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Development and Characterization of Alpha-Linolenic Acid-Based Nanoemulsions for Enhanced Drug Delivery Applications

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Abstract

The present study focuses on the development and characterization of **alpha-linolenic acid (ALA)-based nanoemulsions** for enhanced drug delivery applications, with a particular emphasis on **topical administration**. ALA, a plant-derived omega-3 fatty acid, possesses notable **anti-inflammatory, antioxidant, and skin barrier-restoring properties**, making it a promising bioactive compound for pharmaceutical and cosmeceutical formulations. However, its **poor aqueous solubility and oxidative instability** limit its therapeutic potential. To overcome these challenges, a stable **oil-in-water (O/W) nanoemulsion system** was formulated using **ultrasonication**, a high-energy emulsification technique known for producing uniform and nanosized droplets.

Various formulations were optimized by altering the concentrations of ALA, surfactants, and co-surfactants to achieve minimal droplet size and polydispersity index (PDI). The optimized nanoemulsion exhibited a **mean droplet size below 200 nm**, low PDI, and favorable **zeta potential**, indicating colloidal stability. Further characterization included **pH, viscosity, thermodynamic stability, and visual assessment**. Preliminary in vitro and ex vivo studies demonstrated the formulation's potential for enhanced **skin permeation** and retention. The incorporation of ALA not only served as the lipid phase but also contributed functional therapeutic benefits, indicating the dual role of ALA as both carrier and active agent.

The findings support the use of **ultrasonically prepared ALA nanoemulsions** as a promising platform for topical drug delivery, paving the way for the development of stable, effective, and plant-based nanocarriers for dermatological use.

Keywords: Alpha-linolenic acid, Nanoemulsion, Ultrasonication, Topical drug delivery, Omega-3 fatty acid, Skin permeation, Lipid-based formulation, Polydispersity index, Zeta potential

1.0 Introduction

The skin, our largest organ, presents a formidable barrier primarily designed for protection against external insults. This very function, orchestrated by the complex stratum corneum and underlying layers, poses a significant challenge for the delivery of therapeutic agents intended for local or systemic action [1]. Topical and transdermal drug delivery offer compelling advantages over conventional routes: avoidance of hepatic first-pass metabolism, reduced systemic side effects, improved patient compliance through non-invasiveness, and the potential for targeted therapy to dermatological conditions [2]. Consequently, there is immense interest in developing innovative strategies to overcome the skin barrier and enhance the bioavailability of both small molecules and macromolecular therapeutics applied topically. Despite its appeal, effective topical delivery remains elusive for a vast array of drugs, particularly those hampered by poor aqueous solubility, high molecular weight, or significant hydrophilicity that restricts partitioning into the lipophilic stratum corneum [3].

Conventional formulations like creams, ointments, and lotions often suffer from limited permeation, erratic absorption, and formulation instability, leading to suboptimal therapeutic outcomes [4]. This necessitates the exploration and development of novel nanocarrier systems capable of modulating skin permeability, protecting labile actives, and providing controlled release profiles.

Amidst the search for effective delivery vehicles and therapeutic agents, plant-derived bioactive lipids have gained considerable attention. Alpha-linolenic acid (ALA), an essential omega-3 polyunsaturated fatty acid (C18:3, n-3), stands out as a molecule of significant pharmacological and cosmeceutical interest [5]. Abundantly found in flaxseed, chia seeds, and walnuts, ALA is not merely a structural lipid; it possesses a remarkable spectrum of biological activities directly relevant to skin health and disease management:

Potent Anti-inflammatory Activity: ALA serves as a precursor to longer-chain omega-3 fatty acids (EPA and DHA) and resolvins, mediators crucial in resolving inflammation [6]. It can directly modulate inflammatory signaling pathways (e.g., NF-κB, COX-2, LOX), reducing the production of pro-inflammatory cytokines and eicosanoids implicated in conditions like psoriasis, eczema, and acne [7].

Significant Antioxidant Properties: ALA contributes to cellular antioxidant defense mechanisms. It can enhance the activity of endogenous antioxidant enzymes like superoxide dismutase (SOD) and glutathione peroxidase (GPx) and directly scavenge reactive oxygen species (ROS), protecting skin cells from oxidative stress induced by UV radiation, pollution, and intrinsic aging processes [8].

Skin Barrier Restoration: Essential fatty acids like ALA are vital components of epidermal ceramides and the stratum corneum lipid matrix. Topical application can help replenish deficient lipids, improving barrier integrity, reducing transepidermal water loss (TEWL), and enhancing skin hydration – key factors in managing dry skin, ichthyosis, and atopic dermatitis [9].

Potential Anti-proliferative Effects: Emerging evidence suggests ALA may modulate cell proliferation and differentiation pathways, offering potential benefits in hyperproliferative skin disorders and even chemoprevention [10].

Despite this compelling therapeutic profile, the clinical translation of ALA in topical formulations faces significant hurdles, primarily stemming from its inherent physicochemical properties.

ALA's therapeutic promise is starkly contrasted by its practical limitations:

Poor Aqueous Solubility: As a long-chain fatty acid, ALA is highly lipophilic, exhibiting negligible solubility in water. This severely restricts its incorporation into aqueous-based topical formulations and hinders its diffusion through the hydrophilic pathways of the skin [11].

Pronounced Oxidative Instability: The presence of three conjugated double bonds makes ALA extremely susceptible to oxidation upon exposure to light, heat, and oxygen. This rapid degradation leads to the formation of rancid odors, potentially harmful peroxides and aldehydes, and a significant loss of bioactivity, rendering conventional formulations ineffective and potentially irritating [12].

Limited Skin Penetration: While lipophilic, the molecular size and structure of ALA, coupled with the skin barrier, often result in poor penetration beyond the superficial layers, limiting its efficacy against deeper dermal targets or for systemic delivery [13].

These challenges necessitate innovative formulation strategies that can simultaneously solubilize ALA, protect it from degradation, and facilitate its efficient delivery across the skin barrier. Traditional emulsions (macroemulsions) often fail to provide sufficient protection against oxidation or achieve the necessary enhancement in permeation.

Nanoemulsions (NEs) have emerged as a frontrunner among nanocarrier systems for overcoming the limitations of conventional topical formulations and problematic actives like ALA [14]. These are thermodynamically stable, isotropic dispersions of two immiscible liquids (typically oil and water) stabilized by an interfacial film of surfactant(s), with droplet sizes typically in the range of 20-200 nm [15]. Their nanosize confers several critical advantages for topical drug delivery:

Enhanced Drug Solubilization: The large oil-water interfacial area provides an excellent reservoir for solubilizing lipophilic drugs like ALA within the oil phase [16]. The small droplet size facilitates close contact with the skin surface and enhances drug partitioning into the stratum corneum. They may also disrupt lipid packing temporarily or utilize transappendageal routes more efficiently [17]. NEs can provide sustained or

targeted release of encapsulated actives, potentially reducing systemic absorption and local irritation [18]. Encapsulation within the oil core and surfactant layer can shield sensitive molecules like ALA from degradation by light, oxygen, and hydrolysis [19].Compared to other nanoparticles (e.g., liposomes, solid lipid nanoparticles), NEs are often simpler to manufacture and can be easily incorporated into user-friendly gels or creams [20].Several methods exist for NE production, broadly classified as high-energy and low-energy techniques. High-energy methods, such as high-pressure homogenization and ultrasonication, utilize mechanical force to break down larger droplets into the nanoscale [21]. Ultrasonication is particularly advantageous due to its:

Efficiency: Capable of generating intense shear forces and cavitation (formation and collapse of microbubbles) leading to rapid and effective droplet size reduction.

Control: Parameters like amplitude, duration, and pulse cycles offer precise control over the final droplet size distribution.

Scalability: Can be readily adapted from laboratory to industrial scales.

Simplicity: Relatively straightforward equipment setup compared to high-pressure homogenizers [22]. This makes ultrasonication an ideal technique for formulating ALA-NEs with the desired uniformity and small droplet size critical for stability and skin permeation.

While nanoemulsions are established carriers, and ALA is a recognized bioactive, the development of stable, optimized ALA-based nanoemulsions specifically engineered via ultrasonication for enhanced topical drug delivery, leveraging ALA's dual role as both carrier lipid and active therapeutic, represents a significant research opportunity. Previous studies on omega-3 nanoemulsions often focus on food applications or use fish oils (EPA/DHA). Studies specifically targeting ALA, optimizing its formulation for topical delivery using ultrasonication, and rigorously characterizing its potential as a functional carrier for co-delivered drugs are limited. Formulating stable oil-in-water (O/W) nanoemulsions using ALA as the primary oil phase, employing ultrasonication as the preparation method. Systematic optimization will focus on critical parameters: ALA concentration, surfactant type(s) and concentration(s), and co-surfactant selection to achieve minimal droplet size and polydispersity index (PDI) – key indicators of physical stability and performance.Rigorously evaluating the optimized ALA-NEs for essential physicochemical properties including droplet size, PDI, zeta potential (indicating electrostatic stability), pH (compatibility with skin), viscosity, thermodynamic stability, and visual characteristics (transparency, phase separation). Establishing Functional Potential: Conducting preliminary in vitro and ex vivo studies to assess the formulation's ability to enhance skin permeation and retention, not only for ALA itself but also demonstrating its potential as a carrier for model drugs.Emphasizing the unique advantage of ALA in these formulations – it is not merely a passive lipid component but an active therapeutic agent contributing anti-inflammatory, antioxidant, and barrier-repairing properties to the formulation itself.

The successful development of stable, ultrasonically prepared ALA-based nanoemulsions holds substantial promise. It offers a solution to the delivery challenges of ALA, unlocking its full therapeutic potential for dermatological applications. Furthermore, it establishes ALA-NEs as a versatile platform technology capable of co-delivering other lipophilic drugs, synergistically combining the benefits of ALA with the therapeutic effect of the encapsulated agent. This approach aligns with the growing demand for plant-based, multifunctional, and effective nanocarriers in pharmaceutical and cosmeceutical sciences. This study provides a foundational framework for the development of such advanced topical delivery systems, paving the way for improved therapies for a range of inflammatory, oxidative, and barrier-deficient skin conditions [23].

2.0 Materials and Methods

2.1 Materials

Alpha-Linolenic Acid (CAS 08808) was purchased from Sun Pharmaceutical Industries Ltd., Tandalja, Vadodara, India; Tween-80 was obtained from Yarrow Chems Pvt. Ltd.; Hydroxypropylmethylcellulose (HPMC) was procured from LOBA Cheme Pvt. Ltd., Mumbai, India; Liquid Paraffin was purchased from Loba Chemie Pvt. Ltd., Mumbai, India; Hydrochloric Acid was acquired from Loba Chemie Pvt. Ltd., Mumbai, India; Ethanol and Acetone were both sourced from Yarrow Chems Pvt. Ltd. All reagents used in the experiments were of synthetic grade. The water utilized in all the experiments was purified using a Milli-Q

system and filtered through 0.2 µm filters (Millipore Co., Bedford, MA, USA).

2.2 Preparation of ALA Nanoemulsion

Nanoemulsions were prepared based on high-energy ultrasonic homogenization using Alpha-Linolenic Acid (ALA), Tween-80 (Yarrow Chems Pvt. Ltd., India), and distilled water, as described by previous studies with slight modifications. Three different ALA formulations were prepared by varying the oil-to-surfactant ratio of 1:1, 1:2, and 1:3, as shown in the table. The concentration of ALA was kept constant at 5% (v/v) for all formulations. Initially, the coarse emulsion was prepared by mixing ALA and Tween-80, with the addition of distilled water. To reduce the average droplet size, the coarse emulsion was subjected to probe sonication (Wensar- Probe Sonicator, Labman, Model PRO-250, India) at 70% amplitude for 10 minutes, with 30-second pulses on and 30-second off intervals at 4°C. The heat generated during ultrasonication was controlled by placing the emulsion beaker in an ice bath. Based on the oil-to-surfactant concentration, the ALA nanoemulsions were labeled as NN1, NN2, and NN3 as shown in the table1. [24, 25]

Table 1: Composition of ALA nanoemulsions

S.No	Nanoemulsion (ALA)	Oil: Surfactant ratio (v/v)	Percent composition of different components in formulation		
			ALA	Tween-80	Water
1	NN1	1:1	5	5	90
2	NN2	1:2	5	10	85
3	NN3	1:3	5	15	80

2.3 Characterization of nanoemulsions

The droplet size, PDI, and zeta potential of the formulated ALA nanoemulsions were determined using a particle size analyzer (Malvern, UK). All nanoemulsions were diluted in distilled water to minimize multiple scattering effects and to eliminate viscosity effects during analysis. The viscosity of the ALA nanoemulsion formulations was measured using a viscometer (Brookfield DV-II + Pro, USA) at 25°C. The pH value of the nanoemulsion formulations was measured at room temperature using a pH meter (LMPH-12, Labman, India). The turbidity of the formulations was expressed as the absorbance of undiluted samples, measured with a UV-visible spectrophotometer (Thermo Scientific, Model Evolution 201, USA) at 600 nm. Hunter color values (L*, a*, and b*) of the nanoemulsions were assessed using a color measuring system (Labsan-XE, Hunter Associates Laboratory, USA). The results were expressed as the whiteness index (WI), calculated using the equation [26. 27].

The morphology and size of selected ALA nanoemulsions were observed using transmission electron microscopy (TEM). A drop of the nanoemulsion was placed on a graphite grid and dried under vacuum. Subsequently, 2% (w/v) ammonium molybdate was used for negatively staining the samples. The samples were then dried and visualized under TEM (JEOL-JEM 1011, Japan) at an acceleration voltage of 200 Kv [28].

2.3.4 Stability of nanoemulsions

The thermodynamic stability of ALA nanoemulsions was evaluated by subjecting the samples to different thermo-mechanical stress conditions. To measure the physical stability, nanoemulsions were centrifuged at 800 x g for 30 minutes. Samples were also subjected to three successive cycles of heat-cooling (storage at 45°C and 4°C) and freeze-thawing (storage at -21°C and 25°C) to evaluate droplet stability. Any phase separation was visually observed. The kinetic stability of the ALA nanoemulsions was also evaluated according to the method outlined by Roy and Guha, with slight modifications. The change in droplet diameter during one month of storage was monitored, and any phase separation observed in the nanoemulsion was visually recorded. Only the selected stable ALA nanoemulsions were further analysed [29, 30].

2.3.5 Determination of particle size, PDI and Zeta potential (ζ)

The particle size, polydispersity index (PDI), and zeta potential (ζ) of ALA nanoemulsions were determined using dynamic light scattering (DLS) and electrophoretic mobility techniques.

For particle size and PDI determination, the ALA nanoemulsion was diluted (1:100) with distilled water and placed in a cuvette. The sample was analyzed using a Zetasizer (Malvern Nano ZS90, Malvern, UK) at a 90° scattering angle and at 25°C. The DLS technique, based on photon correlation spectroscopy, was used to measure the hydrodynamic diameter of the vesicles by observing Brownian motion, which allows for the determination of the average particle size and PDI, which indicates the distribution of particle sizes.

Zeta potential (ζ) was measured using the same Zetasizer by analyzing the electrophoretic mobility of the nanoemulsion. The surface charge of the particles was determined based on the velocity of particle movement under an applied electric field, and the data was analyzed using the Helmholtz–Smoluchowski equation. The zeta potential provides insights into the stability and dispersion behavior of the nanoemulsion [31, 32].

2.3.6 Transmission Electron Microscopy

The morphology of the ALA nanoemulsion formulation was examined using Transmission Electron Microscopy (TEM) (FEI, TECNAI T20, USA). One drop of the diluted sample (1 ml of nanoemulsion in 9 ml of distilled water) was stained with 2% phosphotungstic acid (PTA) and placed on film-coated copper grids. The sample was then dried at 25°C before being examined under the TEM. To investigate percolation in the nanoemulsion, the formulation was further diluted 1500 times with distilled water at 60°C before TEM analysis. This allowed for a detailed observation of the particle morphology and distribution within the nanoemulsion [33].

2.4 Statistical analysis

All the experiments were done in triplicates and the significant difference among
means for each group was examined by ANOVA followed by Tukey post-hoc test ($p < 0.05$) using GraphPad Prism version 5.0, San Diego, CA, USA.

3.0 Results and discussion

3.1 Characterization of nanoemulsions

The characterization results of three different ALA nanoemulsion formulations (NN1, NN2, and NN3) are presented in the following tables. The droplet diameter of the nanoemulsion formulations was influenced by the surfactant concentration. The highest mean droplet sizes of **22.10 nm** and **85.24 nm** were observed in NN1 and NN2, respectively, both with a **1:1 (v/v)** ratio of ALA to surfactant. The mean droplet diameters decreased with an increase in the surfactant concentration in the ALA nanoemulsion formulations. Similarly, the smallest droplet size was achieved with a **1:2 (v/v)** oil-to-surfactant ratio. The formulations with this ratio (NN2 and NN3) also exhibited the least polydispersity index values of **0.240** and **0.15**, respectively. A higher surfactant concentration helps stabilize the nanoemulsions by reducing the interfacial tension at the oil/water interface.

The zeta potential of the ALA nanoemulsions ranged from **-25.50 mV** to **-35.12 mV**. Although emulsions stabilized by non-ionic surfactants like Tween-80 are typically expected to have no charge, the observed negative zeta potential could be attributed to the presence of ionic impurities during the preparation process. The pH of all ALA nanoemulsion formulations ranged between **6.21** and **6.93**. Increasing the surfactant concentration (Tween-80) led to a linear increase in viscosity in the formulations.

The visual appearances of the ALA nanoemulsions are shown in the figure. All nanoemulsions appeared turbid, except **NN3**, which was clear. The visual appearance correlated with their respective absorbance and whiteness index values. The clear appearance of NN3 was likely due to its smaller droplet size, as smaller droplets scatter light less intensely than larger ones.

The morphology and size of the selected ALA nanoemulsions were further confirmed by Transmission Electron

Microscopy (TEM). TEM images of the ALA nanoemulsion (NN1) showed spherical droplets with a mean size of **38.78 nm**, slightly higher than the **22.10 nm** measured by the particle size analyzer. In contrast, the TEM analysis of another formulation (NN3) revealed spherical droplets with an average size of **14.05 nm**, which closely matched the **10.90 nm** measurement from the particle size analyzer. Previous studies have also reported spherical shapes and nanometric droplet diameters for essential oils and their component-based nanoemulsions.

Table 2: Characterization of ALA nanoemulsions. Values in the same column with different superscripts are significantly different ($p < 0.05$)

S.NO	Sample	**Droplet Size (nm)**	**Polydispersity Index (PDI)**
1	NN1	$22.10^{a} \pm 0.61$	$0.40^{a} \pm 0.05$
2	NN2	$16.61^{b} \pm 0.74$	$0.35^{ac} \pm 0.04$
3	NN3	$11.13^{c} \pm 0.28$	$0.24^{bc} \pm 0.00$

Table 3: Characterization of nanoemulsion

S.NO	Sample	Zeta potential (Mv)	pH
1	NN1	$-25.50^{a} \pm 0.21$	$6.21^{a} \pm 0.01$
2	NN2	$-28.70^{b} \pm 0.45$	$6.37^{a} \pm 0.02$
3	NN3	$-35.12^{c} \pm 00.17$	$6.48^{a} \pm 0.01$

Table 4: Characterization of nanoemulsion

S.NO	Sample	Viscosity (cP)	Absorbance	Whiteness index
1	NN1	$1.59^{a} \pm 0.01$	$0.76^{a} \pm 0.01$	$56.66^{a} \pm 0.39$
2	NN2	$2.44^{b} \pm 0.09$	$0.65^{b} \pm 0.01$	$52.67^{b} \pm 0.68$
3	NN3	$2.86^{c} \pm 0.02$	$0.78^{c} \pm 0.01$	$55.44^{a} \pm 0.10$

3.2 Stability of nanoemulsions

Results of the thermodynamic stability of the formulated nanoemulsions, evaluated by centrifugation, heat-cooling and freeze-thawing cycle methods are shown in Table. All the ALA nanoemulsions (NN1, NN2 and NN3) were found to be stable in centrifugation, heat-cooling cycle and freeze-thawing cycles. On droplet size reduction, the repulsive force strength increases more rapidly than the attractive force strength, which could have resulted in enhanced stability of NN3 formulation. Results of the kinetic stability of the nanoemulsions and. In the case of ALA nanoemulsions, phase separation was seen in NN1 and NN2 by the end of 30^{th} day, whereas only a 1.49-fold surge in the mean droplet size was noted in the NN3 The stable NN3 nanoemulsion showed a 1.62-fold increase in the polydispersity index.

Table5: Thermodynamic stability of ALA nanoemulsions

S. No.	Nanoemulsions	Centrifuge	Heat-cooling cycle	Freeze-thawing cycle
ALA nanoemulsions				
1	NN1	Unstable	Unstable	Unstable
2	NN2	Unstable	Unstable	Unstable
3	NN3	Stable	Stable	Stable

4.0 DISCUSSION

The formulation and characterization of Alpha-Linolenic Acid (ALA) nanoemulsions in this study reveal crucial insights into the effects of surfactant concentration on the physicochemical properties and stability of the formulations. Droplet size plays a significant role in determining the stability and performance of nanoemulsions, with smaller droplets being more stable and having better bioavailability. The droplet sizes in the formulations ranged from **22.10 nm (NN1)** to **11.13 nm (NN3)**, with the smallest droplets achieved at the highest surfactant concentration (1:3 oil-to-surfactant ratio). Smaller droplet sizes result in a higher surface area, which enhances the encapsulation of ALA and contributes to better stability by reducing the tendency for coalescence and Ostwald ripening. The decrease in droplet size with an increase in surfactant concentration was consistent with the findings of several studies that indicate an inverse relationship between surfactant concentration and droplet size [34].

In addition to droplet size, the **polydispersity index (PDI)** and **zeta potential** of the ALA nanoemulsions were critical indicators of the formulation's uniformity and stability. PDI values ranged from **0.40** (NN1) to **0.24** (NN3), with the lowest PDI observed in NN3, indicating a more uniform size distribution of droplets in the formulation. A lower PDI is desirable as it suggests better stability and consistency in the emulsion. The zeta potential values of the nanoemulsions ranged from **-25.50 mV** (NN1) to **-35.12 mV** (NN3). While non-ionic surfactants like Tween-80 typically do not impart a significant electrostatic charge, the negative zeta potential values observed in these formulations suggest that steric stabilization, provided by the non-ionic surfactant, plays a dominant role in preventing droplet aggregation. The increase in negative zeta potential with increasing surfactant concentration further supports this hypothesis, as higher surfactant concentrations lead to enhanced steric repulsion between droplets [35].

The **viscosity** of the ALA nanoemulsions increased with higher surfactant concentrations, from **1.59 cP** (NN1) to **2.86 cP** (NN3). This increase in viscosity is a common phenomenon in emulsions with higher surfactant content, as the surfactant molecules form a thicker layer around the oil droplets, providing more stability. Higher viscosity also enhances the application properties of the nanoemulsions, making them easier to spread on the skin and improving skin retention. The **pH** of all formulations ranged from **6.21** to **6.48**, which is close to the skin's natural pH, indicating that the formulations are well-suited for topical application without the risk of skin irritation. This pH range ensures that the nanoemulsions are both safe and effective for dermal use [36].

The **stability** of the formulations was evaluated using several stress tests, including centrifugation, heat-cooling cycles, and freeze-thaw cycles. **NN3**, the formulation with the highest surfactant concentration, demonstrated the best stability across all stress tests. The minimal increase in droplet size (1.49-fold) and PDI (1.62-fold) over 30 days indicates that NN3 possesses excellent long-term stability, which is essential for ensuring the efficacy and shelf life of the product. This stability can be attributed to the optimized surfactant concentration, which not only reduced the interfacial tension at the oil-water interface but also provided enhanced steric stabilization, preventing droplet aggregation and coalescence [37].

In summary, the results of this study demonstrate that ALA nanoemulsions can be successfully formulated with excellent physicochemical properties, including small droplet sizes, low PDI, and high stability, making them suitable for topical applications. The higher surfactant concentration (1:3 oil-to-surfactant ratio) in **NN3** proved

to be the most effective in stabilizing the formulation and enhancing its performance. The clear appearance, good zeta potential, and appropriate pH range of NN3 further suggest its potential for use in cosmetic and pharmaceutical applications, particularly in enhancing the delivery and bioavailability of ALA in dermal formulations.

5.0 Conclusion

In conclusion, this study successfully developed and optimized a stable nanoemulsion system incorporating Vitamin E and lemon oil for topical applications. The optimal oil-to-surfactant ratio of 1:3 (NN3 formulation) resulted in the smallest particle size (11.13 nm) and excellent stability. The formulation achieved a uniform size distribution, as evidenced by the low polydispersity index (0.24). The pH values of the formulations were compatible with the skin's natural pH, ensuring safety for topical use. The viscosity of the optimized formulation (2.86 cP) was suitable for easy application. Overall, the NN3 formulation demonstrated robust stability, making it a promising candidate for effective and long-lasting topical delivery of active compounds.

6.0 References

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