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Nanoencapsulation of Licorice Extract as a Skin Anti-Inflammatory

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Abstract

Chronic inflammatory diseases such as lupus are commonly managed using Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and corticosteroids; however, these medications often cause multiple adverse effects, including skin dryness, itching, abnormal discoloration, gastrointestinal discomfort, loss of appetite, and blurred vision. In recent years, researchers have sought alternative therapeutic strategies with fewer side effects by combining traditional and modern medicine. Licorice (Glycyrrhiza glabra) extract, owing to its strong anti-inflammatory and anti-pruritic activities as well as its low toxicity, has shown promise as a natural therapeutic agent for managing inflammatory and autoimmune conditions. In the present study, nanotechnology was employed to encapsulate licorice extract in order to improve its stability and therapeutic efficiency. The extract was prepared by maceration and concentrated, followed by niosomal encapsulation using the thin-film hydration method. The morphology and stability of the synthesized noisome were analyzed using Scanning Electron Microscopy (SEM) and a Zeta sizer. The Encapsulation Efficiency (EE), determined from the supernatant after centrifugation, was found to be 98.64%, indicating high loading capacity. The resulting formulation exhibited satisfactory stability after one month of storage. Overall, the thin-film hydration method proved to be an efficient approach for the encapsulation of herbal extracts and niosomal carriers, due to their structural similarity to biological membranes, demonstrating great potential for targeted and sustained delivery of licorice extract as a skin anti-inflammatory agent.

Keywords: Niosomal encapsulation, Licorice extract, Anti-inflammatory, Drug delivery.

1 | Introduction

Chronic inflammatory diseases such as lupus erythematosus, rheumatoid arthritis, and psoriasis impose a considerable global health burden due to their long-term nature and complex pathophysiological mechanisms [1]. The conventional therapeutic regimen for these disorders primarily involves Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and corticosteroids, which effectively suppress inflammatory responses but

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are frequently associated with adverse effects, including gastrointestinal irritation, skin dryness, pruritus, hyperpigmentation, and visual disturbances [2]. Prolonged use of such medications can also lead to systemic toxicity, reduced patient compliance, and impaired quality of life [3], [4]. Therefore, the search for safer and more effective anti-inflammatory alternatives has become a central focus of pharmaceutical research.

In recent years, the integration of traditional herbal medicine with modern drug delivery technologies has gained considerable attention as a promising approach for developing natural therapeutic agents with improved efficacy and safety profiles [5]. Among the various medicinal plants, Glycyrrhiza glabra (licorice) has demonstrated potent pharmacological properties, including anti-inflammatory, antioxidant, antimicrobial, and anti-pruritic effects [6]. The principal bioactive constituents of licorice, such as glycyrrhizin, liquiritin, and glabridin, modulate pro-inflammatory cytokines and oxidative stress pathways, thereby contributing to its therapeutic potential in autoimmune and inflammatory skin conditions [7], [8]. However, the clinical application of licorice extract is limited by its poor solubility, chemical instability, and low bioavailability in biological systems [6–9].

Nanotechnology-based drug delivery systems have emerged as a powerful tool to overcome these challenges by enhancing the stability, solubility, and targeted delivery of bioactive compounds [7–9]. In particular, niosomes, which are nonionic surfactant-based vesicular carriers, offer advantages such as biocompatibility, chemical stability, low cost, and the ability to encapsulate both hydrophilic and lipophilic drugs [10–15]. Due to their structural similarity to biological membranes, niosomes facilitate efficient transdermal and intracellular drug delivery, making them suitable for dermatological applications [16].

Encapsulation of licorice extract within niosomal vesicles represents an innovative strategy to enhance its pharmacological performance and ensure sustained anti-inflammatory activity with minimal side effects. The thin-film hydration method, widely used for niosomal synthesis, allows for high Encapsulation Efficiency (EE) and controlled particle size distribution [17]. Therefore, the present study aimed to formulate and characterize niosomal nanocapsules containing licorice extract, evaluate their physicochemical properties, and assess their potential as a novel natural anti-inflammatory formulation for skin applications. This approach bridges traditional herbal medicine and modern nanotechnology, contributing to the development of safer and more effective therapeutic systems.

2 | Materials and Methods

2.1 | Preparation of Licorice Extract

Dried roots of licorice (Glycyrrhiza glabra, 50 g) were washed with distilled water, air-dried, and then finely powdered. The powdered material was macerated for 72 hours in a 140 mL mixed solvent system composed of 80 mL 96% ethanol, 40 mL propanol, and 20 mL distilled water to achieve maximum extraction of bioactive compounds. After maceration, the extract was filtered to remove plant residues and prepare it for solvent removal. The filtrate was concentrated using a rotary evaporator at 50 °C and 90 rpm until a viscous extract was obtained. The concentrated extract was stored at 4 °C until further use.

2.2 | Preparation of Licorice-Loaded Niosomal Nanocapsules

Niosomal nanocapsules containing licorice extract were prepared using the thin-film hydration method. Briefly, Span 60 and cholesterol, in a 1:1 molar ratio, were dissolved in a chloroform–methanol mixture (2:1, v/v) in a round-bottom flask. The concentrated licorice extract (prepared as described above) was subsequently added to the organic phase. The solvents were evaporated under reduced pressure using a rotary evaporator at 45 °C to form a thin lipid film on the inner wall of the flask. The dry film was hydrated with 20 mL of Phosphate-Buffered Saline (PBS, pH 7.4) at 60 °C for 1 h under gentle stirring to facilitate vesicle formation. The resulting suspension was sonicated for 5 min using a probe sonicator to reduce vesicle size

and ensure uniform dispersion. The prepared niosomal formulation was stored at 4 °C for further characterization.

2.3 | Determination of Encapsulation Efficiency

The EE of licorice extract within the niosomal nanocapsules was determined using the indirect method. The niosomal suspension was centrifuged at 15,000 rpm for 30 minutes at 4 °C to separate the free (unencapsulated) extract from the vesicles. The supernatant was carefully collected, and the concentration of unencapsulated licorice extract was quantified spectrophotometrically at 254 nm using a UV–Vis spectrophotometer (Shimadzu, Japan). The EE was calculated using the following equation:

$$\mathrm{EE}(\%) = \left(\frac{\text{Total amount of extract} - \text{Free extract}}{\text{Total amount of extract}}\right) \times 100.$$

All measurements were performed in triplicate, and the mean values were reported. This method provided an accurate estimation of the loading capacity and encapsulation performance, ensuring reliable evaluation of the niosomal formulation stability [18].

2.4 | In Vitro Drug Release Study

The in vitro release profile of licorice extract from niosomal nanocapsules was evaluated using the dialysis bag diffusion method. Briefly, the niosomal suspension containing licorice extract was centrifuged at 50,000 rpm for 30 minutes at 4 °C to remove any unencapsulated extract. The supernatant was discarded, and the pellet was washed once with distilled water to ensure complete removal of free drug. The washed pellet was then re-dispersed in 10 mL of PBS (PBS, pH 7.4). The resulting suspension was transferred into a pre-soaked dialysis bag (molecular weight cut-off: 12,000–14,000 Da), which was immersed in 100 mL of PBS maintained at 37 ± 0.5 °C under constant magnetic stirring. At predetermined time intervals (3, 5, 7, 9, 21, 24, 27, 30, and 48 h), 5 mL samples of the release medium were withdrawn and replaced with an equal volume of fresh PBS to maintain sink conditions. The concentration of licorice extract released was determined spectrophotometrically at 254 nm using a UV–Vis spectrophotometer (Shimadzu, Japan). The cumulative percentage of drug release was calculated and plotted as a function of time [10], [19].

2.5 | Morphological Analysis of Niosomal Nanocapsules Using Scanning Electron Microscopy

The morphology of the licorice-loaded niosomal nanocapsules was examined using Scanning Electron Microscopy (SEM). A small amount of the niosomal suspension was placed on a clean glass slide and allowed to air-dry at room temperature. The dried samples were then mounted on aluminum stubs using double-sided conductive carbon tape and coated with a thin layer of gold using a sputter coater to improve conductivity.

SEM imaging was performed at an accelerating voltage of 15 kV to observe the shape, surface characteristics, and approximate size of the niosomes. Micrographs were captured at various magnifications to assess the uniformity and structural integrity of the vesicles [11].

2.6 | Particle Size and Zeta Potential Analysis

The particle size distribution and zeta potential of the licorice-loaded niosomal nanocapsules were measured using a Zetasizer (Malvern Instruments, UK) at 25 °C. Before analysis, the niosomal suspension was appropriately diluted with distilled water to prevent multiple scattering effects and equilibrated for 2 minutes at room temperature.

Dynamic Light Scattering (DLS) was used to determine the mean hydrodynamic diameter and Polydispersity Index (PDI) of the vesicles. The zeta potential, which reflects surface charge and colloidal stability, was

measured using laser Doppler electrophoresis. All measurements were performed in triplicate, and the mean values were reported [13].

3 | Results and Discussion

3.1 | Encapsulation Efficiency Results

The EE of the prepared licorice-loaded niosomal formulation was found to be 98.64 %, indicating highly efficient entrapment of the bioactive compounds within the niosomal vesicles. This remarkably high EE value demonstrates the strong compatibility between the hydrophobic components of licorice extract and the lipid bilayer of niosomes. Such interaction promotes efficient drug entrapment and minimizes leakage during the hydration and sonication processes.

The high EE also suggests that the thin-film hydration method was effective in producing stable vesicles capable of incorporating a significant amount of the herbal extract. The result is consistent with previously reported findings for niosomal systems encapsulating plant-derived compounds [20–24].

Moreover, the formulation remained physically stable over a storage period of one month at 4 °C, with no noticeable phase separation or change in particle size, indicating good retention of the encapsulated extract. The obtained EE value of 98.64 % confirms that the developed niosomal carrier system is an excellent candidate for efficient delivery of licorice extract, providing high loading capacity and improved therapeutic potential for topical anti-inflammatory applications.

3.2 | Drug Release Results

The in vitro release profile of the licorice extract from the liposomal nanocarrier demonstrated a very slow and sustained release behavior, indicating a strong retention capability of the vesicular system. As shown in *Fig. 1*, only about 4% of the encapsulated licorice extract was released after 48 hours of incubation, confirming the high stability of the liposomal formulation and its strong interaction with the encapsulated phytoconstituents.

The minimal release observed over the 48 hours suggests that the liposomal bilayer effectively limited the diffusion of the extract molecules into the surrounding medium. This high retention capacity can be attributed to the lipid composition and the hydrophobic nature of certain bioactive components of the licorice extract, which promote stronger association within the liposomal membrane [25], [26].

Such a controlled and prolonged release pattern is desirable for topical and transdermal drug delivery, as it allows for a gradual and sustained availability of the active compounds, potentially reducing the frequency of application and improving therapeutic efficacy while minimizing side effects.

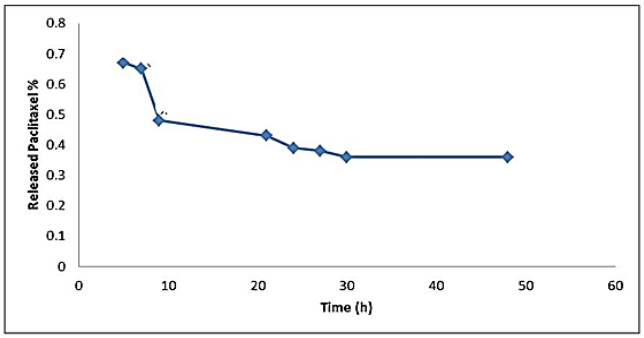


Fig. 1. Licorice extract release from liposomal nanocarriers after 48 h.

3.3 | Stability Evaluation of Licorice-Loaded Niosomal Nanocarriers

The stability of licorice extract-loaded niosomal nanocarriers was evaluated by measuring the zeta potential, particle size, and size distribution using a Zetasizer instrument. The results indicated that the prepared nanoparticles exhibited acceptable physicochemical stability under laboratory conditions. As shown in Table 1, the zeta potential value of the extract-loaded niosomes was recorded as -18.00 mV on the first day and 17.8 mV after 30 days of storage. This slight variation in surface charge suggests good electrostatic stability of the vesicles over time. It is well known that a higher absolute zeta potential value (either positive or negative) contributes to increased electrostatic repulsion between nanoparticles, thereby preventing their aggregation or coalescence. For comparison, the zeta potential of blank (drug-free) niosomes was found to be –13.4 mV, which is consistent with the expected lower surface charge due to the absence of bioactive components. The presence of licorice extract likely enhanced the surface charge, improving overall nanoparticle stability.

Table 1. Zeta potential values of licorice-loaded niosomal nanoparticles.

Sample	Day 1 (mV)	Day 30 (mV)
Licorice extract-loaded niosomal nanoparticles	–18.00	–17.8

According to *Table 2*, the average particle size of the niosomal suspension at the time of preparation was 345 nm, with a PDI of 0.2, indicating a narrow and uniform particle size distribution. After 30 days of storage, the particle size and PDI were measured as 343 nm and 0.2, respectively, showing no significant change. These results confirm that the niosomal formulation maintained a stable particle size and uniform distribution over time.

Table 2. Particle size and size distribution of licorice-loaded niosomal suspensions.

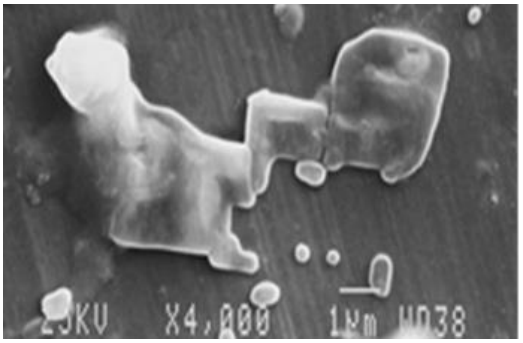
No.	Sample Description	Particle Size (nm)	PDI
1	Licorice-loaded niosomal suspension (Day 1)	345	0.2
2	Licorice-loaded niosomal suspension (Day 30)	343	0.2

Overall, it can be concluded that the licorice-loaded niosomal nanocarriers exhibited good physicochemical stability, and that optimized lipid composition combined with controlled pH conditions played a crucial role in maintaining particle size and surface charge. Indeed, when the pH of the dispersion medium remains within its optimal range, electrostatic repulsion among nanoparticles increases, thereby preventing aggregation and ensuring long-term stability of the niosomal system.

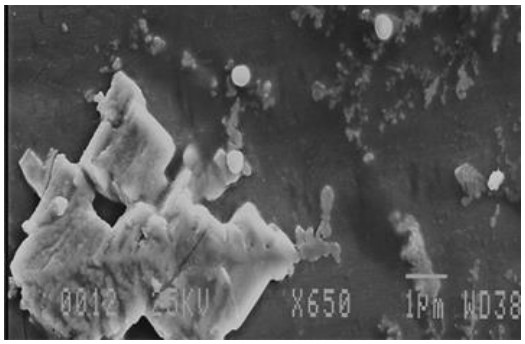
3.4 | Scanning Electron Microscopy Analysis (Morphological Characterization of Niosomal Capsules)

To examine the morphology of the capsules, the nanoparticles were separated from the suspension using a centrifuge at 50,000 rpm and subsequently dried using a lyophilizer. The morphology of the dried nanoparticles was then analyzed using a scanning electron microscope SEM [27–29].

Fig. 2 illustrates the morphological stability of the particles. The results showed that the more spherical the nanoparticles were, the higher their stability in terms of mass and heat transfer efficiency. Accordingly, the niosomal nanoparticles without the extract exhibited a more spherical and uniform shape, as observed in the images. This can be explained by the absence of the extract, which eliminates additional surface charges that could distort the spherical shape of the nanocarriers. In terms of particle size, the niosomal nanoparticles containing licorice extract had an approximate diameter of 300 nm, while the empty nanoparticles exhibited a smaller size of about 200 nm.



a.



b.

Fig. 2. SEM images of licorice extract–loaded; a. and blank, b. liposomal nanocapsules.

4 | Conclusion

In this research, licorice (Glycyrrhiza glabra) extract was successfully encapsulated into niosomal nanocarriers using the thin-film hydration method, aiming to enhance its physicochemical stability and therapeutic efficacy as a potential topical anti-inflammatory agent. The formulation process led to the formation of uniform, spherical, and smooth-surfaced nanocapsules, as evidenced by SEM micrographs, confirming successful vesicle formation and structural integrity. The EE (EE%) was found to be remarkably high at 98.64%, reflecting the strong affinity of the bioactive compounds of licorice for the lipid bilayer of niosomes. This high encapsulation capacity ensures maximum drug retention and minimizes premature leakage of the extract [30].

The zeta potential analysis revealed values of –18.00 mV on the first day and –17.8 mV after 30 days of storage, indicating excellent electrostatic stability and minimal particle aggregation over time. Furthermore, the particle size (345 nm) and PDI (0.2) remained almost unchanged after 30 days, confirming that the niosomal suspension maintained its physical stability and homogeneous size distribution under laboratory conditions. Such stability is crucial for ensuring reproducible drug delivery performance, as both particle size and surface charge directly influence skin penetration and drug release kinetics.

The in-vitro drug release profile demonstrated a sustained and controlled release pattern, with only about 4% of the encapsulated extract released after 48 hours, which highlights the strong entrapment capability of the niosomal matrix. This slow-release behavior can be attributed to the bilayered structure of the niosomes, which acts as a diffusion barrier, allowing for the gradual release of the active compounds. Sustained release not only improves therapeutic efficacy but also reduces dosing frequency and minimizes potential side effects associated with conventional anti-inflammatory therapies [31].

Taken together, these results confirm that niosomal nanocarriers represent a promising platform for the delivery of licorice extract and possibly other plant-based therapeutics. The optimized formulation demonstrated high EE, good morphological uniformity, strong zeta stability, and excellent drug retention

capacity. Moreover, the integration of traditional herbal medicine with nanotechnology provides a synergistic approach to developing modern, biocompatible, and safe therapeutic systems [32].

Therefore, the licorice-loaded niosomal formulation can be considered a potential alternative to conventional anti-inflammatory drugs, offering prolonged release, reduced systemic side effects, and improved patient compliance for the management of chronic inflammatory skin disorders. Further in vivo and clinical evaluations are recommended to validate its pharmacodynamic performance and safety profile for potential pharmaceutical and cosmeceutical applications.

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Data Availability

All data generated or analyzed during this study are included in this published article.

Conflicts of Interest

The author declares that there are no conflicts of interest relevant to the content of this article.

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