

Nanostructured Lipid Carriers Coenzyme Q10 with Stearic Acid as Solid Lipid Phase and Nyamplung Oil (*Calophyllum inophyllum* L.) as Liquid Lipid Phase

M Fatchur Rochman^{1*}, Yulias Ninik Windriyati¹, Malinda Prihantini¹, Kiki Damayanti², Junvidya Heroweti², Arisna Ayuningtyas³, Defa Putra Ardiansa³

¹Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, Universitas Wahid Hasyim, Semarang, Indonesia
²Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Universitas Wahid Hasyim, Semarang, Indonesia
³Undergraduate Program, Faculty of Pharmacy, Universitas Wahid Hasyim, Semarang, Indonesia

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Correspondence:

M Fatchur Rochman
fatchur.rochman@unwahas.ac.id



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Abstract

Background: Coenzyme Q10 is a lipophilic antioxidant with limited aqueous solubility, poor stability, and susceptibility to photodegradation, necessitating an effective delivery system. Nanostructured Lipid Carriers (NLC) offer a promising approach to enhance its bioavailability and therapeutic efficacy.

Objective: This study aims to determine the physicochemical characteristics of the NLC system incorporating stearic acid as the solid lipid phase and nyamplung oil as the liquid lipid phase to enhance the delivery of Coenzyme Q10.

Methods: Preparation of NLC using ultra-turrax equipment with a high shear homogenization technique. Preparation was evaluated for physicochemical characteristics such as pH test, viscosity, spreadability, particle size, polydispersity index, zeta potential, entrapment efficiency, and determination of Q10 levels.

Results: All formulations met the acceptable pH range (5.46-5.72), Viscosity F1: 73.16 cPs, F2: 102.82 cPs, F3: 110.09 cPs. Entrapment efficiency F1: 95.56%, F2: 96.20%, F3: 96.14%. F2 exhibited the most favorable characteristics with a particle size of 492.1 nm and polydispersity index of 0.4194, F1 (761.4 nm, PDI 0.6947) and F3 (4009 nm, PDI 1.00). All formulations showed zeta potential values F1: -39.76 mV, F2: -37.73 mV, F3: -35.44 mV. However, spreadability values 11.81-11.99 cm.

Conclusions: NLC formulations were successfully prepared from stearic acid and nyamplung oil, with F2 (4:2 ratio) demonstrating the most optimal overall characteristics, including monodisperse particle size distribution and high entrapment efficiency. F3 (5:1) failed to achieve nano-scale particle size (4009.0 nm), highlighting the critical importance of maintaining an appropriate solid-to-liquid lipid balance for successful NLC formation.

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INTRODUCTION

Coenzyme Q10 (ubiquinone) is a naturally occurring lipid-soluble antioxidant that plays a critical role in cellular energy production within the mitochondrial electron transport chain. Despite its therapeutic potential for various conditions, including cardiovascular diseases, neurodegenerative disorders, and skin aging, its clinical application is significantly limited by several physicochemical drawbacks: extremely low water solubility, high lipophilicity, poor oral bioavailability, chemical instability, and susceptibility to photodegradation. These inherent limitations necessitate the development of an appropriate delivery system to enhance its stability and therapeutic effectiveness.¹ Thus, an appropriate delivery system is needed to increase the effectiveness of coenzyme Q10, one of which is NLC (Nanostructured Lipid Carrier). The NLC system is the latest generation of the SLN (Solid Lipid Nanoparticle) system, developed to overcome the limitations of SLN, such as long release time, limited entrapment efficiency, and the need to improve the effectiveness of coenzyme Q10.² NLC can increase the trapping efficiency of active compounds, improve physical stability, and reduce particle size.³ Previous research has shown that coenzyme Q10 formulation in an NLC (Nanostructured Lipid Carrier) system is more effective than an SLN (Solid Lipid Nanoparticle) system.⁴

The selection of appropriate lipid components is crucial in determining NLC characteristics and physicochemical stability. The NLC system comprises liquid and solid lipids homogenized into a surfactant-stabilized lipid core matrix.⁵ The lipid components greatly influence the characteristics of NLCs, such as particle size, zeta potential, entrapment

efficiency, pH, viscosity, polydispersity index, and physicochemical stability.⁶ The reason for choosing stearic acid is based on previous research using glyceryl monostearate solid lipids, which produced larger particle sizes than stearic acid, with a range of 458.1 nm to 900.9 nm.⁷ While stearic acid solid lipids in previous studies have a particle size in the range of 214.7 nm to 237.3 nm, previous comparative studies have demonstrated that coenzyme Q10 formulated in NLC systems exhibits significantly higher entrapment efficiency and better stability compared to SLN formulations. This study will develop an NLC system with a stearic acid solid lipid phase that can minimize particle size to increase trapping efficiency.⁸

The liquid lipid phase in NLC can increase the trapping efficiency of active compounds.⁹ This study used the liquid lipid phase of nyamplung oil (*Calophyllum inophyllum* L.). Nyamplung oil (*Calophyllum inophyllum* L.) was chosen as the liquid lipid phase due to its favorable fatty acid composition, particularly its high content of oleic acid (41.27%). Oleic acid offers the advantage of resistance to oxidation during the cooling process in NLC preparation, as it can inhibit the crystallization process and maintain lipid matrix imperfections that accommodate greater drug entrapment. The combination of stearic acid as the solid lipid and nyamplung oil as the liquid lipid represents a novel approach for coenzyme Q10 delivery that remains underexplored in the scientific literature. While separate studies have investigated NLC formulations with these individual components, the specific combination of stearic acid and nyamplung oil for coenzyme Q10 delivery has not been systematically characterized.^{10,11}

Previous research has formulated NLC systems with various lipid combinations for coenzyme Q10 delivery. A recent study by Rochman et al. (2025) investigated NLC formulations composed of mixed solid lipids (cetyl palmitate and stearic acid) with nyamplung oil as the liquid lipid phase without coenzyme Q10, evaluating three solid-to-liquid ratios (3:3, 4:2, and 5:1). While that study provided valuable insights into the feasibility of using nyamplung oil as a liquid lipid phase, and stearic acid as the solid lipid phase resulted in favorable characteristics, thus enabling its use as an effective carrier. Based on the above considerations, this study aims to develop and comprehensively characterize NLC formulations containing coenzyme Q10 with stearic acid as the solid lipid phase and nyamplung oil as the liquid lipid phase, and to evaluate the physicochemical characteristics of the resulting formulations. The significance of this study lies in its contribution to the understanding of NLC formulation design for lipophilic active compounds. By systematically characterizing the physicochemical properties of NLC formulations with varying solid-to-liquid lipid ratios, this study provides practical guidance for the development of stable, high-loading NLC systems.

METHODS

Instrument. Tools used for the study were analytical balance (Ohaus, PR Series), magnetic stirrer (MS-H280-Pro), object glass, test tube (Iwaki CTE33), ultra-turrax (IKA T25), cone & plate viscometer, pH meter (SI Analytics GmbH), Particle Size Analyzer (PSA) (Malvern), centrifuge (Hettich Zentrifugen-2002), UV-Vis spectrophotometer (Shimadzu, UV-1800).

Materials. The materials used for the study were coenzyme Q10 (PT. Chemco Prima Mandiri, Pharmaceutical grade), nyamplung oil (PT. Syailendra Bumi Investama, Food grade), stearic acid (PT. Banusaha Mandiri, Technical grade), tween 80 (PT. Banusaha Mandiri, Technical grade), propylene glycol (PT. Banusaha Mandiri, Technical grade), distilled water, acetonitrile, and 2-propanol (PT. Banusaha Mandiri, Analytical grade).

Research Procedure

NLCs were prepared using the emulsification with the High-Shear Homogenization (HSH) technique. The NLC formulas are presented in **Table 1**. Each ingredient served specific functions: coenzyme Q10 as active substance, nyamplung oil as the liquid lipid, stearic acid as the solid lipid, tween 80 as the surfactant, propylene glycol as the cosurfactant, and distilled water as the solvent.²

Stearic acid, nyamplung oil, tween 80, and coenzyme Q10 were accurately weighed and combined in a 100 mL beaker. The mixture was heated to $65^{\circ}\text{C} \pm 1^{\circ}\text{C}$ using a magnetic stirrer with hot plate at 500 rpm until all components were completely melted and homogenized (approximately 15 minutes). The temperature was monitored continuously using a calibrated thermocouple. Propylene glycol and distilled water were combined in a separate 100 mL beaker and heated to $65^{\circ}\text{C} \pm 1^{\circ}\text{C}$ with stirring at 500 rpm until homogeneous (approximately 10 minutes). The aqueous phase mixture was poured into the lipid phase mixture at 65°C and immediately homogenized using an Ultra-Turrax device at 24,000 rpm for 3 minutes. The homogenization was performed with the dispersing tool immersed approximately 1 cm above the bottom of the beaker to ensure efficient mixing and avoid air incorporation. The NLC mixture was immediately cooled to room temperature ($25^{\circ}\text{C} \pm 2^{\circ}\text{C}$) using an ice bath with gentle stirring at 300 rpm for 10 minutes. The NLC

preparations were stored in amber glass vials at $25^{\circ}\text{C} \pm 2^{\circ}\text{C}$ and evaluated within 24 hours of preparation. Three independent batches were prepared for each formulation (F 1, F 2, F 3), with each batch produced on separate days using freshly prepared materials to account for batch-to-batch variability. All measurements were performed in triplicate for each batch.¹²

Table 1. Coenzyme Q10 Nanostructured Lipid Carriers Formula

Formula	Concentration (% b/b)		
	F 1	F 2	F 3
Coenzyme Q10	2.4	2.4	2.4
Nyamplung oil	3	2	1
Stearic acid	3	4	5
Tween 80	23	23	23
Propylene glycol	10	10	10
Distilled water	100	100	100

Note:

F 1 : Nyamplung oil : Stearic acid (3:3)

F 2 : Nyamplung oil : Stearic acid (2:4)

F 3 : Nyamplung oil : Stearic acid (1:5)

Evaluation of Nanostructured Lipid Carriers

The pH testing was performed using a calibrated pH meter. The electrode was immersed in the NLC preparation, and the pH value was recorded after stabilization. The measurement was repeated three times for each formulation.² The acceptable pH range for topical preparations is 4.5-6.8 to avoid skin irritation.¹³

Viscosity was determined using a cone and plate viscometer (Brookfield DV-II+ Pro, CP-40 spindle, cone angle 0.8° , radius 24 mm). A 13 mL sample of NLC was carefully pipetted onto the plate, ensuring uniform distribution and absence of air bubbles. The cone was lowered to the measurement position (gap setting: 0.013 mm), and the measurement was performed at $25^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$. The viscometer was operated at a shear rate of 100 s^{-1} , with the viscosity value recorded after stabilization (defined as $< 2\%$ variation over 30 seconds).¹⁴

The spreadability test aims to determine the preparation's ability to spread on the skin. This test is carried out by weighing the preparation as much as 0.5 grams and placing it on a watch glass; the preparation is given a load of 150 grams for 1-2 minutes, and then the diameter spread is measured. A good spreadability value is 5-7 cm.¹⁵

Particle size and polydispersity index tests were conducted using a Particle Size Analyzer (PSA). The NLC sample was weighed as much as 1 gram, added to 10 ml of distilled water, and then homogenized. The sample was put into the cuvette and inserted into the sample holder. The PSA tool was turned on, clicked on the particle size menu, and waited 10 minutes. Results were recorded as data. Readings were taken 3 times.¹¹

The zeta potential assay is measured by Electrophoretic Light Scattering (ELS). This test reflects the particles' surface charge and indicates their stability and potential to aggregate.¹⁶ Electrostatically stable NLC values and zeta potential should be less than -30 mV or above +30 mV.¹⁷

The entrapment efficiency was measured using UV-Vis spectrophotometry. A coenzyme Q10 stock solution of 200 ppm was prepared. 100 mg of coenzyme Q10 was weighed and placed into a 500 mL volumetric flask. The solvent (acetonitrile : 2-propanol) was added at a ratio of (84:16) up to the mark. The volumetric flask was then shaken until homogeneous and labeled (Coenzyme Q10 200 ppm). Determination of Maximum Wavelength, 1.5 mL of the 200 ppm stock solution was taken and diluted using the acetonitrile: 2-propanol solvent mixture in a 10 mL volumetric flask, yielding a concentration of 30 ppm. The solution was placed into a cuvette, the UV-Vis spectrophotometer was operated, and the absorbance was observed at a wavelength range of 200–400 nm, using the acetonitrile : 2-propanol mixture as the blank. The theoretical wavelength of coenzyme Q10 is 275 nm. The standard curve was prepared by making a series of concentrations from the 200 ppm stock solution. The concentration series prepared were 15, 20, 25, 30, 35, and 40 ppm. 0.75; 1; 1.25; 1.5; 1.75; and 2 mL of the coenzyme Q10 stock solution were taken, respectively, and then diluted using the acetonitrile : 2-propanol (84:16) solvent mixture in a 10 mL volumetric flask. The volumetric flask was shaken until homogeneous, the solution was transferred into test tubes, and each test tube was labeled accordingly. The absorbance was then read at the previously obtained maximum wavelength, and a linear regression equation between concentration (x) and absorbance (y) was generated, yielding the standard curve equation $y = bx + a$. Determination of Untrapped Coenzyme Q10 Content. 1 gram of the NLC sample was dissolved in 10 mL of the acetonitrile : 2-propanol (84:16) solvent mixture. The mixture was centrifuged for 15 minutes at a speed of 2500 rpm. The supernatant was then separated and its volume was measured. The supernatant indicates the coenzyme Q10 that was not trapped in the NLC system, while the precipitate indicates the coenzyme Q10 that was trapped in the NLC

system. The absorbance of the supernatant was read using a UV-Vis spectrophotometer by taking 2 mL and placing it into a cuvette. If the absorbance did not fall within the range of 0.2–0.8, dilution was performed to obtain a suitable absorbance. The entrapment efficiency value was then calculated using the linear regression equation.¹¹

$$\text{Entrapment Efficiency (\%)} = \frac{[(\text{Total Q10} - \text{Free Q10})]}{(\text{Total Q10})} \times 100\%$$

Where:

Total Q10 = The total amount of coenzyme Q10 added to the formulation (2.4% b/b)

Free Q10 = The amount of coenzyme Q10 in the supernatant (unentrapped)

All measurements were performed in triplicate for each batch, except particle size, index polydispersity, and zeta potential. Statistical analysis was performed using one-way analysis of variance (ANOVA) to determine significant differences among formulations. The assumptions of ANOVA (normality and homogeneity of variance) were tested using the Shapiro-Wilk test and Levene's test, respectively. Where significant differences were found, post-hoc comparisons were performed using Tukey's Honestly Significant Difference (HSD) test. A p-value < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 20.0.

RESULT AND DISCUSSION

The NLC formulations were successfully prepared using the high-shear homogenization technique, yielding visually distinct preparations. **Figure 1** shows the NLC preparations containing coenzyme Q10 with stearic acid and nyamplung oil. The color variations observed among formulations F1, F2, and F3 were attributed to the different solid-to-liquid lipid ratios, with higher stearic acid concentrations producing visually more opaque preparations



Figure 1. Coenzyme Q10 Nanostructured Lipid Carriers

Figure 1 shows the preparation of coenzyme Q10 with stearic acid solid lipid and nyamplung oil liquid lipid prepared using an ultra-turrax with a high shear homogenization technique. The colors in formula 1, formula 2, and formula 3 are different due to the concentration ratio between solid and liquid lipids. The results of the evaluation of the physicochemical characteristics of nanostructured lipid carrier preparations can be seen in **Table 2**, which shows the ratio of liquid lipids and solid lipids in formula 1 (3:3), formula 2 (2:4), and formula 3 (1:5).

Table 2: Evaluation Results of Physicochemical Characteristics of Nanostructured Lipid Carriers

Parameters	F 1	F 2	F 3
pH (mean ± SD)	5.46 ± 0.02	5.50 ± 0.07	5.72 ± 0.11
Viscosity (mean ± SD) (cPs)	73.156 ± 11.40	102.821 ± 19.96	110.09 ± 12.95
Spreadability (mean ± SD) (cm)	11.96 ± 0.05	11.99 ± 0.01	11.81 ± 0.07
Entrapment Efficiency (mean ± SD) (%)	94.27 ± 0.04	93.61 ± 0.36	93.80 ± 0.24
Particle size (nm)	761.4	492.1	4009.0
Polydispersity index	0.6947	0.4194	1.0
Zeta potential (mV)	-39.76	-37.73	-35.44

Note:

F 1 : Nyamplung oil : Stearic acid (3:3)

F 2 : Nyamplung oil : Stearic acid (2:4)

F 3 : Nyamplung oil : Stearic acid (1:5)

pH test

The pH of topical formulations is a critical parameter that influences both skin compatibility and formulation stability. The acceptable pH range for skin preparations is 4.5–6.8.¹³ The pH values obtained for F 1 (3:3), F 2 (2:4), and F 3 (1:5) were 5.46 ± 0.02, 5.50 ± 0.07, and 5.72 ± 0.11, respectively, all within the acceptable range. The observed pH

trend, where higher stearic acid concentrations correlated with increased pH values (less acidic), can be attributed to the presence of carboxyl groups (-COOH) in stearic acid. These functional groups release protons (H⁺) in aqueous media, contributing to the acidic nature of the formulation. However, the data shows that as the stearic acid proportion increased from F1 to F3, the pH also increased. This is because the relative decrease in the liquid lipid proportion and the overall formulation matrix composition, rather than just the absolute stearic acid concentration, may affect the microenvironment and the dissociation of the carboxyl groups. The higher concentration of the total lipid phase in F3 could have altered the partitioning of water and the effective concentration of free protons in the bulk aqueous phase, leading to a less acidic reading. Statistical analysis using one-way ANOVA revealed a significant difference among formulations ($p = 0.016$, $p < 0.05$), confirming that variations in the solid-to-liquid lipid ratio significantly affected the pH values.

Viscosity test

Viscosity is an important rheological property that influences product consistency, stability, and ease of application. Viscosity measurement aims to determine the viscosity value of nanostructured lipid carriers preparations using a cone and plate viscometer.¹⁴ The viscosity results in **Table 2** show that formula F 1 (3:3) obtained an average value of 73.156 cps, F 2 (2:4) 102.821 cps, and F 3 (1:5) of 110.09 cps. The range of viscosity values in nanostructured lipid carriers preparations ranged from 32.5 to 2499.5 cPs.¹² Formula F 1 (3:3) viscosity is lower than that of F 2 (2:4) and F 3 (1:5), which shows that the three formulas have increasing viscosity values. One-way ANOVA analysis indicated no significant difference among formulations ($p = 0.054$, $p > 0.05$), suggesting that while viscosity increased with higher solid lipid content, the variations were not statistically significant at the evaluated concentration range. This finding suggests that formulations require optimization to reduce viscosity for better patient acceptability and ease of application.

Particle size and polydispersity index test

Particle size testing aims to determine the particle size contained in the nanostructured lipid carriers preparation. Particle size is a critical parameter influencing NLC stability, drug release kinetics, and bioavailability. The acceptable particle size for NLC systems is <1000 nm to ensure colloidal stability and prevent sedimentation. Particle size and polydispersity index were measured using *particle size analyzer*. Large particle sizes in nanostructured lipid carriers preparations will settle more easily than preparations that have small particle sizes. The particle size that meets the requirements is <1000 nm.¹⁸ **Table 2** shows that the particle size of the three formulas varies greatly. The particle size results of F 1 amounted to 761,4 nm and F 2 492,1 nm, which still meet the particle size range of nanostructured lipid carriers preparations, which is <1000 nm.¹⁸ Meanwhile, the particle size in F 3 is 4009,0 nm, which does not meet the requirements.

The particle size in F3 is larger than in F1 and F2, which is 4008 nm, where the results do not meet the requirements. This is due to the composition of nyamplung oil liquid lipid and stearic acid solid lipid in formula 3 (1:5), the more dominant concentration of stearic acid solid lipid will form a lipid matrix as during the manufacturing process with temperature, formula 3 tends to have a higher viscosity than formula 1 (3:3) and formula 2 (2:4). High viscosity can inhibit the reduction of droplets to nano-sized during the homogenization process. Another factor causing the large particle size is the time and speed of stirring during the manufacturing process, which is less than optimal, so it cannot reduce the particle size of nanostructured lipid carriers. In addition, unstable physical changes in the nanostructured lipid carriers cause an increase in particle size during storage. Particle size observed in F3 can be attributed to the higher proportion of stearic acid (1:5).¹⁸

The polydispersity index test measures particle size uniformity in the nanostructured lipid carriers system.² **Table 2** shows the polydispersity index results, obtained by F1 (3:3) 0.6947, F2 (2:4) 0.4194, and F3 (1:5) of 1. The polydispersity index describes the particle size distribution in a nanostructured lipid carriers system. Uniform particle size distribution in a system is indicated by a polydispersity index value of <0.5, which indicates homogeneous and monodisperse properties. Conversely, a polydispersity index value >0.5 indicates a non-uniform particle size distribution or a heterogeneous and polydisperse nature.³ The results of the three formulas showed that formula F2 was monodispersed, while F1 and F3 were polydisperse. The ideal PDI of F2 correlates with its optimal particle size distribution, suggesting that the 4:2 solid-to-liquid ratio provides the most balanced formulation for producing uniform nanoparticles.

Zeta potential test

Zeta potential reflects the surface charge of colloidal particles and is indicative of electrostatic stability. Values exceeding ± 30 mV are generally considered sufficient for physical stability due to strong repulsive forces preventing particle aggregation.^{16,17} All formulations exhibited zeta potential values below -30 mV (F1: -39.76 mV, F2: -37.73 mV, F3: -35.44 mV).

The zeta potential measurement results of the three formulas, which means that they are negatively charged and indicate a reduction in particle aggregation due to the repulsive force between particles.²¹ This negative surface charge creates an electrostatic barrier that prevents particle coalescence and aggregation.^{18,21}

Spreadability test

The spreadability determines the ease of application and coverage on the skin surface.²² The results of the spreadability test can be seen in the following table shows the results of the spreadability test in formula F1 (3: 3) obtained 11.96 ± 0.0577 , formula F2 (2: 4) 11.99 ± 0.0115 and formula F3 (1: 5) 11.81 ± 0.0763 . The spreadability values of 11.81-11.99 cm exceeded the ideal range of 5-7 cm for topical preparations. This result suggests that the formulation viscosity was too low to achieve optimal consistency for topical application. The lower viscosity observed in this study resulted in excessive spreadability, which may affect the retention of the preparation on the skin. One-way ANOVA analysis revealed significant differences among formulations ($p = 0.017$, $p < 0.05$), Post-hoc analysis using Tukey's HSD test revealed significant differences between F1 and F3 ($p = 0.038$) and F2 and F3 ($p = 0.019$), confirming that lipid ratio variations significantly affect spreadability. This finding is important for formulation optimization, as spreadability must be balanced with other characteristics to achieve optimal skin application properties.

Entrapment efficiency

Entrapment efficiency (EE) is a crucial parameter indicating the ability of the NLC system to encapsulate the active compound. The calibration curve for coenzyme Q10 was established using six concentrations (15, 20, 25, 30, 35, and 40 ppm), yielding the regression equation $y = 0.02009x + 0.05699$ with correlation coefficient $r = 0.9997$, indicating excellent linearity.¹⁹

The value of trapping efficiency was calculated using the linear regression equation of the calibration curve. Based on **Table 2**, the results of trapping efficiency in F1 (3:3) obtained a trapping value of $94,27\% \pm 0,04$, F2 (2:4) of $93,61\% \pm 0,36$, and F3 (1:5) of $93,80\% \pm 0,24$. The results of the three formulas meet the requirements. The trapping efficiency test aimed to determine the level of drug trapped in the nanostructured lipid carriers system. The trapping efficiency test was carried out by making a standard solution of coenzyme Q10 using a solvent mixture of acetonitrile: 2-propanol (84:16). Coenzyme Q10 is very difficult to dissolve in polar solvents. The results of determining the maximum wavelength in this study obtained 273.80 nm; in theory, the maximum wavelength of coenzyme Q10 is 275 nm. The change in wavelength is due to the auxochrome group in coenzyme Q10, which binds to the chromophore group.¹⁹

The high trapping value can be caused by the high concentration of liquid lipids in the nanostructured lipid carriers system, resulting in higher trapped compounds.²³ This is because the liquid lipids in the nanostructured lipid carriers system can form imperfections in the crystalline lipid structure, which causes more compounds to be trapped in the system.²⁴ Previous research showed that the average trapping efficiency of coenzyme Q10 in the nanostructured lipid carriers system was 85.54%.¹⁴ Incorporation of nyamplung oil into the NLC system demonstrated good entrapment efficiency and favorable formulation characteristics.²⁵ Although the EE values were consistently high, one-way ANOVA showed significant differences among formulations ($p < 0.05$), indicating that the lipid ratio influences entrapment capacity. Post-hoc analysis using Tukey's HSD test revealed significant differences between F1 and F2 ($p = 0.029$).

The results of this study demonstrate the successful development of NLC systems for coenzyme Q10 using the combination of stearic acid and nyamplung oil. Among the three formulations, F2 (4:2 ratio) exhibited the most favorable overall characteristics with optimal particle size (492.1 nm), monodisperse distribution (PDI 0.4194), high entrapment efficiency (96.20%), and zeta potential (-37.73 mV).

The unsuccessful formulation F3 (1:5) highlights the importance of maintaining an appropriate solid-to-liquid lipid balance. The excessive solid lipid content led to failure in achieving nano-scale particle size, likely due to increased viscosity impeding the homogenization process and the formation of a highly ordered crystalline structure limiting particle size reduction. This finding emphasizes the critical role of liquid lipids in creating structural imperfections essential for NLC formation and drug encapsulation.

The critical analysis of these results reveals several important considerations for future formulation development. First, the selection of stearic acid as the solid lipid phase, despite the small particle size advantage, must

be balanced with appropriate liquid lipid content to prevent excessive particle growth. Second, the high entrapment efficiency suggests that the NLC system effectively protects coenzyme Q10 from degradation, which is crucial for maintaining its antioxidant activity. Third, the good zeta potential values indicate formulation stability, which is essential for practical applications and long-term storage.

These findings guide the rational design of NLC formulations, suggesting that a ratio of approximately (2:4) represents an optimal balance for achieving desirable physicochemical characteristics.

Limitation

The present study has several limitations that should be acknowledged. First, the study focused primarily on physicochemical characterization without investigating the *in vitro* release kinetics, skin penetration, or biological activity of the coenzyme Q10-loaded NLCs. Second, the long-term stability of the formulations, particularly with respect to particle size and entrapment efficiency, was not evaluated. Third, the study did not explore the effect of homogenization parameters (speed, time, temperature) on formulation characteristics, which could further optimize particle size reduction.

Future research should address these limitations by conducting comprehensive stability studies, releasing kinetics evaluation, and dermatokinetic studies to assess skin penetration and antioxidant activity. Additionally, formulation optimization using design of experiments (DoE) approaches, such as Box-Behnken design, could systematically investigate the effects of multiple variables and identify optimal formulation parameters. The incorporation of other lipid components or surfactants could also be explored to further enhance the formulation characteristics.

CONCLUSION

The nanostructured lipid carrier system containing coenzyme Q10 was successfully developed using stearic acid as the solid lipid and nyamplung oil as the liquid lipid. Among the formulations evaluated, F2 (2:4) demonstrated the most favorable among the tested formulations characteristics, with a particle size of 492.1 nm, PDI of 0.4194, zeta potential of -37.73 mV, and entrapment efficiency of 96.20% and despite the spreadability test results not meeting the requirements. The lipid ratio significantly influenced pH, spreadability, and entrapment efficiency, while particle size was critically dependent on maintaining an appropriate balance between solid and liquid lipids. The findings confirm that stearic acid and nyamplung oil are suitable lipid components for NLC formulation of coenzyme Q10, offering excellent entrapment efficiency and zeta potential. However, formulation F3 (1:5) failed to achieve nano-scale particle size, indicating that excessive solid lipid content compromises the formation of NLC systems.

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GENERATIVE AI DISCLOSURE STATEMENT

The authors acknowledge the use of generative artificial intelligence (Deepseek) solely for editing language and enhancing the manuscript's readability. Critically, all scientific and scholarly contributions, from the experimental design and data analysis to the interpretation of results and formulation of conclusions, were performed exclusively by the authors, who assume complete liability for the final submission.

AUTHOR CONTRIBUTION STATEMENT

M Fatchur Rochman: Constructing an idea or hypothesis for research and a manuscript, **Yulias Ninik Windriyati:** Organizing and supervising the course of the project or the article, and taking responsibility, **Malinda Prihantini:** Taking responsibility for the construction of the entire manuscript, **Kiki Damayanti:** Taking responsibility for the presentation

of the results, **Junvidya Heroweti**: Taking responsibility for the construction of a substantial part of the manuscript, **Arisna Ayuningtyas**: Analyzing data results, **Defa Putra Ardiansa**: Analyzing data results.

CONFLICT OF INTEREST DECLARATION

The authors declare no conflicts of interest regarding the publication of this manuscript.

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