Optimization of Tween 80 and Span 80 Combination in the Formulation of Niacinamide-Containing Body Lotion

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ABSTRACT

Body lotion is a liquid emulsion preparation consisting of an oil phase and a water phase stabilized by emulsifiers, functioning to maintain skin moisture and provide protection. One of the most widely used active ingredients in current cosmetic formulations is niacinamide, known for its effectiveness in brightening the skin, enhancing the skin barrier function, and reducing hyperpigmentation. The success of a body lotion formulation depended largely on the appropriate selection and concentration of emulsifiers to achieve emulsion stability and optimal physical characteristics. This study aimed to optimize the combination of Tween 80 and Span 80 emulsifiers in a body lotion formulation containing niacinamide using a 2^2 factorial design method with the assistance of Design-Expert software. The formulation was evaluated based on several physical parameters, including pH, adhesiveness, spreadability, viscosity, homogenity, emulsion type, and physical stability. Optimization results indicated that the best formulation was obtained from a combination of 10% Tween 80 and 1% Span 80. The resulting product had a pH of 6.4, adhesiveness of 112 seconds, spreadability of 6.1 cm, viscosity of 16,568.3 cps, good homogenity, and demonstrated a stable oil-in-water (O/W) emulsion type without phase separation. Therefore, the optimum combination of Tween 80 and Span 80 in concentrations of 1% and 10%, respectively, yields a physically stable niacinamide-containing body lotion.

Keywords: Body lotion, niacinamide, tween 80, span 80, design-expert.

INTRODUCTION

The growing public awareness of the importance of skin health care is one of the main factors driving the increasing demand for cosmetic skincare products (Megantara et al., 2017). The skin is not indefinitely resistant to climate conditions and environmental temperatures. Exposure to sunlight and polluted air can generate free radicals, which are harmful to the skin. Free radicals are strong oxidizing agents that can damage the body's defense systems, leading to cellular damage and premature aging. Excessive free radicals can also degrade lipid compounds, reducing skin elasticity and resulting in dry and dull skin (Oktaviana et al., 2021).

Dry skin is a common dermatological issue, especially in tropical regions like Indonesia. However, many individuals underestimate the consequences of prolonged untreated dry skin, often considering it a minor concern. Several factors contribute to dry skin, including dehydration, reduced sebum production, surface roughness, and diminished skin hydrophilicity. Environmental conditions, aging, and inappropriate skincare product use also play significant roles. Among these, skin dehydration is considered the most dominant factor, thus requiring appropriate skin care measures (Butarbutar & Chaerunisaa, 2021).

Proper skin care is essential to prevent dryness, roughness, and dullness. Naturally, the skin is protected by a thin lipid layer produced by sebaceous glands, which helps prevent excessive water loss and maintains hydration (Oktaviana et al., 2021). In recent years, extensive research has focused on developing innovative cosmetic products to address dry skin conditions. One of the most effective solutions is the use of moisturizers, which are designed to enhance skin hydration. Among commercially available moisturizers, body lotions are widely used (Butarbutar & Chaerunisaa, 2021).

Body lotion is a liquid emulsion consisting of oil and water phases stabilized by emulsifiers, functioning to protect and maintain skin moisture. It is favored for its ease of application and suitability for covering large skin areas compared to creams or ointments, which are typically used for localized application. Its fluid consistency allows for quick and even distribution on the skin surface, promoting rapid absorption and improved moisturization (Megantara et al., 2017). One of the active ingredients commonly used in skincare products is niacinamide.

Niacinamide, also known as vitamin B3 or nicotinamide, is a water-soluble vitamin with numerous skin benefits. It helps to reduce and tighten pores, even out skin tone, brighten dull skin, fade signs of aging, prevent acne, and protect the skin from harmful UV radiation. Due to these properties, niacinamide has become one of the most sought-after and widely used active ingredients in modern skincare formulations (Hartini & Haqq, 2023). Achieving an optimal and stable lotion formulation requires careful selection and combination of emulsifiers (Astuti & Dita, 2020).

Emulsifiers are added to reduce the coalescence of dispersed droplets in the continuous phase. These surfactants stabilize emulsions by forming a physical barrier around droplets and reducing interfacial tension, thereby enhancing emulsification during mixing. Typically, emulsifiers are used at concentrations of 5% to 20% of the oil phase weight. Commonly used emulsifiers in body lotion formulations include Tween 80 and Span 80 (Rusmin, 2021).

Tween 80, with a hydrophilic-lipophilic balance (HLB) value of 15, and Span 80, with an HLB value of 4.3, are non-ionic emulsifiers that provide a balance between lipophilic and hydrophilic properties. Combining surfactants often results in more stable emulsions than using a single surfactant (Bagiana, 2015). The recommended concentration for Tween 80 and Span 80 in oil-in-water emulsions is typically between 1% and 10%. This combination improves emulsion consistency and enhances physical stability. To determine the optimum formulation, a factorial design method can be employed (Wikantyasning & Indianie, 2021).

A factorial design is a statistical method using regression equations to model the relationship between response variables and one or more independent variables. It is a commonly used experimental design in process optimization, enabling researchers to identify the effects and interactions of multiple variables (Hidayat et al., 2021).

Based on the aforementioned background, this study aims to optimize the combination of Tween 80 and Span 80 in the formulation of a body lotion containing niacinamide.

METHODS

Materials

The equipment used in this study included an analytical balance, measuring cylinder, porcelain dish, horn spoon, parchment paper, dropper pipette, stirring rod, spreadability tester, watch glass, microscope slide, pH meter, viscometer, mortar, stamper, spatula, ruler, and body lotion containers. The materials used in this study were niacinamide, olive oil, Tween 80, Span 80, propylene glycol, DMDM hydantoin, phenoxyethanol, vitamin E, and distilled water (aquadest).

Methods

A body lotion formulation containing niacinamide was developed. The composition of the formulation was optimized using the Design Expert® version 13 software. The concentration range of Tween 80 and Span 80 used in this study was 1–10%, as recommended by Rowe et al. (2009). These concentration ranges served as the reference in determining the optimum formula through a factorial design approach in Design Expert® version 13. Based on the input data, a total of 12 formulations were generated, evaluated using three response parameters: viscosity, spreadability, and adhesiveness (Ittiqo & Anderiani, 2017).

Table 1. Independent and Dependent Variables in the 2^2 Factorial Design for Optimum Formula Determination

Experimental Variables	**Limitation**		
Dependent	**Lower Limit**	**Upper Limit**	**Targets**
Tween 80	1%	10%	In range
Span 80	1%	10%	In range
Independent			
Viscosity	200 cps	50000 cps	Minimize
Spreadability	3 cm	7 cm	Maximize
Adhesion	4 s	300 s	Maximize

The composition of the optimum Body Lotion formulation is presented in Table 2.

Table 2. Design of Body Lotion Formulation

Ingredients	Functions	Concentrations (%)*			
		1	2	3	4
Niacinamide	Active Ingredients	4	4	4	4
Olive oil	Oil Phase	12,5	12,5	12,5	12,5
Tween 80	Emulsifier	1	10	1	10
Span 80	Emulsifier	10	10	1	1
Propylene Glycol	Humectant	10	10	10	10
DMDM Hydantoin	Preservative	1	1	1	1
Phenoxy ethanol	Preservative	1	1	1	1
Vitamin E	Antioxidant	0,05	0,05	0,05	0,05
Distilled Water	Solvent	Ad 100	Ad 100	Ad 100	Ad 100

** Each formulation was replicated three times*

The lotion formulation was prepared by melting the oil phase, which consisted of Span 80, in a porcelain dish. It was heated separately and melted at 70°C using a water bath. The aqueous phase, consisting of Tween 80, propylene glycol, DMDM hydantoin, and one-third of the total amount of distilled water, was also placed in a separate porcelain dish and melted at 70°C in a water bath. A warm mortar was prepared by filling it with hot water and immersing the pestle in it. Once the outer surface of the mortar felt warm to the touch, the water was discarded. Put the oil phase (mixture 1) into the hot mortar while stirring with rapid and constant stirring until the preparation is homogeneous. Put the water phase (mixture 2) into the oil phase in the mortar little by little, do rapid stirring until homogeneous and forms a good lotion mass. Add the remaining distilled water (2/3 parts) little by little while continuing to stir until homogeneous until the desired volume (Kristianingsih, 2022).

Evaluation of Body Lotion Formulation

Organoleptic Test

This test is conducted by visually observing the physical appearance of the formulation, including its shape, color, and odor (Kristianingsih, 2022).

Homogenity Test

This test aims to assess how well the ingredients in the lotion formulation are uniformly mixed. Approximately 1 gram of each lotion sample is applied onto a piece of glass or other transparent material. A homogeneous formulation is indicated by the absence of coarse granules when the lotion is spread over the glass surface (Noer & Sundari, 2016).

pH Test

The pH test is performed to determine whether the body lotion formulation is acidic or basic. Topical formulations that are too acidic may irritate the skin, whereas those that are too basic can cause dryness and flakiness. The acceptable pH range for skin moisturizers is 4.5–8.0 (Rahayu, 2016).

Spreadability Test

This test aims to determine whether the active ingredient is evenly dispersed on the skin, thereby maximizing therapeutic effect (Amatullah et al., 2017). The acceptable spread diameter for lotion formulations is between 5 cm and

7 cm (Salsabila et al., 2021). A total of 1 gram of the lotion sample is placed at the center of a diameter-marked glass plate. Another glass plate or transparent material is placed on top, followed by specific weights of 50 grams, 100 grams, and 150 grams. After 1 minute, the spread diameter is recorded (Kristianingsih, 2022).

Adhesion Test

A sample of 0.25 grams is placed between two object glasses and pressed with a 1 kg weight for 5 minutes. After removing the weight, the object glass is mounted on a testing device. An 80-gram weight is applied, and the time it takes for the sample to detach is recorded (Suena et al., 2017).

Viscosity Test

Viscosity is measured using a Brookfield LV Viscometer. The formulation is placed in a cup, and spindle No. 4 is used. The rotor operates at a speed of 30 rpm. According to Indonesian National Standard (SNI 16-4399-1996), the acceptable viscosity range for lotion is between 2000–50000 centipoise (cP) (Rahayu, 2016).

Stability Tests

Cycling Test

Stability testing is conducted using a cycling test method for 6 cycles over 12 days. The initial step involves storing the sample at 4°C for 24 hours, followed by placement in an oven at 40°C for another 24 hours. This constitutes one cycle. The process is repeated for a total of 6 cycles, with organoleptic observations (color, odor, and shape) made during each cycle. A cosmetic product is considered stable if it maintains its characteristics during storage and usage as it had when freshly prepared (Hamdhani et al., 2023). Additionally, the lotion is monitored for physical stability over 4 weeks, including organoleptic properties, pH, viscosity, adhesion, and spreadability (Labibah & Zulkarnain, 2023).

Phase Separation Test

A 5 g sample of the lotion is weighed and placed in a centrifuge tube, then centrifuged at 3750 rpm for 5 hours or at 5000–10000 rpm for 30 minutes. This test determines whether the formulation undergoes phase separation (Pratasik et al., 2019).

RESULTS AND DISCUSSION

Optimization of Body Lotion Formulation

Optimization was carried out to facilitate the arrangement and mathematical interpretation of data obtained from the test results. The optimization method used was a 2^2 factorial design to determine the dominant effects influencing the physical properties of the body lotion formulation and to identify the optimal formula from the combination of Tween 80 and Span 80. The data entered into the Design Expert software resulted in 4 formulas, each with 3 replications. The percentage values of each factor produced 12 formula runs, and 12 formulations were prepared based on these runs. The variables entered, along with their upper and lower limits, included Tween 80 (1–10%) and Span 80 (1–10%). The responses measured were viscosity (200–50000 cps), adhesion (2–300 seconds), and spreadability (3–7 cm).

The number of trials in the factorial design was 2^n, where 2 represents the number of levels (high and low) and *n* is the number of factors. The data entered into the Design Expert software using the 2^2 factorial design method produced 4 formulas with 3 replications each. The percentage values of each factor generated 12 formula runs, and 12 formulations were subsequently prepared according to these runs. The responses from each formula, including viscosity, spreadability, and adhesion, were then evaluated. These responses are the factors that may affect the quality characteristics of the body lotion formulation. The results of the response measurements from the 12 formula runs evaluated can be seen in Table 3.

Table 3. Results of Viscosity, Adhesion, and Spreadability Measurements

Run	Factors		Responses		
	Tween 80 (%)	Span 80 (%)	Viscosity (cps)	Spreadability (cm)	Adhesion (s)
1	1	10	17251.8	6.5	135
2	10	1	22918.3	5	155
3	10	1	1758.12	5.5	128
4	10	10	1806.32	6.5	120
5	10	1	22086.4	5.5	146
6	10	10	15942.7	5.5	120
7	10	10	15347.1	6.5	112
8	1	1	20981.5	5	67
9	1	1	21992.4	5	134
10	1	10	20743.8	5.5	68
11	1	1	21034.9	6.5	45
12	1	10	16408.2	5.5	103

The most optimal formula is the one with the highest desirability value. Desirability is a function value used for optimization purposes, indicating the program's ability to meet the desired outcomes based on the predefined criteria of the final product. A desirability value approaching 1.0 signifies that the program's ability to produce the desired product is increasingly ideal (Ramadhani et al., 2017) The Design Expert® application generated five formula options, from which the first formula was selected as the most optimal, having the highest desirability value of 0.559, as shown in Table 4.

Table 4. Formula Solutions Based on Desirability Values

Tween 80 (%)	Span 80 (%)	Viscosity (cps)	Spread ability (cm)	Adhesion (s)	Desirability
10.000	**1.000**	**10138.964**	**6.048**	**121.952**	**0.559**
10.000	1.095	10218.698	6.043	121.931	0.558
9.783	1.000	10278.185	6.042	121.704	0.557
8.932	1.000	10822.409	6.022	120.732	0.550
8.775	1.000	10923.271	6.018	120.552	0.548

The results in Table 4 indicate that the optimal formula has a desirability value of 0.559, with a Tween 80 concentration of 10.000% and a Span 80 concentration of 1.000%. These values fall within the 1–10% range used in the optimization formulation. Desirability is a target value in an optimization process, ranging from 0 to 1, where higher values indicate a better match to the desired outcome. The predicted responses from Design Expert® for this formula include a viscosity of 10,138.964 cps, a spreadability of

6.048 cm, and an adhesion time of 121.952 seconds. Among the five proposed formulas, the first was selected due to its desirability value and its viscosity, which is appropriate for a body lotion formulation and also relevant to the formulation's stability. Interaction and contour plots illustrate how the responses vary depending on the levels of the factors applied.

Viscosity Response

Based on the contour plot in Figure 1, it can be observed that increasing the amount of either Tween 80 or Span 80 leads to an increase in the viscosity of the formulation. The transition from blue to red areas indicates regions of low to high viscosity. The use of Tween 80 and Span 80 contributes to an increase in the cream's viscosity. Tween 80 is hydrophilic; at higher concentrations, it binds the water phase in the cream, resulting in a formulation with higher viscosity. Similarly, increasing the concentration of Span 80 also raises the viscosity. This occurs because Span 80 can absorb more water molecules from the cream, thereby increasing its viscosity (Sandhi et al., 2022).

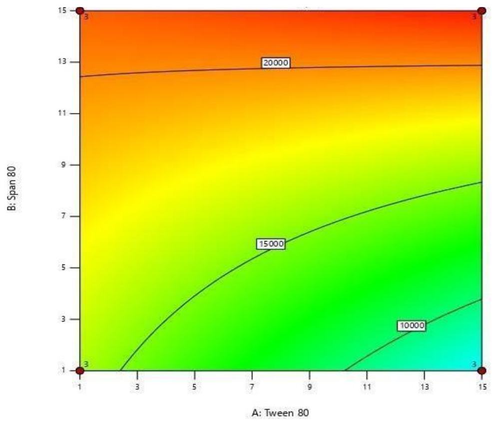

Figure 1. Contour plot of Viscosity

Spreadability Response

Based on the contour plot in Figure 2, it can be seen that higher concentrations of Tween 80 and Span 80 can increase the spreadability of the formulation. The blue area indicates a low level of Tween 80, while the red lines indicate a high level of Span 80. As the concentration of Tween 80 increases, the spreadability of the cream also increases, as reflected by the transition from red to blue in the contour plot, which indicates the most significant change in spreadability. Lower concentrations of Tween 80 result in higher spreadability, whereas higher concentrations of Span 80 tend to decrease spreadability, as shown in the green-colored regions of the plot. Tween 80 is hydrophilic and binds to the water phase, allowing more water molecules to be retained in the cream, thereby enhancing the spreadability of the formulation (Oktavia, 2008).

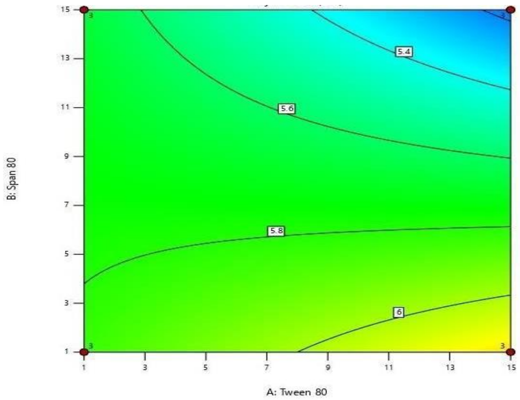

Figure 2. Contour Plot of Spreadability

Adhesion Response

Based on the contour plot in Figure 3, it can be observed that increasing the concentration of Tween 80 enhances the adhesiveness of the formulation. However, increasing the concentration of Span 80 decreases its adhesiveness. The transition from blue to red regions in the contour plot represents areas of low to high adhesiveness. This phenomenon may be influenced by the viscosity of the formulation, where higher viscosity causes the formulation to remain in place longer and flow less easily, thereby increasing its adhesiveness.

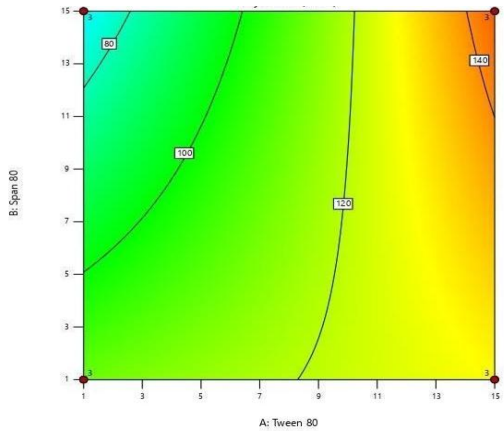

Figure 3. Contour plot of Adhesion

The next step in the optimization process involved testing the formulation using the obtained optimum formula to verify the response based on experimental results and software predictions. The predicted values were: viscosity of 10,138.964 cps, spreadability of 6.048 cm, and adhesiveness of 121.952 seconds. The experimental results were considered acceptable, as they fell within the upper and lower limits defined by the Design Expert® software. The confirmation data are presented in Table 5.

Table 5. Confirmation of Experimental Design Results

Analysis	Predicted mean value	Experimental mean Value	95% Prediction Index	
			Low	High
Viscosity	16522.6	16526.7	9851.77	23193.5
Spreadability	5.7	5.8	4.84894	6.56773
Adhesion	114	112	89.7458	138.254

Two-sided Confidence = 95%

The interaction between Tween 80 and Span 80 in the moisturizing cream formulation is expected to produce the desired optimum formulation. After the Design Expert® software generated the optimum formula based on the experimental design, the formulation was prepared accordingly using the specified composition. The details of the optimum formulation are presented in Table 6.

Table 6. Optimum Body Lotion Cream Formula Based on Design Expert® Optimization

Ingredients	Concentrations (%)
Niacinamide	4
Olive Oil	12,5
Tween 80	10
Span 80	1
Propylene Glycol	10
DMDM Hydantoin	1
Phenoxyethanol	1
Vitamin E	0,05
Distilled Water	Ad 100

Physical Stability Test of the Optimum Body Lotion Formula

Cycling Test

The physical stability test of the optimum body lotion formulation was conducted using the cycling test method over six cycles. The evaluation parameters included organoleptic properties, pH, viscosity, spreadability, adhesiveness, and homogenity. The results of the stability test are presented in Table 7.

Table 7. Stability Test Results of the Optimum Body Lotion Formula

No	Tests	Stability Tests	
		Before	After
1	Organoleptic	White, characteristic odor, thick	White, characteristic odor, thick
2	pH	6,2	6,4
3	Viscosity	16526.7 cps	16568.3 cps
4	Spreadability	5,8 cm	6,1 cm
5	Adhesion	112,3 s	112 s
6	Homogenity	Homogen	Homogen

The formulation was examined and found to have a characteristic odor, white color, thick consistency, and no phase separation. Observations showed no changes in organoleptic properties before and after the cycling test.

The pH evaluation of the moisturizing cream formulation was carried out to determine the acidity level of the preparation. If the cream formulation has a pH that is too alkaline, it may cause the skin to become scaly. Conversely, if the pH is too acidic, it may cause skin irritation. The measurement results based on Table 6 show that the average pH of the formulation after the cycling test indicated a change in pH, which, according to the theory, can be caused by chemical changes in the active ingredients or excipients in the formulation, the influence of the storage container, and environmental factors. The measured pH of the cream formulation was still within the ideal pH range for creams. The ideal cream pH corresponds to the skin's natural pH (Thomas et al., 2024). A good and non-irritating formulation will have a pH within the normal skin range of 4.5–6.5 (Unique, 2018).

Viscosity is a measure of a liquid formulation's resistance to flow and is a critical parameter in determining emulsion stability. An increase in the volume of the cream formulation typically leads to higher viscosity, which enhances stability by limiting the mobility of dispersed particles within the thicker matrix. According to SNI 16-4399-1996 regarding quality standards for cream preparations, good cream viscosity ranges between 2000–50,000 cps (Thomas et al., 2024). The test results showed a viscosity value of 16,526.7 cps before the cycling test, which increased to 16,568.3 cps after the test. This is due to the use of Tween 80 and Span 80 in the formulation. Tween 80 is hydrophilic and, at high concentrations, can bind water in the cream composition, resulting in a formulation with higher viscosity (Sandhi et al., 2022).

The spreadability test was conducted to determine the ability of the formulation to spread on the skin, where a formulation should ideally have good spreadability to ensure effective and even application. The formulation met the requirements for good spreadability, which fall within the range of 5–7 cm (Megantara et al., 2017). The broader the spreading area produced by the cream, the better its ability to spread when applied (Thomas et al., 2024). This occurs because creams with high spreading ability generally have optimal viscosity, meaning they are not too thick and can spread evenly over the skin surface with only light pressure. A wide spreading area indicates that the cohesive forces between the molecules in the cream are relatively low, while the adhesive forces between the cream and the skin surface are relatively high, allowing the cream to spread more easily and adhere to the skin (Lachman et al., 1976). Based on the test results, the spreadability value before the cycling test was 5.8 cm and increased to 6.1 cm after the cycling test. Thus, it can be concluded that the formulation meets the requirement for good spreadability, falls within the acceptable range, and is considered stable.

Adhesiveness serves to determine the ability of the formulation to adhere to the skin surface after application. A good cream should provide effective contact time with the skin to ensure optimal therapeutic effect. The adhesiveness test results before the cycling test showed an average value of 112.3 seconds, and after the cycling test, the value increased to 122 seconds. Therefore, it can be stated that all three replications met the criteria for semi-solid formulations with an adhesiveness range of 4–300 seconds. The relatively long adhesiveness of the formulation was due to its higher oil content, which allows for longer contact with the skin.

The homogenity test of the optimum formula showed homogeneous results if the texture and color are evenly distributed and free of clumps (Wardani et al., 2023). Based on the obtained results, the body lotion formulation was found to be homogeneous. Each formulation was observed to have good homogenity with no coarse particles present.

Phase Separation Test

The phase separation test was conducted to determine the instability indicated by phase separation in the formulation. This test aims to evaluate the durability and stability of the formulation against gravitational forces applied to the preparation after vigorous shaking. Centrifugation demonstrates the stability of the formulation over the equivalent of one year, as indicated by the absence of phase separation during centrifugation (Sari et al., 2021). The test was performed by centrifuging the body lotion formulation in a centrifuge tube at a speed of 50 rpm for 30 minutes. Based on the results, the formulation was stable, as no phase separation occurred. This was indicated by the absence of any liquid separating to form a layer above or below the formulation. The lack of phase separation after exposure to centrifugal force indicates that the formulation remained stable under stress conditions.

CONCLUSION

Based on the results of the study, it can be concluded that the optimal body lotion formulation containing niacinamide is obtained from a combination of 10% Tween 80 and 1% Span 80, as determined through analysis using the Design Expert® software. This formula demonstrated acceptable physical characteristics, including a viscosity of 16,568 cps, pH of 6.4, spreadability of 6.1 cm, adhesion time of 112 seconds, and favorable organoleptic appearance. The formulation also maintained good stability, as confirmed by phase separation and cycling tests conducted over six cycles, which included evaluation of organoleptic properties, viscosity, pH, spreadability, and adhesion.

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REFERENCES

Amatullah, L., Cahyaningrum, T. N., & Fidyaningsih, A. N. (2017). Antioxidants effectivity in skin lotion formulation of mesocarp fruit extract lontar (Borassus Flabellifer) against white rats wistar male in-situ. *JPSCR: Journal of Pharmaceutical Science and Clinical Research*, *2*(1), 25–34.

Astuti, R. N. D., & Dita, D. (2020). Formulasi Dan Evaluasi Hand And Body Lotion Ekstrak Daging Buah Labu Kuning (Cucurbita Moschata Duch.) Dengan Variasi Setil Alkohol Sebagai Emulgator. *Jurnal Kesehatan Farmasi*, 1–12.

Bagiana, I. S. I. K. (2015). Optimasi tween 80 dan span 80 dalam sediaan krim ekstrak etanol daun iler (coleus atropurpureus (l) benth) dan aktivitas antibakteri Staphylococcus aureus ATCC 25923. *Media Farmasi Indonesia*, *10*(2), 151299.

Butarbutar, M. E. T., & Chaerunisaa, A. Y. (2021). Peran pelembab dalam mengatasi kondisi kulit kering. *Majalah Farmasetika*, *6*(1), 56–69. https://doi.org/10.24198/mfarmasetika.v6i1.28740

Hamdhani, Saputri, M., Sudewi, & Margata, L. (2023). Formulation of Ethanol Extract for Peel Avocado (Persea Americana Mill.) as Foundation Cream. *Journal Pharmaceutical And Sciences*, *6*.

Hartini, T., & Haqq, B. N. (2023). Perancangan Animated Infographics Mengenai Fungsi Niacinamide untuk Kesehatan Kulit untuk generasi Z. *IKRA-ITH HUMANIORA: Jurnal Sosial Dan Humaniora*, *7*(1), 71–81.

Hidayat, I. R., Zuhrotun, A., & Sopyan, I. (2021). Design-expert software sebagai alat optimasi formulasi sediaan farmasi. *Majalah Farmasetika*, *6*(1), 99–120. https://doi.org/10.24198/mfarmasetika.v6i1.27842

Kristianingsih, I. (2022). Optimasi dan Karakterisasi Sediaan Body Lotion Ekstrak Etanol Daun Kelor (Moringa Oleifera L.) Menggunakan Tween 80 dan Span 80 Sebagai Emulgator. *Jurnal Pharma Bhakta*, *2*(2).

Labibah, K., & Zulkarnain, A. K. (2023). Optimasi Formula Dan Uji Aktivitas Secara In Vitro Lotion O/W Senyawa Kalkon Sebagai Tabir Surya. *JIIS (Jurnal Ilmiah Ibnu Sina): Ilmu Farmasi Dan Kesehatan*, *8*(1), 114–124.

Lachman, L., Lieberman, H. A., & Kanig, J. L. (1976). *The theory and practice of industrial pharmacy*. Lea & Febiger Philadelphia.

Megantara, I., Megayanti, K., Wirayanti, R., Esa, I. B. D., Wijayanti, N., & Yustiantara, P. S. (2017). Formulasi lotion ekstrak buah raspberry (Rubus rosifolius) dengan variasi konsentrasi trietanolamin sebagai emulgator serta uji hedonik terhadap lotion. *Jurnal Farmasi Udayana*, *6*(1), 1–5.

Noer, B. M., & Sundari, S. (2016). Formulasi Hand And Body Lotion Ekstrak Kulit Buah Naga Putih (Hylocereus undatus) dan Uji Kestabilan Fisiknya. *JPP (Jurnal Kesehatan Poltekkes Palembang)*, *11*(1), 101–113.

Oktavia, M. (2008). Optimasi Komposisi Tween 80 dan Span 80 sebagai Emulsifying Agent dalam Formula Emulgel Anti-Aging Ekstrak Teh Hijau (Camellia sinensis (L.) OK): Aplikasi Desain Faktorial. *Skripsi. Fakultas Farmasi. Universitas Sanata Dharma*.

Oktaviana, M., Rejeki, D. P., Ceriana, R., Mardiana, R., & Dita, S. F. (2021). Formulasi Sediaan Lotion Dari Ekstrak Buah Alpukat (Persea Americana) dan Lidah Buaya (Aloe Vera) Untuk Kulit Kering. *Journal of Pharmaceutical and Health Research*, *2*(2), 50–53.

Pratasik, M. C. M., Yamlean, P. V. Y., & Wiyono, W. I. (2019). Formulasi dan uji stabilitas fisik sediaan krim ekstrak etanol daun sesewanua (Clerodendron squamatum Vahl.). *Pharmacon*, *8*(2), 261–267.

Rahayu, S. (2016). Hubungan Perbedaan Konsentrasi Ekstrak Kunyit Putih (Curcuma mangga Val.) Terhadap Sifat Fisik Lotion. *Prosiding Rakernas Dan Pertemuan Ilmiah Tahunan Ikatan Apoteker Indonesia*, 50–56.

Ramadhani, R. A., Riyadi, D. H. S., Triwibowo, B., & Kusumaningtyas, R. D. (2017). Review pemanfaatan design expert untuk optimasi komposisi campuran minyak nabati sebagai bahan baku sintesis biodiesel. *Jurnal Teknik Kimia Dan Lingkungan*, *1*(1), 11–16.

Rusmin, R. (2021). Formulasi Dan Uji Stabilitas Sediaan Krim Ekstrak Rimpang Iris (Iris Pallida Lamk.) Menggunakan Emulgator Anionik dan Nonionik. *Jurnal Kesehatan Yamasi Makassar*, *5*(2), 50–58.

Salsabila, S., Fitriani, E., & Safitri, C. I. N. H. (2021). Formulasi dan Stabilitas Mutu Fisik Losion Pencerah dari Minyak Atsiri Temu Kunci (Boesenbergia pandurata Roxb.). *Prosiding SNPBS (Seminar Nasional Pendidikan Biologi Dan Saintek)*, 219–227.

Sandhi, B. G. F., Cahyani, I. M., Purwanto, U. R. E., & Indriyanti, E. (2022). Optimasi span 80 dan tween 80 dalam krim alas bedak dibenzalaseton sebagai tabir surya. *Jurnal Farmasi Medica/Pharmacy Medical Journal (PMJ)*, *5*(1), 14–19. https://doi.org/10.35799/pmj.v5i1.41439

Sari, N., Samsul, E., & Narsa, A. C. (2021). Pengaruh Trietanolamin pada Basis Krim Minyak dalam Air yang Berbahan Dasar Asam Stearat dan Setil Alkohol: Effect of Triethanolamine on Oil-in-Water Cream Base Based on Stearic Acid and Cetyl Alcohol. *Proceeding of Mulawarman Pharmaceuticals Conferences*, *14*, 70–75.

SUENA, N. I. M. D. S., ANTARI, N. I. P. U., & CAHYANINGSIH, E. (2017). Physical Quality Evaluation Of Body Butter Formulation From Etanol Extract Of Mangosteen (Garcinia Mangostana L.) Rind. *Jurnal Ilmu Kefarmasian Indonesia*, *15*(1), 63–69.

Thomas, N. A., Muâ, A., Latif, M. S., Hutuba, A. H., & Susanti, S. (2024). Formulasi dan Uji Stabilitas Fisik Krim Pelembab Ekstrak Rumput Laut (Eucheuma cottonii). *Indonesian Journal of Pharmaceutical Education*, *4*(1).

Unique, I. G. A. N. P. (2018). Optimasi konsentrasi setil alkohol sebagai agen pengental pada formula krim ekstrak rimpang kunyit (Curcuma domestica). *Jurnal Farmasi Udayana*, *7*(2), 40–44.

Wardani, G. A., Ruswanto, R., Lestari, T., Sari, T. P., & Fauziah, S. N. (2023). Penyuluhan Pembuatan Sediaan Serbuk Herbal Jahe Zingiber Officinale Dan Kunyit Curcuma Domestica Sebagai Imunomodulator. *JMM (Jurnal Masyarakat Mandiri)*, *7*(2), 1229–1240.

Wikantyasning, E. R., & Indianie, N. (2021). Optimisasi tween 80 dan span 80 sebagai emulgator dalam formula krim tabir surya kombinasi ekstrak etanol daun alpukat (Persea americana M.) dan nanopartikel seng oksida dengan metode simplex lattice design. *CERATA Jurnal Ilmu Farmasi*, *12*(1), 20–28. https://doi.org/10.61902/cerata.v12i1.198