrifuged the niosomes and the unentrapped drug at 15,000 rpm for 60 min at 4 c. using a UV-Visible Spectrophotometer with the wavelength set to 225 nm, the concentration of free medication in the supernatant was calculated. Drug entrapment within niosomes was determined using the formula.

$$\% \text{ Drug entrapment} = \frac{(\text{Total drug- Drug in supernatant liquid})}{\text{Total drug}} \text{X } 100$$

***In vitro* release study**

In vitro drug release analysis was done to study drug release profile. After free medication was eliminated, a glass tube's end was sealed with a dialysis membrane to create a niosomal preparation. The receptor compartment was a beaker containing 100 ml of phosphate buffered saline pH 7.4 that was put over the tube's open end. The receptor medium was kept at 37 °C and 100 rpm of agitation using a magnetic stirrer.

A 5 ml sample was taken at regular intervals and promptly swapped out for new PBS buffer, pH 7.4. In this investigation, we used a continuous sink condition. A UV-Visible spectrophotometer, with the wavelength set at 225 nm, was used to examine the samples.

Scanning electron microscopy

Scanning electron microscopy was used for measurement of diameter of vesicle membranes (HITACHI S-150). The cover slip of the specimen stub was used to collect a little amount of niosomes suspension. A layer of carbon and subsequently a layer of gold vapor was applied using a Hitachi vacuum evaporator, model HITACHI S 5 GB. Examined the materials and took photos using a scanning electron microscope at 15 kV.

Zeta potential analysis

Niosome stability was evaluated by investigating its colloidal characteristic using zeta potential analysis. The vesicle surface charge is thought to be reduced during aggregation due to the ions in solution acting as a shield. The Zeta potential may be used to get a rough idea of the surface charge of a vesicle by measuring the electrophoretic mobility of its particles.

Formulation of niosome loaded azelaic acid gel

Carbopol 940 (1.5%), Glycerol (10%), Triethanolamine (q. s.), and distilled water up to 15g were used to make the gel base. The promising niosome suspension (a formulation of niosomes prepared using the optimised ratio of surfactants) and azelaic acid equivalent to 2 percent w/w was infused into the gel base.

Evaluation of niosomal gel

This research looked at the aesthetics, pH, viscosity, content homogeneity, and entrapment effectiveness of niosomal gels. The gel's clarity, colour, consistency, and possibility for contamination were all evaluated visually. A digital pH metre was used to determine the gel dispersion's pH value. To determine the ultra-viscosity, a programmed Brookfield DV III ultra-viscometer was used. The gel's drug concentration and content uniformity were analysed using a UV/visible spectrophotometer. Centrifuging the gel and evaluating the free drug concentration in the supernatant using a UV/visible spectrophotometer allowed us to determine the trapping effectiveness of the gel. The amount of medication encapsulated by the niosomes was then determined.

***In vitro* drug diffusion study**

In vitro drug diffusion studies used a dialysis membrane. The dialysis membrane was connected to one end of a glass tube with niosomal gel containing 10 mg of the drug. This room served as the donor's freezer. A beaker holding 100 ml of phosphate buffered saline pH 7.4 served as the receptor compartment, which was placed over the tube's open end. Using a magnetic stirrer, the receptor media was maintained at 37 °±2 °C with agitation at 100 rpm. At the designated interval, a 5 ml sample was withdrawn and immediately replaced with a fresh PBS buffer, pH 7.4. The sink condition persisted throughout the trial. The acquired samples were analysed at 225 nm in a UV-Visible spectrophotometer.

Stability studies

The best niosomal formulations were subjected to stability testing, during which changes in physical attributes, entrapment efficiency, and drug content were tracked as a function of temperature. Two millilitre samples were taken every 15 d from niosomal dispersions kept at 2-8 °C and at room temperature (30±2 °C), yielding 45 millilitres in total. After dissolving the vesicles in 50% n-propanol, the samples were analysed by spectrophotometry at max 225 nm.

RESULTS AND DISCUSSION

Drug excipient compatibility studies

Through capturing the FT-IR spectra, looked at the potential for interactions between the drug and the excipients (cholesterol, nonionic surfactant). Drug and formulation FT-IR spectra (F3 20-3, F9 40-4, and F15 60-5) are shown graphically.

Standard curve for azelaic acid

Azelaic acid's standard curve was prepared using UV spectrophotometry. The drug's absorbance at 225 nm was determined in phosphate-buffered saline (pH 7.4) containing a trace amount of methanol. Fig. reports the results.

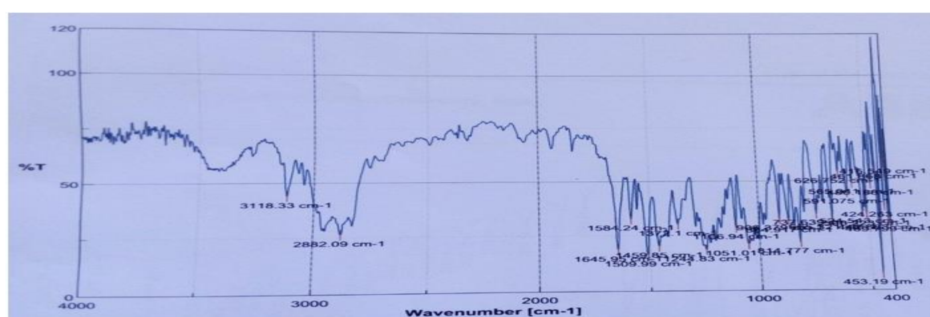


Fig. 1: FT-IR spectra of azelaic acid

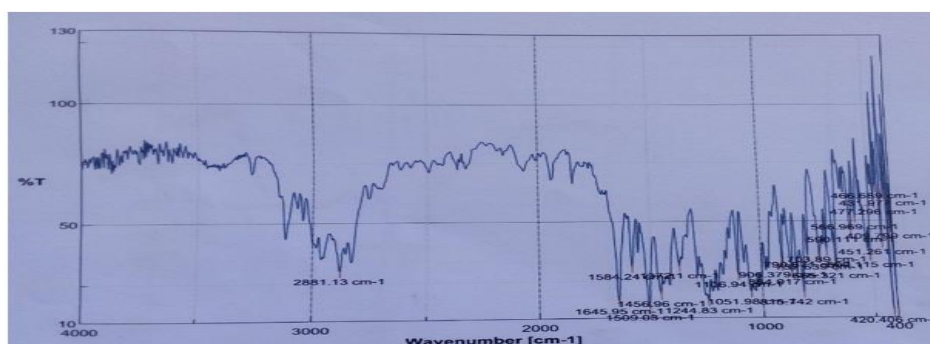


Fig. 2: FT-IR spectra of azelaic acid with Span 20, comparing the spectra of unloaded and loaded niosomes, it is established that there is no significant shifting or loss of functional peaks

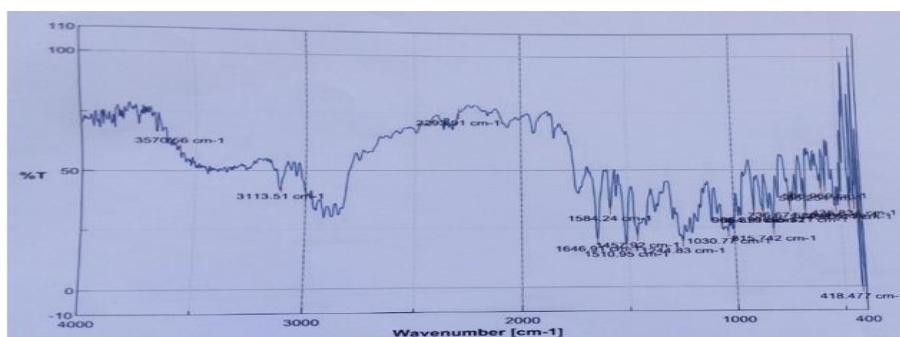


Fig. 3: FT-IR spectra of azelaic acid with span 40, the spectra of both unloaded and loaded niosomes show that the drug peaks are present and unaltered

Fig. 4: FT-IR spectra of azelaic acid with Span 60, from comparing the spectra of unloaded and loaded niosomes, it is clear that there is no significant difference in peak position or functional loss

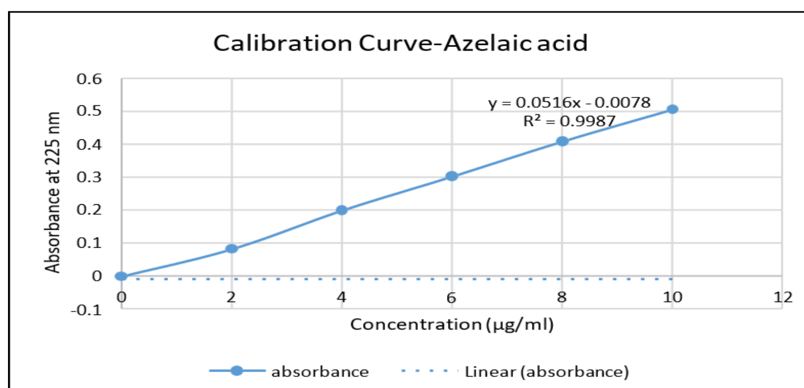


Fig. 5: Standard curve of azelaic acid in PBS pH 7.4, azelaic acid's standard curve was linear from 2 to 10µg/ml, with a starting point at the origin, when measured in PBS at a pH of 7.4. Beer-Lambert law can be applied to this curve with ease

Drug content and entrapment efficiency

Table 2: Drug content and entrapment efficiency of azelaic acid niosome

Formulation code	Drug content (% w/w)	Entrapment efficiency (% w/w)
F1 20-1	94.64±0.32	41.7±0.11
F2 20-2	93.41±0.12	52.1±0.74
F3 20-3	95.22±0.05	56.1±0.10
F4 20-4	91.73±0.09	46.2±0.24
F5 20-5	97.7±0.14	43.2.±0.03
F6 40-1	94.06±0.24	51.7±0.07
F7 40-2	87.61±0.17	59.1±0.09
F8 40-3	95.37±0.02	65.3±0.42
F9 40-4	88.81±0.12	72.3±0.26
F10 40-5	92.31±0.15	69.2±0.35
F11 60-1	98.44±0.20	51.8±0.41
F12 60-2	97.57±0.07	52.8±0.16
F13 60-3	95.81±0.03	56.21±0.08
F14 60-4	94.64±0.18	56.6±0.10
F15 60-5	99.6±0.08	60.2±0.14

Data presented as mean±SEM (n=3)

The formulations' entrapment efficiencies ranged from 41.7% to 72.1%. The F3 20-3 formulation had an entrapment efficiency of 56.1%, the F9 40-4 formulation had 72.3%, and the F15 60-5 formulation had 60.2%. Niosomes prepared using the Span 40 formulation had the maximum entrapment efficiency, followed by those prepared using the Span 60 formulation. One of them is that Span 40 has a better HLB value than Span 60. From Span 40's 6.7 to Span 60.15's 4.7 HLB, entrapment efficiency fell. Although Span 20 had the highest HLB value, 8.6, its entrapment efficiency lagged below that of the other two formulations. A disparity in the phase transition temperature may be the reason. Trapping effectiveness increases with increasing amounts of non-ionic surfactants. Span 40 showed the greatest entrapment effectiveness of the studied surfactants, followed by Span 60 and Span 20.

Span 40>Span 60>Span 20

In vitro release study

An *in vitro* release study of azelaic acid niosomes was conducted to determine how much of the drug was really released after 24 h. Dialysis membranes were placed in a tube-beaker arrangement with phosphate-buffered saline (PBS) at pH7.4 and 10% methanol to test the diffusion of the solution. The results revealed that the cumulative percent drug release at 24 h increased from 65.77 percent for F1 20-1 to 69.43 percent for F2 20-2 and 82.21 percent for F3 20-3 in the formulations with lower surfactant ratios. F4 20-4 and F5 20-5 had a release of 73.99 and 64.14 percent, respectively, however the release progressively decreased with increasing surfactant ratios. F6 40-1 from the Span 40 series had a 72.97 percent cumulative drug release after 24 h. The percentage was higher for the formulation F7 40-2 (74.72 percent), F8 40-3 (72.58 percent), and F9 40-4 (82.69 percent), but significantly lower for F10 40-5. (7.96 percent). When comparing the Span 60 niosomes, the F11 40-1 (57.45%), F12 60-2 (63.25%), and F13 60-3 (67.25%) exhibited the greatest cumulative percent drug release after 24 h (76.68 percent). The findings suggest that the surfactant ratio is related to the rate of drug release from niosomal formulations, with higher ratios leading in slower drug release over time, falling from 63.96 percent for F14 60-4 to 58.47 percent for F15 60-5. The Span 40 series was deemed more effective in dispensing medicine than the Span 60 series. Niosomes are proved to be effective a delivery system that allows for the regulated and prolonged release of the medicine [12].

Particle size

The mean particle size of F3, F9 and F15 preparation were found to be 260.1 nm, 272.3 nm, and 226.3 nm respectively.

Kinetics of drug release

In vitro release data applied to numerous kinetic models predicted the mechanism of drug release from niosomal formulations prepared with different nonionic surfactants.

A regression coefficient (r2) was determined using the information on drug distribution.

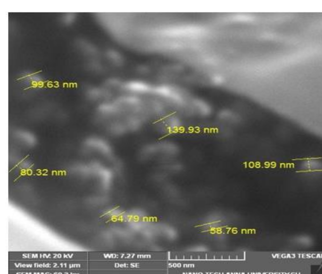
Table 3: Drug release kinetics

	Formulation code	F3 20-3	F9 40-4	F15 60-5
Zero order	R2	0.966	0.976	0.95
First order	R2	0.985	0.97	0.991
Higuchi model	R2	0.949	0.956	0.936
Korsemeyer peppas	R2	0.975	0.994	0.99
	N	0.75	0.771	0.937
Hixson crowell	R2	0.996	0.993	0.989

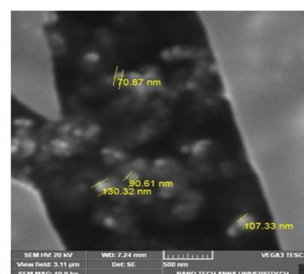
The release was found to be dose-dependent across all formulations, with R2 values between 0.97 and 0.99, confirming first-order kinetics. Azelaic acid was revealed to be diffusely controlled released from niosomes, with a release rate proportional to the square root of time.

Consistent with the anomalous Non-Fickian type diffusion and the Super case-II report, we find that the n value for the korsemeyer-peppas model for azelaic acid niosomal formulation ranges from 0.750 to 0.937. First-order release, the korsemeyer-peppas model, and the Higuchi model are all consistent with the observed release profile of azelaic acid from niosomes. Niosomes enhance medication solubility, permit longer release, and decrease the frequency of administration and related negative effects by encapsulating hydrophobic medicines like azelaic acid [13, 14].

a) Span 20 (F3 20- 3)



b) Span 60 (F9 40-4)



c) Span 60 niosomes (F15 60-5)

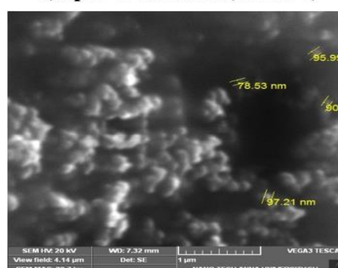


Fig. 6: Scanning electron microscopic images of azelaic acid niosomes

Scanning electron microscopy

The SEM pictures showed the improved niosomal formulations. These fig. illustrate our findings. Niosomes loaded with azelaic acid had a spherical form and measured an average of 260 nm in size, according to scanning electron microscopy.

Formulation of azelaic acid niosomal gel

Carbopol 940 was used as a gelling agent in azelaic acid niosomal gel formulations with an ideal ratio of the surfactants, extending the drug's residence time at the site of absorption through contact with the mucosa due to its hydrophilic nature and bio-sticky qualities. The gel was evaluated for appearance, pH, viscosity, and drug content, in addition to the *in vitro* drug diffusion studies. The F15 60-5 formulation provided the highest possible entrapment efficiency. The higher phase transition temperature of Span 60 might be the reason.

In vitro drug diffusion studies

In vitro drug diffusion study of azelaic acid niosomal gel was conducted using phosphate buffered saline (PBS) at pH 7.4 and a tube-beaker assembly with an open end as the diffusion medium and dialysis membrane. Tables and charts are used to visually display data.

Stability studies of azelaic acid niosomal gel

Three distinct azelaic acid gel formulations (F3 20-3, F9-40-4, and F15-60-5) were stored for 45 d at 4 °C to 8 °C (refrigeration temperature) and 25 °C±2 °C by ICH (International Conference on Harmonization) guidelines.

Table 4: The pH, viscosity, and drug content of gel formulations

S. No.	Formulation code	Viscosity	Entrapment	Drug content
01	F3	8320±0.225	52.4±0.225	98.13±0.14
02	F9	8256±0.562	63.8±0.558	96.10±0.25
03	F15	8675±0.551	65.2±0.789	94.34±0.35

Data presented as mean±SEM (n=3)

Table 5: *In vitro* release of azelaic acid niosomal gel in the optimized ratio of surfactants

Time (H)	Plain azelaic acid gel	F15 60-5
0	0	0
1	5.96	4.77±0.21
2	8.9	13.04±0.78
3	15.97	20.4±0.02
4	19.73	26.49±0.04
5	22.84	32.41±0.85
6	25.86	37.56±0.22
7	28.78	42.89±0.22
8	34.79	47.07±0.54
9	40.84	50.52±0.36
10	45.72	54.38±0.56
11	47.76	59.02±0.52
12	49.81	63.49±0.22
24	60.87	75.59±0.23

Data presented as mean±SEM (n=3)

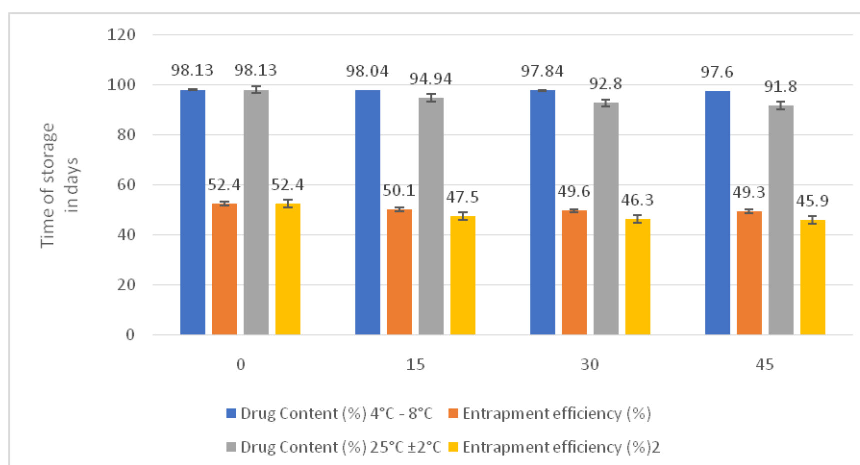


Fig. 7: Stability study of azelaic acid niosomal gel formulation F3 20-3 at different temperature, Error bars are represented as mean±SEM (n=3)

The drug entrapment efficiency in the niosomal gel was determined immediately after production and then every 15 d for 45 d. Heating the vesicles to 4 degrees celsius resulted in the lowest drug release. This might be because the phase shift of the surfactant and lipid causes vesicle leakage at higher storage temperatures. That's why 4-8 degrees celsius is a good range for storing niosomes. Niosomes may be more stable when embedded in a gel matrix, which prevents them from aggregation. Niosomal gel may have a reservoir effect on the skin, leading to increased medication skin retention. Niosomal gel compositions were shown to be most stable when stored between 4 and 8 degrees celsius, as determined by stability study.

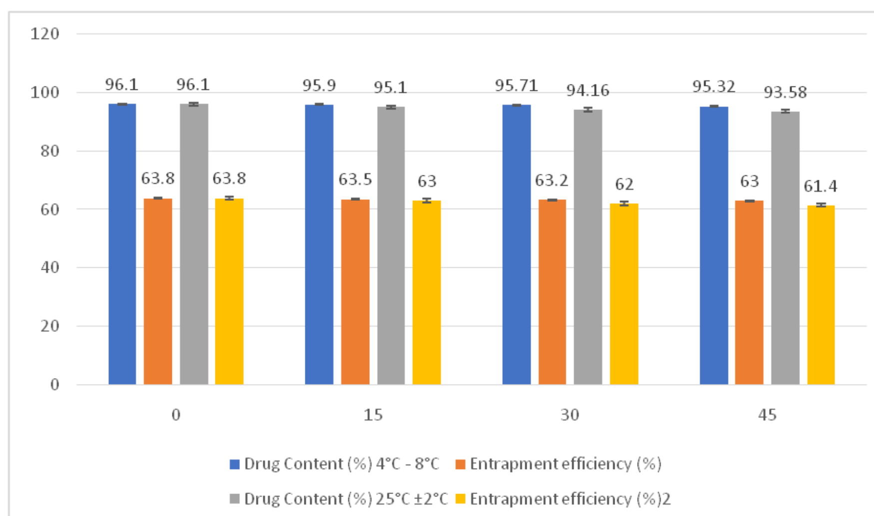


Fig. 8: Stability study of azelaic acid niosomal gel formulation F9 40-4 at different temperature, error bars are represented as mean±SEM (n=3)

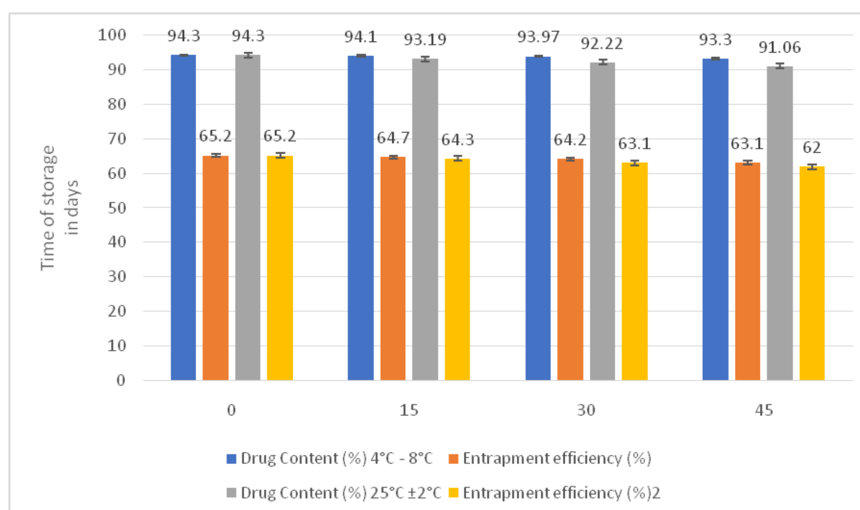


Fig. 9: Stability study of azelaic acid niosomal gel formulation F15 60-5 at different temperature, error bars are represented as mean±SEM (n=3)

CONCLUSION

This research demonstrates the successful development of a niosomal gel formulation for sustained-release delivery of azelaic acid, addressing the need for an effective and well-tolerated anti-acne treatment. The thin film hydration technique proved to be a viable approach for encapsulating the hydrophobic azelaic acid within niosomes with high entrapment efficiency. Acne sufferers will have a better quality of life thanks to this research since it paves the way for the creation of safer and more effective treatments.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

Both authors have contributed equally.

CONFLICT OF INTERESTS

The authors have no conflicts of interest regarding this investigation.

REFERENCES

1. Fox L, Csongradi C, Aucamp M, du Plessis J, Gerber M. Treatment modalities for acne. Molecules. 2016 Aug 13;21(8):1063. doi: 10.3390/molecules21081063, PMID 27529209, PMCID PMC6273829.
2. Barros BS, Zaenglein AL. The use of cosmeceuticals in acne: help or hoax? Am J Clin Dermatol. 2017 Apr;18(2):159-63. doi: 10.1007/s40257-016-0249-6, PMID 28063095.
3. Sahni K, Singh S, Dogra S. Newer topical treatments in skin and nail dermatophyte infections. Indian Dermatol Online J. 2018 May-Jun;9(3):149-58. doi: 10.4103/idoj.IDOJ_281_17. PMID 29854633, PMCID PMC5956860.
4. Walocko FM, Eber AE, Keri JE, Al-Harbi MA, Nouri K. The role of nicotinamide in acne treatment. Dermatol Ther. 2017 Sep;30(5). doi: 10.1111/dth.12481. PMID 28220628.
5. Vyas A, Kumar Sonker A, Gidwani B. Carrier-based drug delivery system for treatment of acne. Scientific World Journal. 2014 Feb 9;2014:276260. doi: 10.1155/2014/276260, PMID 24688376, PMCID PMC3934386.
6. Shahmoradi Z, Iraji F, Siadat AH, Ghorbaini A. Comparison of topical 5% Nicotinamid gel versus 2% clindamycin gel in the treatment of the mild-moderate acne vulgaris: a double-blinded randomized clinical trial. J Res Med Sci. 2013 Feb;18(2):115-7. PMID 23914212, PMCID PMC3724370.
7. Kaufman BP, Aman T, Alexis AF. Postinflammatory hyperpigmentation: epidemiology, clinical presentation, pathogenesis and treatment. Am J Clin Dermatol. 2018 Aug;19(4):489-503. doi: 10.1007/s40257-017-0333-6, PMID 29222629.
8. Taherzade SD, Rojas S, Soleimannejad J, Horcajada P. Combined cutaneous therapy using biocompatible metal-organic frameworks. Nanomaterials (Basel). 2020 Nov 25;10(12):2296.

doi: 10.3390/nano10122296, PMID 33255580, PMCID PMC7760737.
9. Hu S, Laughter MR, Anderson JB, Sadeghpour M. Emerging topical therapies to treat pigmentary disorders: an evidence-based approach. J Dermatolog Treat. 2022 Jun;33(4):1931-7. doi: 10.1080/09546634.2021.1940811. PMID 34114938.
10. Babbush KM, Babbush RA, Khachemoune A. Treatment of melasma: a review of less commonly used antioxidants. Int J Dermatol. 2021 Feb;60(2):166-73. doi: 10.1111/ijd.15133. PMID 32815582.
11. Hekmatpou D, Mehrabi F, Rahzani K, Aminiyan A. The effect of aloe vera clinical trials on prevention and healing of skin wound: a systematic review. Iran J Med Sci. 2019 Jan;44(1):1-9. PMID 30666070, PMCID PMC6330525.
12. Liu H, Yu H, Xia J, Liu L, Liu GJ, Sang H. Topical azelaic acid, salicylic acid, nicotinamide, sulphur, zinc and fruit acid (alpha-hydroxy acid) for acne. Cochrane Database Syst Rev. 2020;5(5):CD011368. doi: 10.1002/14651858.CD011368.pub2. PMID 32356369.
13. Li N, Su Q, Tan F, Zhang J. Effect of 1,4-cyclohexanediol on percutaneous absorption and penetration of azelaic acid. Int J Pharm. 2010 Mar 15;387(1-2):167-71. doi: 10.1016/j.ijpharm.2009.12.025. PMID 20025951.
14. MS, Buddha S, Kumari PVK, Rao YS. Proniosomes: a vesicular drug delivery system. Int J Curr Pharm Sci. 2021 Nov 15;13(6):32-6.