Al-Mustaqbal Journal of Pharmaceutical and Medical Sciences

Volume 3 | Issue 3 Article 2

2025

Green Pharmaceutical Systems: Alpha-Tocopherol Encapsulation in Nanostructured Lipid Carriers via Microwaves-Based Technique as Advanced Topical Drug Delivery Systems

Hayder Kadhim Drais
Department of Pharmaceutics, College of Pharmacy, Al-Mustaqbal University, Babil, Iraq, hayder.kadhim.drais@uomus.edu.iq

Mohammed A Albarki
Department of Pharmaceutics, College of Pharmacy, Al-Mustaqbal University, Babil, Iraq

Hayder Ridha-Salman
Department of Pharmacology, College of Pharmacy, Al-Mustaqbal University, Babil, Iraq

Ahmed Abbas Hussein
Department of Pharmaceutics, Baghdad College of Medical Sciences, Baghdad, Iraq

Ashraf Abbas Drais
Nursing Techniques Department, Babylon Technical Institute, Al-Furat Al-Awsat Technical University, Najaf, Iraq

ISSN: 2959-8974 – e-ISSN: 3006-5909

ORIGINAL STUDY

Green Pharmaceutical Systems: Alpha-Tocopherol Encapsulation in Nanostructured Lipid Carriers via Microwaves-Based Technique as Advanced Topical Drug Delivery Systems

Hayder Kadhim Drais [a,*], **Mohammed A Albarki** [a], **Hayder Ridha-Salman** [b], **Ahmed Abbas Hussein** [c], **Ashraf Abbas Drais** [d]

[a] Department of Pharmaceutics, College of Pharmacy, Al-Mustaqbal University, Babil, Iraq
[b] Department of Pharmacology, College of Pharmacy, Al-Mustaqbal University, Babil, Iraq
[c] Department of Pharmaceutics, Baghdad College of Medical Sciences, Baghdad, Iraq
[d] Nursing Techniques Department, Babylon Technical Institute, Al-Furat Al-Awsat Technical University, Najaf, Iraq

ABSTRACT

Alpha tocopherol (Vitamin E) is practically insoluble in water. It is important for skin health due to its many therapeutic actions, such as antioxidant, anti-inflammatory, and photoprotection. Therefore, the purpose of this study is to develop, prepare, and evaluate nanostructured lipid carriers (NLCs)-based hydrogels as a topical dosage form to improve stability and therapeutic activity of vitamin E. The microwave-based method prepared five lavender oil-based NLCs (LN1–LN5) formulations that were assessed thermodynamically and entered into characterization processes. Hydrogels formulations based on NLCs (LNG1–LNG5) were prepared and evaluated. All of the lavender oil-based NLC formulations (LN1–LN5) had suitable surface charge, a low polydispersity index, robust thermodynamic stability, and nanosized particles. Stable organoleptic qualities, reasonable pH and spreadability coefficient values, acceptable viscosity, and no erythemic reaction are all reflected in the evaluation procedures for NLCs- based hydrogels (LNG1–LNG5) formulations. According to the thermodynamic stability study and characterization processes, the lavender oil-based NLCs (LN1–LN5) formulations can be considered suitable nanocarriers for the delivery of various therapeutic agents. The vitamin E loaded in NLC-based hydrogels (LNG1–LNG5) formulations is a promising cosmetic product for protection against photoaging and chronological aging.

Keywords: Alpha tocopherol, Lavender oil, NLCs, Microwave-based method, Aging

1. Introduction

Multiple changes in cellular functions in the human body continue with age. These changes may lead to a reduction in the functioning of organic functions, and they appear clearly in the skin with the appearance of cracks and wrinkles, especially in the presence of factors that accelerate them. The skin is the external covering of the body. The skin primarily expects to safeguard individuals against ecological hostilities. Since it communicates with the climate, the skin assumes a critical part in securing the human body against microorganisms and unnecessary water misfortune [1, 2]. Beauty care product or cosmetics is substance or formulations planned to be put in touch with the different pieces of the human body epidermis, nails, lips, hair framework, and outside genital organs or with the teeth and the mucous layers of the oral hole with a view only or fundamentally to perfuming them, cleaning them, changing their

Received 2 September 2025; revised 9 December 2025; accepted 10 December 2025.
Available online 22 December 2025

* Corresponding author.
E-mail address: hayder.kadhim.drais@uomus.edu.iq (H. K. Drais).

https://doi.org/10.62846/3006-5909.1033

appearance or potentially amending stenches and additionally safeguarding them or keeping them looking great [3–5]. Antiaging beauty care products are a part of beauty care products that bargain with the elimination of maturing and wrinkle impact on skin. Aging is a collection of harm to macromolecules, cells, tissues, and organs. Two particular kinds of maturing: 1. Internal aging maturing caused mainly by hereditary qualities, breakdown of cell designs and cycles, diminished bone thickness, and hormonal changes. 2. External aging maturing is caused mainly by photoaging, smoking, facial expression, sleep position, and gravity. Antiaging agents such as antioxidant agents reduce the effects of aging on the skin, which helps maintain its freshness and vitality. Antioxidant agents decrease damage caused by free radicals, in this way forestalling weakness at the cell level. They repress inflammation, which prompts collagen consumption, and they offer insurance against photo harm and skin disease [5–7]. Vitamin E is a lipid-soluble antioxidant that is fundamental for the support of normal skin. Vitamin E is ordinarily given to the skin through the sebum. The effective application can likewise supply the skin with vitamin E and may give explicit vitamin E frames that are not accessible from the eating regimen. Vitamin E mostly reacts with reactive oxygen species as an antioxidant. Vitamin E is also capable of absorbing the energy produced by ultraviolet (UV) light. Consequently, it assumes significant parts in photoprotection, inhibiting UV-actuated free extreme harm to the skin. In the skin, vitamin E may also play related anti-inflammatory roles. Vitamin E suffers from degradation by photolysis and photooxidation after exposure to light [8–10]. Nano-structured lipid carriers (NLCs) are lipid-based nanocarriers that have emerged as drug delivery systems composed of liquid lipids and solid lipids for the delivery of different therapeutic agents. Numerous highlights, which these transporter frameworks show for dermal utilization of beauty care products and pharmaceutics, have been called attention. NLCs are made out of biodegradable lipids that show low poisonousness. The small size guarantees a nearby contact with the layer of stratum corneum and can expand much of the medication infiltrated into the skin. NLCs can improve the vitamin E stability against light sensitivity, oxidation, and hydrolysis [11–13]. Lavender oil, or Lavender Angustifolia, is a commonly used aromatic plant throughout the world that is a member of the Labiatae (Lamiaceae) family [15]. For millennia, lavender has been regularly employed as a herbal cure in traditional medicine. Many chemical components were found in the lavender oil, with linalool, linalyl acetate, α-pinene, limonene, 1,8-cineole, cis- and trans-ocimene, 3-octanone, caryophyllene, camphor, terpinene-4-ol, and linalyl acetate being the primary elements. It has been demonstrated that the anti-inflammatory properties of lavender essential oil are associated with its main constituents, linalool and linalyl acetate [16]. Additionally, several investigations have demonstrated the strong antioxidant, antimicrobial, and anxiolytic qualities of linalool and linalyl acetate. Linalool has been shown to enhance immune system performance, minimize inflammation, and fight against oxidative stress [17, 18]. When lavender oil-based NLCs combine with gelling agents results in a more attractive delivery system to deliver vitamin E safely across human skin [19, 20]. Therefore, the objective of this research was to develop, prepare, and evaluate NLCs-based hydrogel as a beauty care product for alpha tocopherol delivery.

2. Materials and methods

2.1. Materials

Alpha-Tocopherol, lavender oil and lauric acid, were purchased from Nanjing Duly Biotech Co., Ltd China. Triethanolamine, pH adjuster/neutralizer, ensures gel consistency and maintains skin-compatible pH, was purchased from Avon Chem, United Kingdom. Propylene glycol, tween 80 (nonionic surfactant/emulsifier), and carbopol 940 were purchased from Beijing Yibai Biotechnology Co., Ltd. China. All solvents and reagents that had been in the experiment were of analytical grade.

2.2. Methods

2.2.1. Preparation of lavender oil-based NLCs using microwaves-based technique

Vitamin E acts as a skin antioxidant — neutralizes free radicals, helping reduce premature aging, provides moisturizing and emollient properties, improving skin softness and supports skin barrier repair and healing.

Lauric acid is fatty acid with strong antimicrobial and surfactant properties (commonly found in coconut oil) helps improve skin penetration of active ingredients, contributes to emollient effect (softening skin). Lavender oil, act as natural essential oil with antimicrobial, anti-inflammatory, and soothing properties. Provides a pleasant fragrance (aromatic acceptability). Propylene glycol as humectant and enhances penetration of active compounds into the skin, tween 80 (nonionic surfactant / emulsifier), and Carbopol 940 as gelling agent Vitamin E, lauric acid and lavender oil were mixed using a magnetic stirrer for 5 minutes. The hydrophilic components which are distilled water tween 80 and propylene glycol were

Table 1. Concentrations of lavender oil-based NLCs (LN1-LN5) formulations and NLCs-based gel (LNG1- LNG5) formulations.

Code	Vitamin E (% w/w)	Lavender oil (% w/w)	L auric acid (% w/w)	Tween 80 and propylene glycol mixture 1:1 (% w/w)	Carbopol 940 (% w/w)	Distilled water up to (%w/w)
LNG1	1.8	3	1	30	0.5	100
LNG2	1.8	5	1	30	0.5	100
LNG3	1.8	7	1	30	0.5	100
LNG4	1.8	9	1	30	0.5	100
LNG 5	1.8	12	1	30	0.5	100

mixed using a magnetic stirrer for 5 minutes. The hydrophobic phase was mixed with the hydrophilic phase. The blend that prepared under 1000 rpm for 5 minutes of magnetic stirrer according to the amounts described in (Table 1). The mixture was inserted in a microwave device where rated microwave-power is 1050 W for 10–15 seconds, then a magnetic stirrer device at 1000 rpm for adequate time (seconds to minutes) until the feature of NLCs (LN1-LN5) was observed [20–23].

2.2.2. The preparation of NLCs-based gel

The hydrogel of carbomer 940 was prepared by adding 0.5% of the gelling agent in distilled water with stirring using an electric homogenizer add a few drops of triethanolamine to obtain a gel of pH around (4.7). The previously prepared NLCs (LN1-LN5) formulations were mixed with hydrogel and continuously slow stirred until clear NLCs-based gel (LNG1-LNG5) formulations were formed. The NLCs-based gel (LNG1-LNG5) formulations were stored in a tightly closed container at 25 ˚C temperatures for experimental processes [24–28].

2.3. Application of thermodynamic stability studies to the screening of lavender oil NLCs (LN1-LN5) formulations

The outcomes of the following experiments established the thermodynamic stability evaluation.

2.3.1. Centrifugation testing

Phase separation, creaming, and cracking were seen in the selected preparations after they were centrifuged for 30 minutes at 5000 rpm. The formulations chosen must show optimum stability, indicating that there shouldn't be any signs of phase separation, creaming, or cracking. The approved formulations were put through additional tests of thermodynamic stability. Three replicates of each measurement were generated [29].

2.3.2. Test of heating and cooling

It is used to demonstrate how heating and cooling affect the stability of lavender oil-based NLCs, with preparations needed to be held at 45 C and 0 C for a minimum of 48 hours for each temperature test. Three duplicates of each measurement were made [29].

2.3.3. Freeze-thaw experiment

This test was completed to expedite the assaying of lavender oil-based NLC formulations for stability. The formulations were exposed to two distinct temperatures (–21oC and 21oC) for a minimum of 24 hours. Three replicas of the metrics were done [29].

2.4. Characterization of lavender oil-based NLCs (LN1- LN5) formulations through determination of particle size, index of polydispersity (PDI), and zeta potential (ZP)

Particulate size, charge on the surface, and index of polydispersity (PDI) of globules of lavender oil-based NLCs (LN1- LN5) formulations have been determined by dynamic light scattering (DLS), a method that was made possible by Horiba Instrument, Ltd., Kyoto, Japan. When a beam of laser energy traverses a sample, the intensity of the scattered light varies over time due to the dispersed lipid-based nanocarriers traveling in a Brownian fashion. The readings obtained in three trials prove the astonishing accuracy of the method used [19, 29].

2.5. Atomic force microscopy (AFM)

For the most optimum formulation, AFM Angstrom Advanced Inc. AA3000 USA determined the nanocarrier morphology. A 100 MV/s scanning range was implemented. On an experimental glass slide, between two and three drops of nanostructured lipid carriers were applied, and outcomes were recorded after three hours [29].

2.6. Evaluation of hydrogel (LNG1–LNG5) formulations based on NLCs

2.6.1. Assessment of organoleptic

To ascertain the physical stability of medicinal preparations, organoleptic testing is crucial. For NLCs-based hydrogel (LNG1-LNG5) formulations, the appearance of colour, sense of smell, uniformity, and

syneresis can be examined at 0, 7, 14, 21, and 28 days. The information was acquired three times [19, 27].

2.6.2. Determination of pH

The stability of the formulation and skin compatibility can be predicted by this crucial characteristic. A ten-gram sample of the NLCs-based hydrogel (LNG1-LNG5) formulations, the digital pH meter was used to measure the pH. The ideal pH range for human skin is between 4.5 and 6.5. Three trials were carried out for the experiment [24, 27].

2.6.3. Measurement of spreadability

It was accomplished using two distinct glass slide pieces, each measuring 10 × 2.5 cm. A wooden foundation containing 0.5 g of NLCs-based hydrogel (LNG1-LNG5) formulations was fastened to the lower slide. When applied to the first glass slide, the second piece of glass was knotted to weigh 25 g, and it took 7.0 cm for the first glass slide to come free. The weight in grams and the length of time in seconds required to move a second glass slide were recorded, and Eq. (1) underneath can be employed to compute the propagation parameter:

$$S = M \times L/T \quad (1)$$

S, stands for spreadability, M, for weight which triggers the first slide, and L, for slide length.

T is the time it takes to fully separate two sides. Three trials were used for the study [19, 24].

2.6.4. Viscosity measurement

It is an essential criterion for analysis and novel formulation creation, as well as for evaluating pharmaceutical formulations. The viscosity of NLCs-based hydrogel (LNG1-LNG5) formulations was determined at 25 °C using a rotational digital viscometer from Biobase Meihua Trading Co., Ltd. with a spindle number (2). The rotational speeds that the samples were subjected to were 0.1, 0.3, 0.6, 1.5, 3, 6, 12, 30 and 60 rpm. Three trials were used to experiment [19, 24, 27].

2.6.5. Skin irritation study

The Al-Mustaqbal University ethics committee accorded the study ethical approval; the approval code used for the study was pha 3/2024 on 5.2.2024. For the skin fumbling test, a male rabbit weighing around 2.1 kg was utilized that had fasted. The experimental animals were allowed free access to water and were fed an appropriate diet. The hair has been removed from its skin and separated into five pieces, with each piece measuring about 4 cm × 2 cm. Every spot was then treated with 0.5 g of NLCs-based hydrogel (LNG1-LNG5) formulations, given twice a day. After conducting the test for 1, 24, 48, and 72 hours, the testing site was checked for any erythemic or swelling response. Based on edema, the response was assessed as 0, 1, 2, and 3 for no response, little irregular inflammation, hazy erythema, and substantial erythema, correspondingly [19].

2.6.6. Ex-vivo skin permeation study

Ex vivo study was achieved on male rabbit weighing around 2.1 kg. The study approval was taken from the institutional animal ethics committee in Al-Mustaqbal University College of Pharmacy where approval code was pha 3/2024 on 5.2.2024. The animal slayed and anatomize and hairless skin of abdominal region was surgically isolated and removed subcutaneous lipid carefully. The experimental skin was cut into pieces of 4 cm^2 (2 cm × 2 cm) to be biological barrier that was inserted between donor and receptor parts of Franz- diffusion cell. The volume of diffusion was 200 mL of phosphate buffered saline pH 7.4. Samples of NLCs-based hydrogel (LNG1-LNG5) formulations where 0.148 gram had been applied in the donor chamber. Samples were withdrawn from the receptor chamber at periodic time intervals and then analyzed for alpha-tocopherol amount that permeated across biological membrane. After each sample withdrawing, replenished with an equal taken volume of by fresh diffusion liquid immediately. The ultraviolet-visible spectrophotometer (Biobase Meihua Trading Co., Ltd) at 295 nm was used to achieve study [27, 29]. The test was performed in triplicate. The permeability coefficients were determined by the following Eq. (1).

$$M = \text{Peff S Cd tres} \quad (2)$$

Where:

M = is the amount of alpha-tocopherol absorbed.

Peff = is the effective permeability of alpha-tocopherol through the membrane.

Cd = is the initial concentration of alpha-tocopherol in the donor chamber.

tres = is the residence time of alpha-tocopherol in the biological membrane.

S = is the surface area of absorption.

2.7. Analytical statistics

The study's observations were the three experimental trials' mean and standard deviation (SD). With excel, the statistical assessment concluded. A statistical test known as one-way analysis of variance (ANOVA) was utilized and the significance threshold was kept at ($P \leq 0.05$) [19, 20].

3. Results

3.1. Characterization of lavender oil-based NLCs (LN1- LN5) formulations through determination of particle size, index of polydispersity (PDI), and zeta potential (ZP)

Nanoparticles which are nanostructured lipid carriers were prepared using a new method based on microwaves. Thus, the work was accomplished with high speed and great accuracy, and samples free of impurities were prepared. Lavender oil was volatile oil and had a high flow rate in preparation and was a good solvent for the lauric acid used in the experiment, to create acceptable nanocarriers for the vitamin E. The results of the thermodynamic analysis include cycles of freezing and thawing, as well as centrifugation showing that every preparation had outstanding physical stability. Five formulas, namely LN1, LN2, LN3, LN4, and LN5, were chosen to characterize globule size, PDI, and zeta potential. As indicated in (Table 2), the particle size results were LN1 = 82.463 nm, LN2 = 111.8 nm, LN3 = 124.33 nm, LN4 = 137.77 nm and LN5=167.78 nm. (Table 2) displays the results of the polydispersity index (PDI) experiment for the lavender oil-based NLCs (LN1-LN5) formulations, which ranged from 0.105 to 0.173. As indicated in (Table 2), the mean zeta potential as absolute value for the formulations of lavender oil-based NLCs (LN1-LN5) ranged from 11.65 to 27.93 mV, confirming the stability of the nanosystem.

Table 2. Characterization results of lavender oil-based NLCs (LN1-LN5) formulations.

Formulation Code	Globule size (nm)*	PDI*	Zeta potential*
LN1	82.463 ± 2.081	0.105 ± 0.004	11.65 ± 1
LN2	111.8 ± 1.442	0.135 ± 0.004	14.81 ± 1.536
LN3	124.33 ± 2	0.152 ± 0.003	18.36 ± 1.501
LN4	137.77 ± 1.527	0.16 ± 0.002	23.81 ± 1.558
LN5	167.78 ± 1.834	0.173 ± 0.004	27.93 ± 1.652

*Values are expressed as mean ± SD (n = 3).

3.2. Atomic force microscopy

The findings demonstrate that the LN5 formula contains nanometer-sized particles with a nearly spherical form and a regular smooth surface as shown in (Fig. 1). Particle aggregation was absent, indicating the preparation's physical stability. The atomic force microscopy (AFM) analysis confirmed that the LN5 formulation exhibited nanosized particles with uniform spherical morphology and smooth surface characteristics, consistent with optimal nanocarrier design.

3.3. Evaluation of hydrogel (LNG1–LNG5) formulations based on NLCs

3.3.1. Assessment of organoleptic

Using only visual observation, the organoleptic test was carried out. Every LNG1–LNG5 formulation exhibits a distinct, uniform aroma of essential oil, which is embodied by lavender oil. High physical stability is shown by the absence of syneresis as shown in (Table 3).

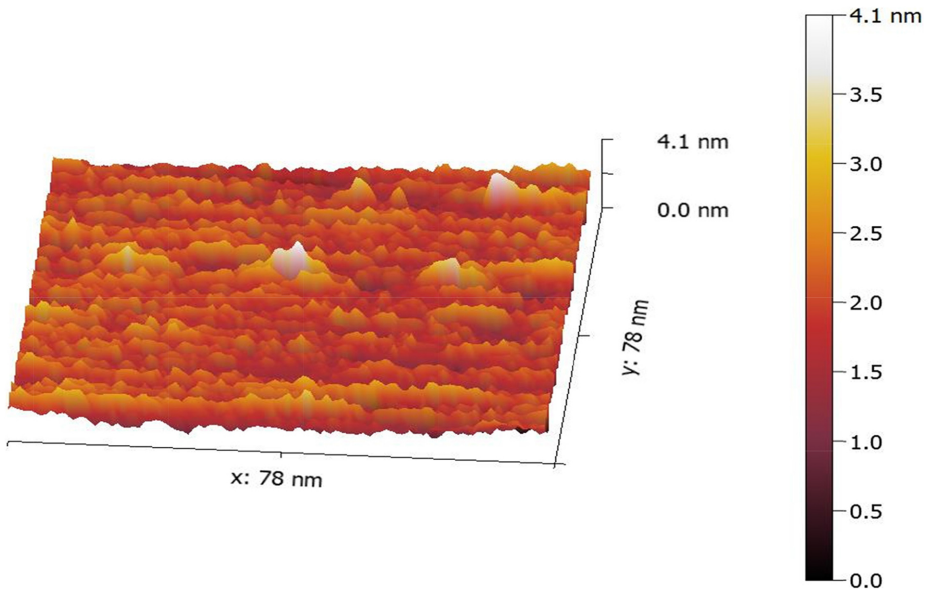

Fig. 1. AFM 3D image of lavender oil-based NLCs (LN5) formulation where scanning area is 78 nm * 78 nm.

Table 3. Test findings for gel (LNG1-LNG5) formulations based on NLCs.

Code	Color	Odor	Syneresis	Homogeneity	pH*	Mean spreadability (g*cm/sec)	Viscosity at 30 pm (mP.s)
LNG1	Colorless	Aromatic smell	No	Homogeneous	4.76 ± 0.152	126.03 ± 0.602	1112.06 ± 1.803
LNG2	Colorless	Aromatic smell	No	Homogeneous	5.2 ± 0.081	123.986 ± 0.571	1131.7 ± 1.473
LNG3	Colorless	Aromatic smell	No	Homogeneous	5.156 ± 0.051	114.496 ± 0.606	1157.1 ± 1.852
LNG4	Colorless	Aromatic smell	No	Homogeneous	5.363 ± 0.055	99.673 ± 1.225	1174.3 ± 1.527
LNG5	Colorless	Aromatic smell	No	Homogeneous	5.86 ± 0.049	92.089 ± 0.995	1187.5 ± 1.501

*Values are expressed as mean ± SD (n = 3).

3.3.2. Determination of pH

An important metric that can be used to prevent improper qualities in gels related to patient satisfaction is the pH evaluation. Table 3 indicates that the gel formulations based on NLCs (LNG1–LNG5) had somewhat acidic pH values ranging from 4.76 to 5.86 as shown in (Table 3).

3.3.3. Measurement of spreadability

The spreadability study was achieved for gel formulations based on NLCs (LNG1–LNG5). The results were (126.03 to 92.089 g*cm/sec) as shown in (Table 3).

3.3.4. Viscosity measurement

To assess the viscosity behavior of gel formulations based on NLCs (LNG1–LNG5), Biobase Meihua Trading Co., Ltd. utilized a viscometer with a spindle number (2) of rotating digital type. The results for viscosity (Table 3) show that an increase in the amount of aromatic oil used will culminate in a viscosity increase at a constant concentration of a 1:1 (% w/w) mixture of tween 80 and propylene glycol. As an outcome, it was found that the viscosity values at 30 rpm in (mP.s) units are LNG1 = 1112.06, LNG2 = 1131.7, LNG3 = 1157.1, LNG4 = 1174.3, and LNG5 = 1187.5 as shown in (Table 3). The viscosity assessment of the NLC-based gel formulations (LNG1–LNG5) demonstrated a direct correlation between aromatic oil concentration and viscosity, confirming the influence of oil content on rheological behavior.

3.3.5. Skin irritation study

A male rabbit was utilized in a study on skin irritation employing gel formulations based on NLCs (LNG1-LNG5). It was found that once the gel was applied, none of the formulations caused any discomfort or signs of allergic reactions or itching as shown in (Fig. 2).

3.3.6. Ex-vivo biological membrane permeation study

The permeability coefficient (cm/min) was determined by measuring the flux of alpha-tocopherol (μg/mL) across a 4 cm^2 area using a Franz diffusion cell. The findings from the ex-vivo biological membrane permeation study showed that the permeability coefficient (cm/min) of alpha-tocopherol was significantly greater (p-value <0.05) for LNG1 and significantly lower (p-value <0.05) for LNG5, as illustrated in (Fig. 3). The release profile comparison of alpha-tocopherol from the NLCs-based gel formulations (LNG1-LNG5) was ranked in the descending order: LNG1 > LNG2 > LNG3 > LNG4 > LNG5, as displayed in (Fig. 3). The LNG1 formulation exhibited a higher permeation coefficient compared to the other formulations due to the smaller size of the nanoglobules. As the particle size decreases, the rate of nanoglobule penetration through the biological skin membrane increases, and the smaller globule size provides a larger surface area for alpha-tocopherol diffusion.

4. Discussion

The characterization of lavender oil-based NLCs (LN1–LN5) provided important insights into the influence of formulation parameters on particle size, homogeneity, and stability. The microwave-assisted preparation method proved efficient in producing nanoparticles rapidly, with minimal impurities, and ensured reproducibility. Particle size analysis revealed that LN1 had the smallest average size (82.46 nm), while LN5 exhibited the largest (167.78 nm). This progressive increase in size could be attributed to variations in lipid and oil ratios, highlighting their critical role in nanocarrier design. The polydispersity index (PDI) values across all formulations ranged between 0.105 and 0.173, which are within the acceptable limit (<0.3), confirming a narrow size distribution and uniformity of nanoglobules. Such monodispersity is crucial for consistent drug release and biological performance. Zeta potential values varied between 11.65 mV and 27.93 mV, indicating moderate electrostatic repulsion sufficient to prevent aggregation under storage conditions, though values closer to ±30 mV would suggest greater stability. These findings confirm that lavender oil is a suitable lipid phase for developing stable NLC systems and suggest that smaller particle sizes, may provide superior permeation and drug delivery properties compared to larger formulations. Overall, the

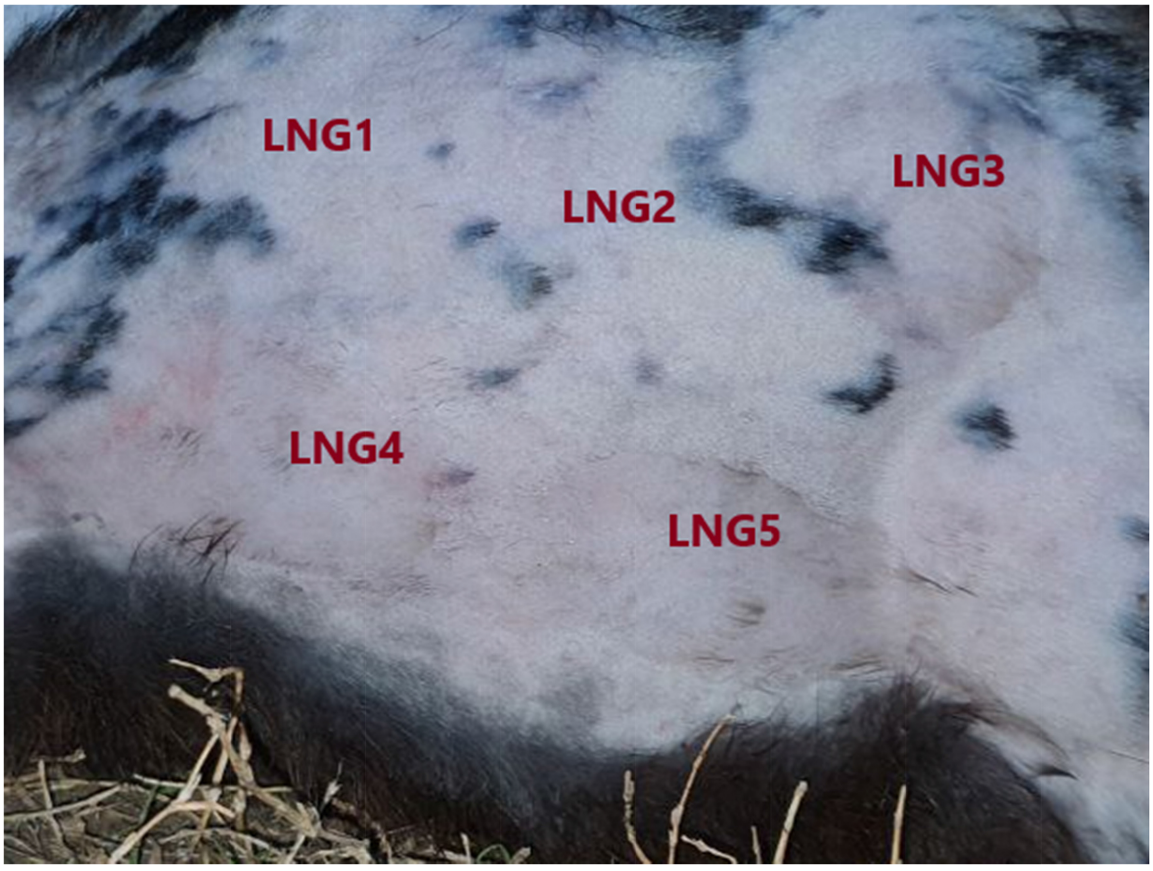

Fig. 2. Skin of experimental rabbit that explain there was not skin irritation after application of of gel (LNG1–LNG5) formulations based on NLCs.

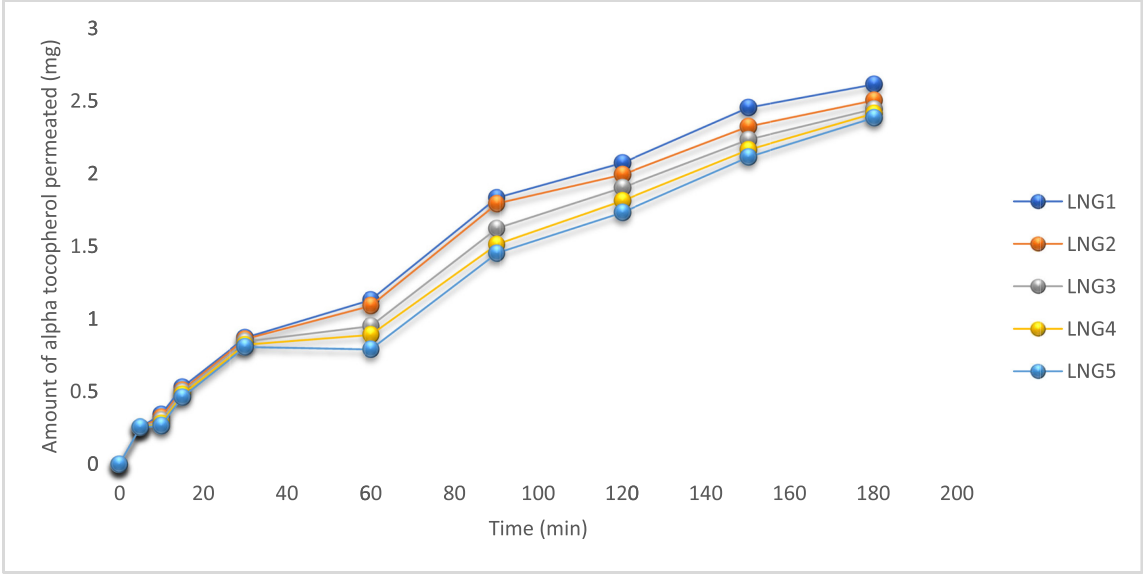

Fig. 3. Amount of alpha tocopherol permeated across skin of experimental rabbit for lavender oil-based NLCs (LNG1-LNG5) formulations during ex vivo study.

Table 4. Slope and permeability coefficient of lavender oil-based NLCs (LNG1-LNG5) formulations.

Code	Slope (mg/mL)	Permeability coefficient (cm/min)
LNG1	0.0145	0.001352
LNG2	0.0138	0.001287
LNG3	0.0133	0.001240
LNG4	0.0129	0.001203
LNG5	0.0126	0.001175

*Values are expressed as mean ± SD (n = 3).

formulations demonstrated favorable physicochemical characteristics suitable for topical applications. Since there was a significant link between the dependent variable (p-value ≤ 0.5) and the oil content, the analysis of variance supported the alternative hypothesis and rejected the null hypothesis [20–24]. Atomic force microscopy (AFM) characterization of the LN5 formulation provided valuable morphological evidence supporting its suitability as a nanostructured lipid carrier system. The particles exhibited a nanoscale size range with spherical geometry and smooth surface features, which are desirable traits for enhancing stability and functionality of nanocarriers. The absence of particle aggregation suggests strong physical stability of the system, minimizing risks of sedimentation or size growth during storage. Such stability is essential for ensuring reproducibility of therapeutic performance. Moreover, the uniform spherical shape and small dimensions are expected to improve dispersion in biological environments, facilitate cellular internalization, and potentially enhance bioavailability of the encapsulated bioactive agent. These morphological traits also support efficient drug loading and controlled release properties. Together, these findings demonstrate that LN5 exhibits the critical physicochemical attributes of a well-designed nanosystem, reinforcing its potential as a promising vehicle for pharmaceutical and biomedical applications where stability and efficacy are required [29]. Organoleptic evaluation of formulations LNG1–LNG5 revealed uniform appearance and a characteristic lavender aroma, attributable to the incorporated essential oil. The consistency in aroma across all formulations reflects homogenous distribution of the oil within the matrix, which is critical for ensuring product quality and consumer acceptability. Notably, the absence of syneresis indicates high physical stability, as phase separation often compromises both functional and sensory attributes of formulations. These findings suggest that the formulations maintained structural integrity during storage, supporting their suitability for further development. The results are consistent with previous reports highlighting organoleptic testing as a reliable preliminary stability assessment [19, 27]. It was found that a small pH increase was caused by an increase in the concentration of essential oil. The results offer a pH that is appropriate for the patient, ensuring their comfort and preventing dermatitis and skin allergies. According to the analysis of variance, there is a significant correlation ($p \leq 0.05$) between the quantity of lavender oil at the level and the pH as a dependent component [24, 27]. It was found that the quantity of lavender oil increased at the constant quantity of tween 80, propylene glycol, and carbomer 940, leading to a decreased spreadability parameter due to increased viscosity of gel formulations based on NLCs (LNG1–LNG5). Generally, the outcome indicates low spreadability time for NLCs-based gel (LNG1–LNG5) formulations that enhance patient compliance upon application on the skin (12–14). The analysis of variance indicates a significant relationship between the spreadability factor and lavender oil as an independent factor at the level ($p \leq 0.05$) [19, 24]. As observed, viscosity values increased progressively from LNG1 to LNG5, indicating that higher aromatic oil levels reduce the proportion of aqueous phase and consequently enhance the resistance of the colloidal dispersion system to flow. This increase in viscosity is favorable for topical formulations, as it can improve spreadability, retention time on the application site, and stability during storage. The statistical analysis (ANOVA, $p \leq 0.05$) further validated the significant impact of aromatic oil concentration on viscosity, highlighting the role of formulation composition in determining physicochemical performance. These findings align with previous reports suggesting that modulation of the oil-to-aqueous ratio is an effective approach for tailoring the mechanical and stability properties of nanostructured gels. Thus, LNG5 exhibited the highest viscosity, suggesting greater structural integrity [19, 24]. The skin irritation study performed using a male rabbit model demonstrated that all NLC-based gel formulations (LNG1–LNG5) were well tolerated, with no evidence of erythema, edema, itching, or allergic manifestations following topical application. The absence of visible irritation or discomfort indicates that the formulations are dermatologically safe and compatible with skin physiology. This favorable outcome can be attributed to the biocompatibility of the excipients employed, including essential oil, surfactants, and stabilizers, which are widely reported for their non-irritant properties at the concentrations used. The findings support the potential of these nanosystems for safe long-term application in topical delivery, particularly in formulations intended for sensitive skin. Furthermore, the absence of irritation enhances user compliance, which is a critical

factor in product development. These results are consistent with prior studies highlighting the safety of nanostructured lipid-based systems, thereby reinforcing the suitability of LNG1–LNG5 gels for further pharmacological and clinical evaluation [19, 20]. The ex-vivo biological membrane permeation study highlighted significant differences in the permeability of alpha-tocopherol across NLC-based gel formulations (LNG1–LNG5). Among these, LNG1 exhibited the highest permeation coefficient, which can be attributed to its smaller nanoglobule size that enhances diffusion by providing a greater surface area for interaction with the biological membrane. Conversely, LNG5 displayed the lowest permeability, likely due to its larger globule size and higher lipid content, which reduced drug release and penetration. The observed trend (LNG1 > LNG2 > LNG3 > LNG4 > LNG5) demonstrates the critical role of particle size and lipid concentration in modulating permeation efficiency. ANOVA analysis further confirmed a statistically significant association ($p < 0.05$) between lipid content and permeability coefficient, supporting the influence of formulation composition on transdermal drug delivery. These results suggest that optimizing particle size and lipid proportion is essential for enhancing the bioavailability of alpha-tocopherol in topical applications [20, 27, 29].

5. Conclusion

The prepared samples of lavender oil-based NLCs (LN1-LN5) formulations, which are characterized by high stability, confirm the great acceptability of the preparation method based on microwaves. The structure of the manufactured nanoparticles can load aqueous and fatty medicinal agents. The alpha tocopherol loaded in NLCs has many supportive cares for skin health such as antioxidant anti-inflammatory and photoprotection in addition lavender oil is antioxidant, and antimicrobial, enhances immune system performance, and minimizes inflammation, this provides a promising skin care product for counteract the photoaging and chronological aging.

Conflict of interest

The author declares there is no conflict of interest.

Acknowledgements

The authors would like to thank Prof. Dr. Hasan Shakir Majdi, President of Al-Mustaqbal University for scientific research support.

Funding

This project was made possible with financial support from Al-Mustaqbal University (grant no.: MUC-M-0222).

References

1. A. Woo and H. S. Kim, “Interaction between the microbiota and the skin barrier in aging skin: a comprehensive review,” *Front. Physiol.*, vol. 15, no. 1322205, pp. 1–13, 2024.
2. M. GarcíaFernández, J. Puig, and L. Toledo, “Changes in human skin composition due to intrinsic aging: a histologic and morphometric study,” *Histochem. Cell Biol.*, vol. 162, pp. 259–271, 2024.
3. A. Moradi and A. D. Widgerow, “Multicenter evaluation of a topical antioxidant serum: clinical, in vitro, and ex vivo assessment of collagen, photodamage, and elastin,” *J. Cosmet. Dermatol.*, vol. 23, no. 16067, pp. 1–12, 2024.
4. D. Romanowitz, J. Zeichner, E. Lain, K. Mariwalla, F. Kirchner, J. Weise, and Z. Draelos, “Evaluation of antioxidants’ ability to enhance hyaluronic acid-based topical moisturizers,” *SKIN J. Cutaneous Med.*, vol. 8, no. s348, pp. 1–8, 2024.
5. N. Jurek and V. Neymann, “The role of the ImmunatuRNA®-complex in promoting skin immunity and its regenerative abilities: implications for anti-aging skincare,” *J. Cosmet. Dermatol.*, vol. 23, pp. 1429–1445, 2024.
6. G. Jin, P. Zhang, H. Liu, J. Jiang, W. Sun, and C. Chang, “Food-derived skin-care ingredient as a promising strategy for skin aging: current knowledge and future perspectives,” *Colloids Surf. B Biointerfaces*, vol. 244, p. 114170, 2024.
7. A. Bajnóczi, M. Kiss, and J. Boros, “Plant-based phytochemicals mitigate oxidative stress and structural degeneration in aged skin: mechanisms and cosmeceutical applications,” *Immunity Ageing*, vol. 22, no. 5, pp. 1–12, 2025.
8. R. Mahfoudh, A.-H. AlRawi, and M. AlAbadie, “The epitome of antioxidants against UV photodamage: VitaminE use in skin protection,” *J. Dermatol. Res.*, vol. 6, pp. 1–9, 2025.
9. Y. T. Silva, A. M. CostaSilva, and R. G. da Silva, “Cosmeceutical formulations of provitaminE phosphate: invitro release testing and dermal penetration into excised human skin,” *Int. J. Pharm.*, vol. 630, no. 123021, pp. 1–12, 2023.
10. A. Jesus, S. Mota, and A. Torres, “Evaluation of vitaminE and derivatives for photoprotection: stability, mechanism, and formulation strategies,” *Antioxidants (Basel)*, vol. 12, no. 138, pp. 1–19, 2023.
11. A. Rani, R. Kaur, A. Aldahish, R. Vasudevan, P. Balaji, C. P. Dora, B. Chandrasekaran, T. G. Singh, and R. Sharma, “Nanostructured lipid carriers (NLC)-based topical formulation of hesperidin for effective treatment of psoriasis,” *Pharmaceutics*, vol. 17, no. 478, pp. 1–12, 2025.
12. A. Morakul, V. B. Junyaprasert, K. Sakchaisri, and V. Teeranachaideekul, “Cannabidiolloaded nanostructured lipid carriers (NLCs) for dermal delivery: enhancement of photostability, cell viability, and antiinflammatory activity,” *Pharmaceutics*, vol. 15, no. 537, pp. 1–12, 2023.
13. R. Koumoulos, L. NižićNodilo, J. Lovrić, A. Hafner, I. Pepić, and M. Jug, “Functional nanostructured lipid carrierenriched hydrogels tailored to repair damaged epidermal barrier,” *Gels*, vol. 10, no. 466, pp. 1–11, 2024.
14. V. M. But, A. E. Bulboacă, V. Rus, T. Ilyés, M. L. Gherman, and S. D. Bolboacă, “Antiinflammatory and antioxidant efficacy of

lavender oil in experimentally induced thrombosis," *Thromb. J.*, vol. 21, no. 85, pp. 1–13, 2023.
15. A. Analytou, I. Voulgari, E. Gogou, and A. Tsaknis, "Antibacterial and synergistic efficacy of Romanian *Lavandula angustifolia* essential oil against Grampositive pathogens: roles of linalool and linalyl acetate," *Plants*, vol. 13, no. 2136, pp. 1–14, 2024.
16. Y. K. Shin and G. H. Seol, "Effects of linalyl acetate on oxidative stress, inflammation and endothelial dysfunction: implications for skin and neuroprotection," *Front. Pharmacol.*, vol. 14, no. 1233977, pp. 1–19, 2023.
17. L. Hareng, S. N. Kolle, C. Gomes, S. Schneider, and M. Wahl, "Critical assessment of the endocrine potential of linalool and linalyl acetate: proactive testing strategy assessing estrogenic and androgenic activity of lavender oil main components," *Arch. Toxicol.*, vol. 98, pp. 347–361, 2024.
18. M. ElAbdali, N. ElBarakaoui, and S. Bellahcen, "Antibacterial, antioxidant and NADPHoxidase inhibition activities of *Lavandula dentata* essential oil: emphasis on linalool content," *Evid. Based Complement. Alternat. Med.*, Article 9766002, pp. 1–11, 2023.
19. H. K. Drais, "Development and evaluation of essential oils nanoemulgel as human skin sanitizer using novel method," *Turk. J. Pharm. Sci.*, vol. 21, pp. 456–462, 2024.
20. H. K. Drais, F. H. Ihmedee, M. K. Sharaf El-Din, and N. A. Naser, "Investigation of biological membrane permeability of nanoemulsion, nanostructured lipid carriers and lipid polymer hybrid nanocarriers based nanogel as transdermal carvedilol delivery system," *Res. J. Pharm. Technol.*, vol. 17, pp. 4947–4952, 2024.
21. S. Lohan, R. Verma, D. Kaushik, and M. Bhatia, "Optimization and evaluation of microwave-assisted curcumin-loaded nanostructured lipid carriers: a green approach," *Future J. Pharm. Sci.*, vol. 9, no. 117, pp. 1–12, 2023.
22. R. Joukhadar, L. NižićNodilo, J. Lovrić, A. Hafner, I. Pepić, and M. Jug, "Amphotericin Bloaded nanostructured lipid carrier gel prepared via microwave-assisted method: enhanced encapsulation efficiency and skin permeation," *Biomed. Pharmacol. J.*, vol. 18, pp. 1–11, 2025.
23. K. Mauludin, A. N. Garmana, and F. Fauzian, "Physicochemical improvement of carvacrol-loaded nanostructured lipid carrier using microwave-assisted synthesis: optimization & characterization," *Biointerface Res. Appl. Chem.*, vol. 14, no. 107, pp. 1–15, 2024.
24. H. K. Drais, "Transdermal delivery of lornoxicam hybrid nanogel: design, preparation, characterization, and in-vitro diffusion evaluation," *Iraqi J. Ind. Res.*, vol. 10, pp. 98–104, 2023.
25. A. Khan, M. Ahmad, and F. Asif, "Development and evaluation of curcumin-loaded nanostructured lipid carrier hydrogel for enhanced topical delivery: formulation, characterization, and stability," *J. Drug Deliv. Sci. Technol.*, vol. 78, no. 103885, pp. 1–12, 2024.
26. S. Gupta, A. Kumar, and M. Singh, "Formulation and characterization of carbomer-based nanostructured lipid carrier gel for improved skin permeation of quercetin," *Pharm. Dev. Technol.*, vol. 28, pp. 950–960, 2023.
27. H. K. Drais, "Design hybrid nanogel of prednisolone for topical application: preparation, characterization, in-vitro and ex-vivo evaluation," *Iran. J. Pharm. Sci.*, vol. 19, pp. 194–207, 2023.
28. P. Singh, R. Kumar, and K. Sharma, "Nanostructured lipid carrier-based carbomer gel: formulation optimization and in vitro skin permeation study," *Drug Dev. Ind. Pharm.*, vol. 49, pp. 569–578, 2023.
29. H. K. Drais and A. H. Ahmed, "Lipid-polymer hybrid nanocarriers for oral delivery of felodipine: formulation, characterization and ex-vivo evaluation," *Adv. Pharm. Bull.*, vol. 12, pp. 791–800, 2022.