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Optimization of a Niosomal Transdermal Delivery System Containing Kojic Acid and Alpha Arbutin

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ABSTRACT

Hiperpigmentasi merupakan gangguan kulit akibat peningkatan produksi melanin. Asam kojic dan alfa-arbutin merupakan agen pencerah kulit yang bekerja menghambat aktivitas enzim tirosinase, namun memiliki keterbatasan penetrasi melalui kulit. Penelitian ini bertujuan untuk memformulasikan dan mengkarakterisasi sistem penghantaran transdermal niosom kombinasi asam kojic dan alfa-arbutin dengan variasi konsentrasi Span 80. Niosom dibuat menggunakan metode ethanol injection dengan tiga formula, yaitu F1 (0,37%), F2 (0,40%), dan F3 (0,42%) Span 80. Evaluasi meliputi uji organoleptik, viskositas, pH, stabilitas, iritasi, ukuran partikel, indeks polidispersitas (PDI), dan zeta potensial. Hasil penelitian menunjukkan bahwa seluruh formula memiliki karakteristik fisik yang baik, stabil, dan tidak menimbulkan iritasi. Ukuran partikel yang diperoleh berturut-turut sebesar 185,1 nm, 372,9 nm, dan 322,6 nm dengan nilai PDI 0,273; 0,295; dan 0,118. Nilai zeta potensial masing-masing formula adalah -18,5 mV, -23,0 mV, dan -18,4 mV. Analisis statistik menunjukkan bahwa variasi konsentrasi Span 80 tidak berpengaruh signifikan terhadap viskositas dan pH ($p>0,05$). Disimpulkan bahwa kombinasi asam kojic dan alfa arbutin berhasil diformulasikan dalam sistem niosom dengan karakteristik fisikokimia yang baik, dimana Formula III merupakan formula yang paling optimal.

Keywords: *Asam Kojic; alpha-arbutin; niosom; Penghantaran Transdermal; Span 80.*

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ABSTRACT

Hyperpigmentation is a skin disorder characterized by excessive melanin production. Kojic acid and alpha-arbutin are skin-lightening agents that inhibit tyrosinase activity; however, their effectiveness is limited by poor skin penetration. This study aimed to formulate and characterize a niosomal transdermal delivery system containing a combination of kojic acid and alpha-arbutin at different Span 80 concentrations. Niosomes were prepared using the ethanol injection method in three formulations: F1 (0.37% Span 80), F2 (0.40% Span 80), and F3 (0.42% Span 80). The formulations were evaluated for organoleptic properties, viscosity, pH, stability, irritation potential, particle size, polydispersity index (PDI), and zeta potential. All formulations exhibited acceptable physical characteristics, remained stable, and caused no irritation. The particle sizes of F1, F2, and F3 were 185.1 nm, 372.9 nm, and 322.6 nm, respectively, with corresponding PDI values of 0.273, 0.295, and 0.118. The zeta potential values were -18.5 mV, -23.0 mV, and -18.4 mV for F1, F2, and F3, respectively. Statistical analysis showed that variation in Span 80 concentration had no significant effect on viscosity or pH ($p > 0.05$). The combination of kojic acid and alpha-arbutin was successfully incorporated into a niosomal system with favorable physicochemical characteristics, and Formula III was identified as the optimal formulation.

Keywords: *Kojic acid; alpha-arbutin; niosomes; transdermal delivery; Span 80.*

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1. Introduction

The skin is the largest organ of the human body and serves as the primary protective barrier against environmental influences while maintaining physiological homeostasis. In addition to functioning as a physical barrier, skin condition reflects an individual's health and may affect self-confidence and quality of life. Therefore, appropriate skin care is essential to preserve skin function and prevent disorders arising from internal and external factors [1].

Facial skin is frequently exposed to ultraviolet radiation, pollution, and chemical substances, making it particularly susceptible to disorders such as hyperpigmentation. Hyperpigmentation results from increased melanin production driven by tyrosinase activity. In addition to being an aesthetic concern, this condition may adversely affect an individual's psychological well-being [2].

Kojic acid is one of the active compounds widely used to manage hyperpigmentation. It acts as a tyrosinase inhibitor and thereby suppresses melanin formation. Kojic acid also exhibits antioxidant and anti-inflammatory activities. However, its effectiveness as a single agent remains limited; therefore, it is frequently combined with other active compounds to achieve more optimal outcomes [3,11].

Alpha-arbutin is another depigmenting agent with a similar mechanism of action, namely the inhibition of tyrosinase activity and suppression of melanin synthesis. It is considered safer than hydroquinone and is effective in managing various forms of hyperpigmentation. The combination of kojic acid and alpha-arbutin may provide a synergistic effect in inhibiting melanogenesis. Nevertheless, its effectiveness is strongly influenced by the ability of the active compounds to penetrate the skin. A major limitation of topical delivery is the lipophilic nature of the stratum corneum, whereas alpha-arbutin is hydrophilic. This mismatch restricts active-compound penetration and reduces therapeutic effectiveness [4,12-14]. Therefore, a delivery system capable of enhancing permeation and improving active-compound release is required.

Niosomes are promising delivery systems because they are composed of nonionic surfactants and cholesterol and can encapsulate both hydrophilic and lipophilic compounds. Their advantages include favorable biocompatibility, improved active-compound stability, enhanced transdermal penetration, and controlled drug release [5,10]. Niosomes can also interact with stratum corneum lipids, thereby facilitating the permeation of active compounds through the skin [6,15].

Accordingly, this study aimed to develop a niosome-based transdermal delivery system containing a combination of kojic acid and alpha-arbutin. This approach is expected to improve the effectiveness, stability, and safety of skin-lightening preparations for the management of hyperpigmentation.

2. Methods

This experimental study aimed to develop and optimize a niosome-based transdermal delivery system containing a combination of kojic acid and alpha-arbutin. This section is optional for original research articles. The methods should be presented descriptively and should clearly explain the methodology applied in the study, enabling readers to understand the procedures performed.

Materials and Equipment

The equipment used in this study included an analytical balance (Ohaus), beakers (Pyrex®), graduated cylinders (Pyrex®), volumetric flasks (Pyrex®), Pasteur pipettes, glass stirring rods (Pyrex®), a climatic chamber, a magnetic stirrer (IKA® C-MAG HS 7), a pH meter (Hanna Instruments), a particle size analyzer based on dynamic light scattering (DLS), syringes, a sonicator (Ultrasonic Cleaner, Power Sonic 405), a centrifuge (Hettich Rotina 380R), a Zetasizer, aluminum foil, spatulas, micropipettes, and sealed glass storage containers.

The materials used in this study were kojic acid, alpha-arbutin, glycerol, Span 80 (sorbitan monooleate), cholesterol, dicetyl phosphate (DCP), and acetate buffer at pH 5.5.

Formulation of the Niosomal Transdermal Delivery System

Table 1. Formulation of the Niosomal Transdermal Delivery System

No.	Material	F1	F2	F3	Function
1.	Kojic acid	1%	1%	1%	Active compound
2.	Alpha-arbutin	2%	2%	2%	Active compound
3.	Glycerol	5%	5%	5%	Humectant/isotonicity agent
4.	Span 80 (sorbitan monooleate)	0.37%	0.40%	0.42%	Primary surfactant
5.	Cholesterol	9.94%	9.94%	9.94%	Stabilizes the vesicular bilayer
6.	Dicetyl phosphate (DCP; negative charge inducer)	0.35%	0.35%	0.35%	Improves zeta stability and prevents aggregation
7.	Acetate buffer, pH 5.5	Ad 100	Ad 100	Ad 100	Hydration medium

Table 1 presents the niosomal transdermal delivery formulations containing a combination of kojic acid and alpha-arbutin with three Span 80 concentrations: F1 (0.37%), F2 (0.40%), and F3 (0.42%).

Preparation of the Niosomal Transdermal Delivery System

1. Preparation of the Aqueous Phase

Kojic acid (1%) and alpha-arbutin (2%) were accurately weighed and dissolved in acetate buffer at pH 5.5. Glycerol (5%) was then added as both a humectant and an isotonicity agent. The mixture was stirred using a magnetic stirrer until a clear and homogeneous solution was obtained [6].

2. Preparation of the Lipid Phase

Span 80 was measured at different volumes for each formulation: 0.111 mL for F1, 0.120 mL for F2, and 0.126 mL for F3. Cholesterol (0.3 mL) was then added, followed by dicetyl phosphate (DCP) at 0.01 mL. All lipid components were dissolved in absolute ethanol without heating. The mixture was homogenized using a vortex mixer until all components were completely dissolved. If necessary, brief sonication was performed at room temperature to facilitate dissolution while preventing a substantial increase in temperature [5].

3. Niosome Formation (Ethanol Injection Method)

The ethanolic lipid solution was slowly injected into the aqueous phase using a syringe while the aqueous phase was vigorously stirred with a magnetic stirrer at room temperature. The solution was added rapidly in a dropwise manner to promote spontaneous niosomal vesicle formation resulting from the polarity difference between the organic and aqueous phases. After injection was completed, stirring was continued for 15-20 minutes until a stable and uniformly dispersed niosomal system was obtained [5].

4. Removal of Residual Ethanol

Residual ethanol was removed by continuing the stirring process in an open system under an airflow or under mild vacuum until the odor of ethanol was no longer detectable. This step was performed to ensure the safety and stability of the niosomal preparation [5].

5. Particle-Size Reduction

The resulting niosomal dispersion was subjected to particle-size reduction using a probe sonicator in pulse mode, for example, 10 seconds of sonication followed by a 20-second pause. The container was placed in an ice bath during sonication to prevent temperature increases that could compromise active-compound stability. Sonication was continued until nanometer-scale particles with a polydispersity index (PDI) below 0.3 were obtained [5].

6. Storage

The prepared niosomal dispersion was stored in tightly closed amber glass bottles at 4°C until further characterization, including particle-size analysis, zeta-potential measurement, entrapment-efficiency determination, and stability testing [5].

Quality Evaluation of the Preparation

1. Organoleptic Evaluation

Organoleptic evaluation of the niosomal preparations was conducted by visual observation of appearance, color, odor, texture, and homogeneity (Zatalini et al., 2023). Sensory assessment of odor, texture, and color was performed using a scoring method based on hedonic-quality and hedonic tests. The evaluation involved 10 untrained panelists (students).

2. pH Evaluation

The pH was measured by immersing a calibrated pH-meter electrode into each test sample. The instrument was calibrated beforehand using standard buffer solutions. The analysis was conducted to determine whether the formulation pH was compatible with the physiological pH range of the skin (4.5-6.5) [5].

3. Viscosity Evaluation

Viscosity was measured using a Brookfield viscometer. The niosomal sample was placed in the test vessel, and viscosity was measured using an appropriate spindle at several rotational speeds, such as 12, 30, and 60 rpm. Values were recorded in mPa·s, and each measurement was performed in triplicate to obtain the mean. This evaluation was important for assessing ease of topical application and the physical stability of the niosomal preparation [5,6].

4. Stability Evaluation

Stability testing was conducted by storing the niosomal samples at 4°C, 25°C, and 40°C for a specified period. The samples were placed in a climatic chamber under controlled conditions. The results were used to assess the physical stability of the preparations during storage assessing ease of topical application and the physical stability of the niosomal preparation [5,6].

5. Irritation Test

The irritation test involved 10 volunteers. The inclusion criteria were students aged 20-55 years. The test preparation was applied to the upper arm for 4 hours. After removal, skin reactions were evaluated at 24, 48, and 72 hours. During the observation period, volunteers were permitted to rinse the application site with water but were instructed not to use soap, detergent, or cosmetic products assessing ease of topical application and the physical stability of the niosomal preparation [5,6].

Niosome Characterization

1. Particle Size and Polydispersity Index (PDI)

Niosomal particle size was determined by dynamic light scattering (DLS) using a particle size analyzer. The niosomal samples were diluted with purified water until an appropriate light-scattering intensity was obtained. Measurements were performed at 25°C. The results were expressed as the mean particle diameter (nm) and PDI, which reflects the homogeneity of the particle-size distribution. Measurements were conducted in triplicate. The target critical quality attributes (CQAs) were a particle size below 1,000 nm and a PDI below 0.500, which were considered indicative of acceptable niosomal quality.

2. Zeta-Potential Measurement

Zeta potential was determined electrophoretically using a Zetasizer. Surface-charge analysis is essential for predicting the long-term physical stability, in vivo performance, and biological fate of niosomal carriers. Niosomes with a high positive or negative surface charge generally exhibit less aggregation than neutral or weakly charged vesicles. Surface charge governs electrophoretic mobility and alters the intensity of scattered light. The samples were diluted and transferred into specialized cuvettes, after which the instrument measured particle mobility in an electric field. Zeta-potential values above +30 mV or below -30 mV are generally indicative of highly stable niosomal dispersions.

Data Analysis

The test results were expressed as mean ± standard deviation (SD). Statistical analysis was performed using one-way analysis of variance (one-way ANOVA) to

identify differences among the formulations. When a significant difference was detected ($p < 0.05$), Fisher's least significant difference (LSD) post hoc test was performed for pairwise comparisons. If the assumptions of normality or homogeneity were not met, the nonparametric Kruskal-Wallis test was used, followed by the Mann-Whitney test. All analyses were conducted at a 95% confidence level.

3. Results and Discussion

Niosomal Formulation Containing Kojic Acid and Alpha-Arbutin

In this study, niosomes were formulated with a combination of kojic acid and alpha-arbutin as the active compounds and varying concentrations of Span 80 as the vesicle-forming nonionic surfactant. Kojic acid and alpha-arbutin were selected because they act as skin-lightening agents by inhibiting tyrosinase and thereby reducing melanin formation [4,13,14]. Span 80 was used because its low hydrophilic-lipophilic balance (HLB) promotes the formation of stable vesicular bilayers and may enhance the penetration of active compounds through the skin. Cholesterol increases the stability and rigidity of the bilayer membrane, whereas dicetyl phosphate (DCP) serves as a charge inducer that prevents vesicle aggregation through electrostatic repulsion. Glycerol functions as a humectant, and acetate buffer at pH 5.5 maintains formulation stability and compatibility with the physiological pH of the skin [10,15].

Organoleptic Evaluation

The organoleptic properties of the niosomal formulations containing kojic acid and alpha-arbutin were evaluated by directly observing their color, physical form, odor, and homogeneity.

Table 2. Results of the Organoleptic Evaluation

Sample	Color	Texture	Odor	Uniformity
F1	Cloudy white	Liquid	Characteristic odor	Homogeneous
F2	Cloudy white	Liquid	Characteristic odor	Homogeneous
F3	Cloudy white	Liquid	Characteristic odor	Homogeneous

Source: Processed primary data, 2026

As shown in Table 2, all niosomal formulations containing kojic acid and alpha-arbutin (F1, F2, and F3) exhibited identical organoleptic characteristics: a cloudy-white appearance, liquid consistency, characteristic odor, and homogeneous dispersion. The cloudy-white appearance is characteristic of niosomal systems formed by the dispersion of Span 80 and cholesterol bilayer vesicles in an aqueous phase. All formulations demonstrated favorable and stable physical characteristics, as indicated by the absence of visible phase separation or particle aggregation. These uniform characteristics suggest that the tested Span 80 concentrations were capable of producing stable and homogeneous vesicular systems. Organoleptically, niosomal preparations generally appear as milky-white to cloudy-white colloidal dispersions with a homogeneous consistency, depending on the surfactant type, cholesterol concentration, and properties of the incorporated active compounds. Therefore, all

formulations met the expected physical characteristics of a niosome-based delivery system [7].

Viscosity Evaluation

Viscosity was evaluated to determine the consistency of the niosomal formulations containing kojic acid and alpha-arbutin, because this property may influence flow behavior, physical stability, and ease of application. Measurements were performed at 60 rpm [7].

Table 3. Results of the Viscosity Evaluation

Speed (rpm)	Viscosity (cP)		
	F1	F2	F3
60 rpm	11.3333 ± 0.65	12.6667 ± 0.65	13.3333 ± 1.35

Source: Processed primary data, 2026

As presented in Table 3, the viscosity values of the niosomal formulations containing kojic acid and alpha-arbutin were 11.3333 ± 0.65 cP for F1, 12.6667 ± 0.65 cP for F2, and 13.3333 ± 1.35 cP for F3. These results indicate that all formulations were liquid preparations with relatively low viscosity. The higher viscosity values observed for F2 and F3 were associated with the increased Span 80 concentration. Increasing the concentration of the nonionic surfactant may promote the formation of a greater number of bilayer vesicles, strengthen intermolecular interactions, and consequently increase resistance to flow within the dispersion. Nevertheless, all formulations retained the favorable flow characteristics expected of a liquid vesicular system. Previous studies have reported that niosomal viscosity is influenced by surfactant and cholesterol composition, both of which contribute to bilayer formation and membrane stability. Thus, the increased viscosity of F2 and F3 suggests the formation of a more stable vesicular system without compromising the principal characteristics of a liquid niosomal delivery system [5].[5]

pH Evaluation

The pH evaluation was conducted to determine the acidity of the niosomal formulations containing kojic acid and alpha-arbutin and to ensure their suitability for application to the skin. pH is an important parameter that may affect vesicle stability, active-compound stability, and skin compatibility.

Table 4. Results of the pH Evaluation

Sample	pH Value
F1	5.0
F2	5.3
F3	5.5

Source: Processed primary data, 2026

As shown in Table 4, the pH values of the niosomal formulations containing kojic acid and alpha-arbutin were 5.0 for F1, 5.3 for F2, and 5.5 for F3. The three formulations therefore exhibited relatively similar pH values within the physiological skin-pH range of 4.5-6.5. The variation in formulation composition did not

substantially affect acidity. A pH close to the physiological pH of the skin is expected to minimize irritation and improve the safety and comfort of topical application.

Furthermore, pH strongly influences the stability of the kojic acid and alpha-arbutin combination. Kojic acid is more stable under acidic to mildly acidic conditions, whereas an increase in pH may promote oxidation and degradation, which can be indicated by color changes and reduced active-compound activity. These findings are consistent with reports that niosomal formulations for dermatological and cosmetic applications are generally developed at a pH close to that of the skin to maintain product stability and minimize irritation. Therefore, all formulations met the expected pH requirements for topical preparations [3,11].

Stability Evaluation

Stability testing was performed to identify changes in the quality of the niosomal formulations containing kojic acid and alpha-arbutin during storage at different temperatures. Organoleptic properties, pH, and viscosity were evaluated to assess physical stability at 4°C, 25°C, and 40°C.

Table 5. Results of the Stability Evaluation

Form.	Temp. (°C)	Color	Odor	Tex.	pH	Visc. (cP)
F1	4	Slightly cloudy	Characteristic odor	Liquid	6	12.0000
	25	Cloudy white	Characteristic odor	Liquid	5	12.0000
	40	Cloudy white	Characteristic odor	Liquid	5	11.3333
F2	4	Slightly cloudy	Characteristic odor	Liquid	6	12.0000
	25	Cloudy white	Characteristic odor	Liquid	5	12.0000
	40	Cloudy white	Characteristic odor	Liquid	5	11.5667
F3	4	Slightly cloudy	Characteristic odor	Liquid	6	15.3333
	25	Cloudy white	Characteristic odor	Liquid	5	12.6667
	40	Cloudy white	Characteristic odor	Liquid	5	11.3333

Source: Processed primary data, 2026

As shown in Table 5, all niosomal formulations containing kojic acid and alpha-arbutin remained organoleptically stable during storage at 4°C, 25°C, and 40°C. F1, F2, and F3 showed no substantial changes in color, odor, or texture, indicating favorable physical stability. The formulations maintained the characteristics of a cloudy-white, characteristically scented, liquid dispersion. Their pH values remained within the range of 5-6, which is compatible with physiological skin pH and is considered suitable for topical use. At 4°C, the pH tended to be higher (pH 6), whereas at 25°C and 40°C it decreased to pH 5; however, these values remained within an acceptable range [8].[8]

Viscosity was the parameter most strongly affected by storage temperature. All formulations exhibited decreased viscosity as temperature increased. This reduction may be attributed to increased fluidity of the niosomal bilayer membrane and weakened intermolecular interactions within the dispersion at higher temperatures. Nevertheless, F3 maintained the highest viscosity among the formulations, suggesting that a higher Span 80 concentration may increase consistency and support physical stability. Overall, all three formulations demonstrated favorable physical stability under the tested storage conditions.

Irritation Test

The irritation test was conducted to determine whether the niosomal formulations containing kojic acid and alpha-arbutin caused skin irritation. A patch-test method was applied to 10 healthy panelists, and itching, swelling, erythema, and burning or warmth were observed at 24, 48, and 72 hours.

Table 6. Results of the Irritation Test

Time	Reaction				n
	Itching	Swelling	Erythema	Burning/Warmth	
24 h	-	-	-	-	10
48 h	-	-	-	-	10
72 h	-	-	-	-	10

Source: Processed primary data, 2026

As shown in Table 6, the niosomal formulations containing kojic acid and alpha-arbutin produced negative irritation-test results. No itching, swelling, erythema, or burning sensation was observed in any panelist during the 72-hour observation period. The absence of irritation indicates favorable skin safety and tolerability. This finding is consistent with reports that niosomes composed of nonionic surfactants and biocompatible components have low irritation potential and are suitable for topical delivery [5].[5]

Particle Size and Polydispersity Index (PDI)

Particle size and polydispersity index (PDI) were evaluated to determine niosomal vesicle size and the uniformity of the particle-size distribution. Particle size is an important parameter influencing active-compound penetration and distribution, whereas PDI reflects the uniformity of particles within a dispersion.

Table 7. Particle-Size and PDI Results

Formulation	Particle Size	PDI
F1	185.1 nm	0.273
F2	372.9 nm	0.295
F3	322.6 nm	0.118

Source: Processed primary data, 2026

As presented in Table 7, the particle sizes of F1, F2, and F3 were 185.1 nm, 372.9 nm, and 322.6 nm, respectively. All formulations met the acceptable niosomal particle-size criterion of less than 1,000 nm. The PDI values of F1, F2, and F3 were 0.273, 0.295, and 0.118, respectively, indicating homogeneous particle-size distributions because all values were below 0.500. Differences in particle size among the formulations may have resulted from variation in the concentration of Span 80 as the nonionic bilayer-forming surfactant. Increasing surfactant concentration may affect vesicle formation and stability, thereby producing different particle sizes. F3 exhibited the lowest PDI (0.118), indicating the most uniform particle-size distribution. Although F1 had the smallest particle size, F3 demonstrated the most favorable overall niosomal characteristics because it maintained a nanoscale particle size with the highest distribution uniformity [7,10,15].

Zeta-Potential Evaluation

Zeta potential was evaluated to determine the electrostatic stability of the niosomal systems. This parameter reflects the magnitude of repulsive forces among particles within the dispersion and can therefore be used to predict physical stability.

Table 8. Zeta-Potential Results

Formulation	Zeta Potential
F1	-18.5 mV
F2	-23.0 mV
F3	-18.4 mV

Source: Processed primary data, 2026

As shown in Table 8, the zeta-potential values of F1, F2, and F3 were -18.5 mV, -23.0 mV, and -18.4 mV, respectively. All formulations exhibited negative zeta-potential values, indicating a negative charge on the surface of the niosomal vesicles. Zeta-potential values above +30 mV or below -30 mV generally indicate strong electrostatic stability. Although the values obtained in this study did not reach these thresholds, all formulations still demonstrated acceptable stability [7,15]. The negative surface charge was attributable to dicetyl phosphate (DCP), which acts as a charge inducer, increases electrostatic repulsion among vesicles, and thereby reduces aggregation. F2 had the highest absolute zeta-potential value (-23.0 mV), indicating greater electrostatic stability than F1 and F3. Overall, the zeta-potential results suggest that all formulations possessed favorable physical characteristics and the potential to form stable niosomal systems [7,15].

Statistical Analysis

One-way ANOVA was used to determine the effect of Span 80 concentration on the viscosity and pH of the niosomal formulations.

Table 9. Statistical Analysis Results

Parameter	Test	p-value	Significant Difference	Summary
Viscosity (60 rpm)	One-Way ANOVA	0.089	None	Similar viscosity across F1-F3
pH	One-Way ANOVA	0.791	None	Similar pH across F1-F3

Source: Processed primary data, 2026

As shown in Table 9, the significance value for viscosity was p = 0.089 (p > 0.05), indicating no statistically significant difference among F1, F2, and F3. Nevertheless, a descriptive increase in viscosity was observed as Span 80 concentration increased. A higher surfactant concentration may enhance interactions among vesicles and thereby increase resistance to flow within the dispersion. However, the relatively small differences in Span 80 concentration were likely insufficient to produce statistically significant changes in viscosity [9].[9]

For pH, one-way ANOVA yielded a significance value of p = 0.791 (p > 0.05), indicating no statistically significant difference among the niosomal formulations. The relatively uniform pH values were likely attributable to the acetate buffer, which maintained system pH during formulation and storage (Zbacnik et al., 2017). Moreover, Span 80 is a nonionic surfactant and therefore has minimal influence on system pH. Thus, variation in Span 80 concentration did not significantly affect the viscosity or pH of the three niosomal formulations.

4. Conclusion

The results demonstrate that variation in Span 80 concentration influenced the physical and physicochemical characteristics of niosomes containing kojic acid and alpha-arbutin. All formulations were stable, homogeneous, and met the expected characteristics of niosomal systems. Formula III was identified as the optimal formulation based on particle size, PDI, stability, and safety for application to the skin.

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