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Original Article

NANOCREAM FOUNDATION FORMULATION LOADED WITH ETHYL ACETATE FRACTION FROM *MELASTOMA MALABATHRICUM l.*

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ABSTRACT

Objective: This study aimed to create a nanocream formula of the ethyl acetate fraction of *Melastoma malabathricum* using Design-Expert software. The objective was to obtain an optimal nanocream formula, analyze its characteristics, test its real-time stability, and measure its free radical scavenging ability using the DPPH method.

Methods: The study began by manufacturing 70% ethanol extract from *Melastoma malabathricum* leaves and fractionating it with ethyl acetate to obtain the desired fraction. The fraction was then used to create a nanocream using cetyl alcohol, liquid paraffin, and propylene glycol in a ratio of 5:5:15. The optimal formula was tested for real-time stability and antioxidant effectiveness using the DPPH method.

Results: Based on the results of the study, the optimal formula of the nanocream foundation preparation of the ethyl acetate fraction of *Melastoma malabathricum* was a combination of cetyl alcohol, liquid paraffin and propylene glycol in a ratio of 5:5:15. The results showed that the optimal nanocream formula had a pH value of 6.1±0.36, a spreadability of 6.57 cm ±0.06, and an adhesion of 22.20 minute±0.03. The particle size was determined to be 47 nm±0.78. The optimal formula also showed practical free radical scavenging ability, with an IC50 value of 556,29±0,155. The nanocream was stable for 28 d of real-time testing, and the honey extract remained stable during freeze-thaw.

Conclusion: In conclusion, using the design-expert software, the study successfully created a nanocream formula from the ethyl acetate fraction of *Melastoma malabathricum* (NFMM). The resulting nanocream had physical characteristics that met the requirements for pH, spreadability, adhesion, and particle size. It was stable for 28 d of real-time testing and showed antioxidant activity when tested with the DPPH method.

Keywords: *Melastoma malabathricum*, Formula design, Nanocream foundation, DPPH

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INTRODUCTION

Exposure to Ultraviolet (UV) light generates Reactive Oxygen Species (ROS) that damage the skin. Antioxidants mitigate this damage by reducing the effects of ROS. Antioxidants could stimulate the production of dermal collagen by increasing the production of matrix metalloproteinase-I (MPP-I) tissue inhibitors that inhibit the breakdown of collagen and elastin in the dermis [1]. Matrix metalloproteinase is an enzyme that can reduce the collagen and elastin content in the skin, leading to aging. UV rays cause a decrease and damage to collagen in the skin and increased MMP-1, which causes aging [2]. One of the plants that have antioxidant activity is *Melastoma malabathricum* l. Thin layer Chromatography (TLC) results showed that the n-hexane and chloroform fractions of *Melastoma malabathricum* extract contain steroid and terpenoid compounds. Antioxidant activity test with DPPH method showed that the n-hexane and chloroform fractions of ethanol extract of *Melastoma malabathricum* L. leaves had IC_{50}values of 49.2±7.9 g/ml and 11.3±3.65 g/ml, respectively. Antioxidant testing with FRAP showed that the IC_{50} values of the n-hexane and chloroform fractions are 365.2±133.6 g/ml and 80.8±8.9 g/ml, categorized as strong and weak antioxidants [3]. The ethyl acetate extract of *Melastoma malabathricum* contains quercetin and quercitrin. These flavonoids have a strong inhibitory activity of more than 90% by the FTC method. Quercetin could fight against free radicals through DPPH method with IC_{50} 0.69 [4].

Flavonoids, secondary metabolites, have phenols that are active antioxidants, so by performing fractionation, it is expected to extract more active compounds to increase their therapeutic activity. The fraction is unacceptable when used without being formulated. The design of the nanocream foundation will affect the amount and penetration of the active substances that can be absorbed. The active substances in the nanocream foundation enter the carrier that brings the drug into contact with the skin surface [5]. Cosmetics with nanotechnology-based delivery systems have attracted considerable attention in recent years. The small size of the 100-600 nm droplets has allowed homogeneous distribution to the skin and improves the efficient delivery of active ingredients through the skin [6-8]. Nanosystems in drug delivery are intended to enhance the biopharmaceutical properties of existing drugs, which often show limited effectiveness in therapy. Such limitations included solids and suspension states instability, poor solubility, and poor drug absorption, which can lead to low bioavailability and inadequate targeting efficiency that can cause an unfavorable ratio between the amount of drug administered and the concentration in the target tissue [9-11]. Topical drug administration was a challenge in pharmacy because of the problem of skin penetration and the determination and reproduction of the right amount of drugs reaching the skin layer at the desired depth; several strategies can be applied to overcome skin problems [12-14]. The purpose of this study was to design a nanocream foundation formula for the *Melastoma malabathricum* Fraction (NFMM) using Design-Expert software to obtain the optimal nanocream formula, analyze the characteristics of the optimal formula, analyze the real-time stability of the formula, and test the radical scavenging by the optimal nanocream formula with DPPH method. In this study, for forming the nanocream, the auxiliary materials that have a large proportion and have a significant effect on the characteristics of the cream were cetyl alcohol, liquid paraffin, and propylene glycol, so it was necessary to study their optimal compositions. This study aimed to design a nanocream formula of the *Melastoma malabathricum* fraction using Design-Expert software to obtain the optimal nanocream formula, analyze the characteristics of the optimal formula, analyze the real-time stability of the formula, and test the free radical scavenging by the optimal nanocream formula with the DPPH method. The novelty of this research is that the nanocream is designed with natural ingredients, namely the *melastoma* fraction, which has characteristics, stability, and antioxidant activity.

MATERIALS AND METHODS

Materials and excipient

The equipment used in this study is analytical balance (Ohaus PA214, USA), homogenizer (IKA RW20), hotplate with magnetic stirer (DLab),

glassware (pyrex), stopwatch, vortex mixer (Thermolyne), ultrasonicator (J. P. Selecta), UV-Vis Spectrophotometer (Shimadzu type 2450), 1 cm-sized quartz cuvette, a magnetic stirrer (Stuart CB162), pH meter (HANNA), filter paper, Particle Size Analyzer (Beckman coulter), Socorex® micro pipette (0.5 – 10; 5–50; 50-200, 200–1000), eppendorf tube, rotary evaporator (Heldolph Hei-VAP type), oven (Memmert), water bath (Memmert type WNB14), 120 mesh-sized sieve, aluminum foil, thermometer. *Melastoma malabathricum* leaves used in the study were freshly harvested from Sekajang village, Sanggau district, West Kalimantan, Indonesia. The botanical identity of Melastoma malabathricum has voucer specimen number is 021/AL/lB/FMIPA/UNTAN/2023. Ethanol 70% (Dwicentra), n-hexane (Merck), ethyl acetate (Merck), stearic acid (Bratachem), liquid paraffin (Nusa Kimia), cetyl alcohol (Pharma chemical), sodium lauryl sulfate (Kimia Jaya labora), Triethanolamine, methylparaben (Kimia Jaya labora), propyl paraben (Kimia Jaya labora), propylenglikol (Bratachem), aquadest (Dwicentra), parfum, the standard of quercetin (Sigma), methanol (Merck), DPPH (Smart-Lab).

Methods

***Melastoma malabathricum* l. preparation**

The collected *Melastoma malabathricum* l**.** leaves were separated from other materials such as sand, stones, and dust that can interfere and were then washed with water and drained. Then, the leaves were chopped to expand them to dry evenly and speed up the drying process. The chopped leaves were dried by aerating. The following steps were dry: the sorting process removes damaged leaves, refine with a blender, and sieve with a 40 mesh sieve [15].

***Melastoma malabathricum* l. fraction preparation**

The dried powder of *Melastoma malabathricum* l. was extracted with 78% ethanol by maceration method, and a rotary evaporator was used to reduce solvent and crude extract [3]. The crude extract was then separated using a funnel with solvents of different polarities: n-hexane and ethyl acetate. Thus, n-hexane and ethyl acetate fractions were obtained. Ethyl acetate fraction was used. The dried fraction was stored at room temperature.

NFMM preparation

Nanocream was made with cetyl alcohol, liquid paraffin, and propylene glycol. Then, EAF was added. The oil phase (liquid paraffin, cetyl alcohol, stearic acid) and the water phase (sodium lauryl sulfate, propylparaben, triethanolamine, methylparaben, propylene glycol, aqua dest) were melted in different containers at 70 ˚C, then mixed in a hot mortar, crushed and added with perfume and ethyl acetate fraction of *Melastoma malabathricum* l. Next, the mixture was put in a homogenizer 750 rpm for 10 min. The physical data from 14 nanocream runs could be used to determine the optimal formula. The determination of the optimal formula was performed by Design-Expert ® version 7.0.0 software with the simplex lattice design method. The characteristics of the physical properties used in determining the optimal formula were pH, spreadability, and adhesion.

Construction of pseudoternary phase diagram

The orientation of the nano cream formula was carried out to compare the cream and carriers that can produce nano cream with cetyl alcohol, liquid paraffin, and propylene glycol. The percentage composition of components in each ternary system is determined and the observation results are plotted on triangular coordinates to create a phase diagram [16].

pH evaluation of the NFMM

The pH test was carried out by dissolving 1 g of the nanocream in 10 ml of distilled water and then measuring the pH of the preparation using a pH meter, standardized using standard pH 4.0 and 7.0 buffers before the pH meter was used [14]. The preparation met the requirements when reaching the skin pH range, which is 4.5-7 [18]. The reading on the pH meter was noted after 5 min to ensure that the fig. is stable and still.

Spreadability evaluation of the NFMM

The spreadability test was carried out by placing 0.5 g of the nano cream on a round glass, then another glass was placed on top of the cream and left for 1 min. The diameter was measured. A load of 50 g was added and allowed to stand for 1 min; then, the diameter was remeasured. The preparation met the requirements if it had a spread of 5-7 cm [19].

Adhesion evaluation of the NFMM

The adhesion test was carried out by placing the gel on a glass object. The glass was pasted with another glass object that was hung with a load of 80 g, and a weight of 1 kg was placed on it for 5 min. The release time was recorded. The requirement for good adhesion was not less than 4 seconds [20].

Particle size determination of the NFMM

A total of 1.5 mg of the sample was analyzed for the droplet size using a Particle Size Analyzer (PSA). The particle size data obtained as an output on a computer were the average particle size, the particle size distribution, and the deviation from the mean [16].

Verification of the optimal NFMM

The verification was done by making the optimal nanocream of the experimental results that are compared with predictive software. Table 1 shows the verification results of the optimal formula.

Antioxidant activity of the NFMM

The nanocream preparation was dissolved in methanol p. a with a 1000 g/ml concentration as the mother liquor. *Melastoma malabathricum* leaves used in the study were freshly harvested from Sekajang village, Sanggau district, West Kalimantan, Indonesia. The preparation solution was then prepared in a concentration of 200, 600, 1000, 1400, 1800, and 2200 g/ml. Each concentration obtained was then put into a 5 ml volumetric flask in each test tube, added with 2 ml of the preparation and 3.0 ml of DPPH. The mixture was then incubated at 37 °C for 30 min. Furthermore, the absorption was measured at a wavelength of 515.5 nm. The IC50 values were calculated using the regression equation formula.

Physical stability test using real storage conditions of the NFMM

Three batches of 50 g were prepared and packed in non-transparent containers. The physical stability of the nanocream was observed on the 0, 3rd, 7th, 14th, 21st, and 28th d under real conditions at 25 °C and 70% RH. The observations were for its organoleptic, pH, spreadability, and adhesion.

Data analysis

The analyses included the test results of pH, spreadability, and adhesion. The test results were obtained and analyzed with the prediction of the optimum formula using the simplex lattice design method. The data were analyzed using the IMB SPSS Statistics using One-Sample T-Test.

RESULTS AND DISCUSSION

Nanocream foundation design based on design expert software

One of the criteria that must be met is pH because it relates to the safety of the preparation when applied to the skin, especially in nanocream foundation preparations. It is essential to do a pH test to ensure that the pH of the preparation is safe when applied to the skin and is closely related to comfort when applied to the skin. The ideal topical preparation pH is 4.5- 6.5. It was feared that irritation would occur if the preparation had a too-acidic pH and that it could cause dry skin if its pH were too alkaline [18]**.**

Based on the results of the pH test (table 1), of the 14 runs, the pH requirements allowed for nanocream foundation preparations are in the range of 4.5-6.5. In all runs, namely run 1 to 14 with a composition ratio of cetyl alcohol, liquid paraffin, and propylene glycol, it entered the permissible pH range, except for run 2. The difference in pH in each run indicated that there is an effect of the combination of cetyl alcohol, liquid paraffin, and propylene glycol on the pH of the preparations. Based on the results of the highest pH, the use of liquid paraffin and high propylene glycol can increase the pH of the preparation. The data were analyzed with the Design-Expert software. Based on the ANOVA test, residual

normal curve analysis plot, and lack-of-fit analysis, the special cubic model in the equation is valid and appropriate for the pH. The ANOVA test results show that the p-value is at a significance level of 95%, meaning that the linear model is the right model to explain the effect of components on the pH. This is also reinforced by the results of the lack-of-fit analysis, which shows a p-value of 0.0014>0.05 at the 95% significance level. This shows no significant difference between the experimental and predicted data from the proposed model. The special cubic model's p-value (0.01340<0.05) indicates a significant difference in the pH from the use of different compositions of cetyl alcohol, liquid paraffin, and propylene glycol. Fig. 1 shows the contour plot of the pH responses.

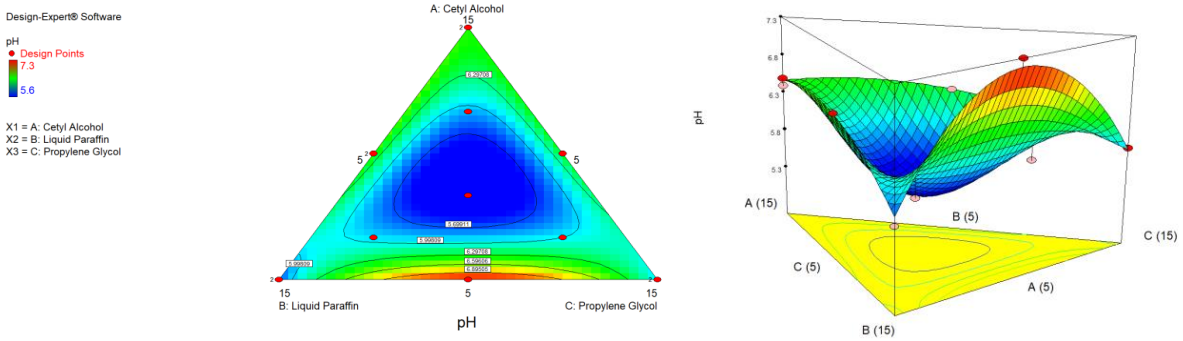

Fig. 1: *Contour plot* pH response: X1=A: Cetyl alcohol, X2 = B: liquid paraffin, X3 = C: Propylene glycol (Design Expert® Ver. 7.0.0.)

The Simplex lattice Design equation obtained can be seen in equation 1.

$$Y = -0.57\,(A) - 0.84\,(B) - 0.83\,(C) + 0.22\,(A)(B) + 0.22\,(A)(C) + 0.26\,(B)(C) - 0.04\,(A)(B)(C) \quad \ldots\ldots (1)$$

Note:

Y = pH

A = Component of cetyl alcohol

B = liquid paraffin component

C = Component of propylene glycol

Based on the pH data and contour plots and equations, the pH value is determined by each optimized component. Cetyl alcohol gave the most significant effect, as indicated by the magnitude of the coefficient in the equation. Propylene glycol more substantially impacted the pH value than liquid paraffin. The interaction of liquid paraffin and propylene glycol increased the pH value much greater than that of cetyl alcohol and liquid paraffin and that of cetyl alcohol and propylene glycol. The interaction of cetyl alcohol, liquid paraffin, and propylene glycol lowered the pH value. Fig. 1 shows that preparing the nano cream foundation with cetyl alcohol, liquid paraffin, and propylene glycol affects the pH responses. The more excellent composition of liquid paraffin and propylene glycol in the preparation can cause the pH of the preparation to increase. This is indicated by the red area, which has a higher pH response.

A spreadability test was carried out to determine the ability to spread on the skin. The results of the dispersion test of the ten nano-cream formulas are presented in table 1. The permissible good dispersion for topical preparations is 5-7 cm [18]. Based on the ANOVA test, residual normal curve analysis plot, and lack-of-fit analysis, the linear model in the equation is valid and appropriate for the pH. The results of the ANOVA test showed that the p-value is at a significance level of 95%, meaning that the linear model is the suitable model to explain the effects of components and their interactions on water content. This is also supported by the results of the lack of fit analysis, which shows the p-value of 0.049>0.05 at the 95% significance level. This indicates no significant difference between the experimental data and the predicted data from the proposed model. The linear model's p-value (0.12<0.05) indicates a significant difference in dispersion from the use of different compositions of cetyl alcohol, liquid paraffin, and propylene glycol. Fig. 2 shows the contour plot of water content responses.

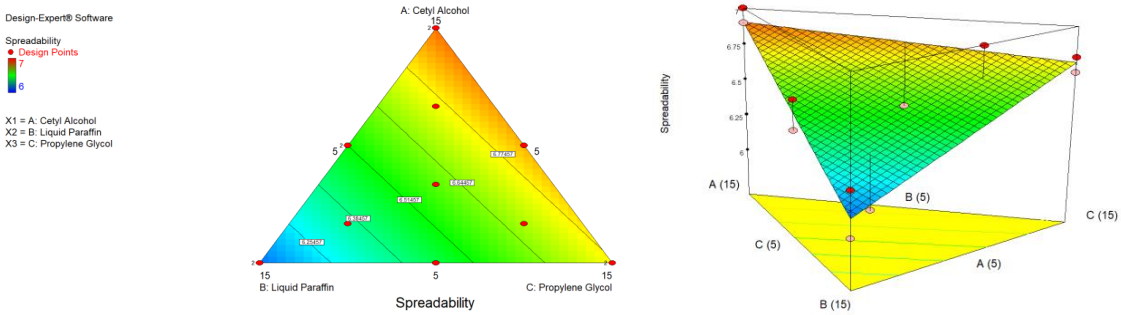

Fig. 2: *Contour plot* spreadability response: X1=A: Cetyl alcohol, X2 = B: liquid paraffin, X3 = C: Propylene glycol (Design Expert® Ver. 7.0.0.)

The Simplex lattice Design equation obtained can be seen in equation 2.

$$Y = 0.29\,(A) + 0.22\,(B) + 0.28\,(C) \quad \ldots\ldots (2)$$

Information:

Y = Scattering power

A = Component of cetyl alcohol

B = Liquid paraffin component

C = Component of propylene glycol

Based on the data of dispersion and contour plot as well as the equation, the value of the dispersion power is determined by each optimized component. Cetyl alcohol gave the most significant effect, as indicated by the magnitude of the coefficient in the equation. Propylene glycol more substantially impacted the dispersion value

than liquid paraffin. Based on fig. 2, preparing the nanocream foundation with a combination of cetyl alcohol, liquid paraffin, and propylene glycol affects the dispersion responses.

Referring to the analyses using the Design-Expert software with a test on the adhesion response, plot of residual average curve analysis, and lack of fit analysis, the quadratic model in the equation is a valid and appropriate model for the pH. The ANOVA test results showed that the p-value is at a significance level of 95%, meaning that the quadratic model is suitable for explaining the effect of components and their interactions on water content. This is also strengthened by the results of the lack-of-fit analysis, which shows a p-value of 0.0085>0.05 at the 95% significance level. This indicates no significant difference between the experimental data and the predicted data from the proposed model. The quadratic models p-value (0.00648<0.05) indicates a significant difference in adhesion from using different compositions of cetyl alcohol, liquid paraffin, and propylene glycol. Fig. 3 describes the contour plot of water content responses.

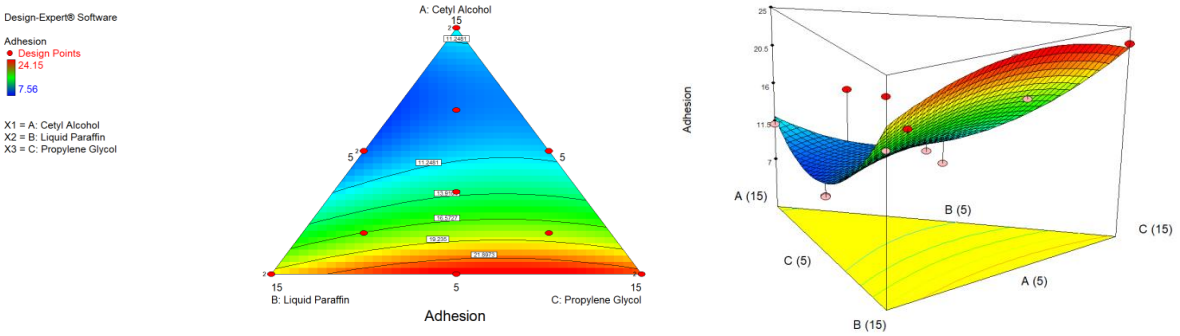

Fig. 3: *Contour plot* Adhesion response: X1=A: Cetyl alcohol, X2 = B: liquid paraffin, X3 = C: Propylene glycol (Design Expert® Ver. 7.0.0.)

The Simplex lattice Design equation obtained can be seen in equation 3.

$$Y = 2.43\ (A)+1.26\ (B)+1.48\ (C) - 0.28\ (A)(B) - 0.27\ (A)\ (C)+0.122\ (B)(C) \ldots\ldots\ldots (3)$$

Information:

Y = Stickiness

A = Component of cetyl alcohol

B = Liquid paraffin component

C = Component of propylene glycol

Based on the analysis of the adhesion and contour plot data, as well as the equation, the dispersion value is influenced by each optimized component. Cetyl alcohol exhibited the most significant impact, as evidenced by the coefficient magnitude in the equation. Propylene glycol had a more substantial effect on the adhesion value compared to liquid paraffin. The preparation of a nanocream foundation using cetyl alcohol, liquid paraffin, and propylene glycol was found to impact the adhesion responses, as depicted in fig. 3. The combination of liquid paraffin and propylene glycol resulted in increased adhesion responses, as shown by the red area.

Optimal formula of NFMM

The graph in fig. 4 illustrates the relationship between the components of cetyl alcohol, liquid paraffin, and propylene glycol on the desirability value, while fig. 5 displays the contour plot of the optimal formula.

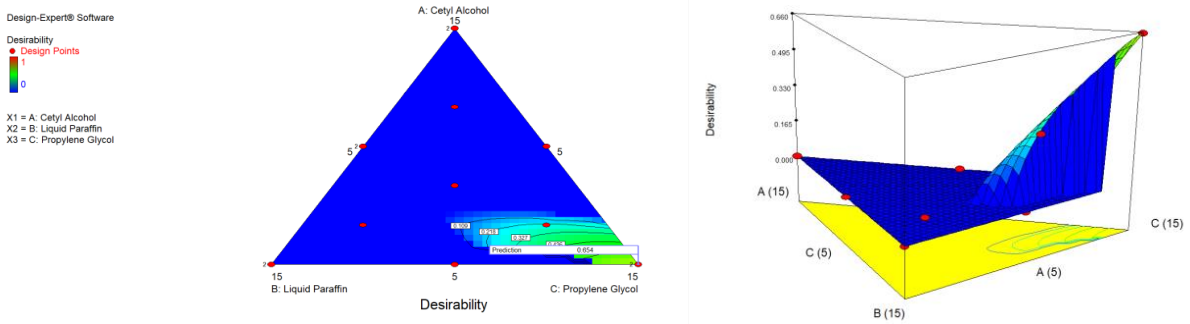

Fig. 4: Contour plot of desirability (Design Expert® Ver. 7.0.0.)

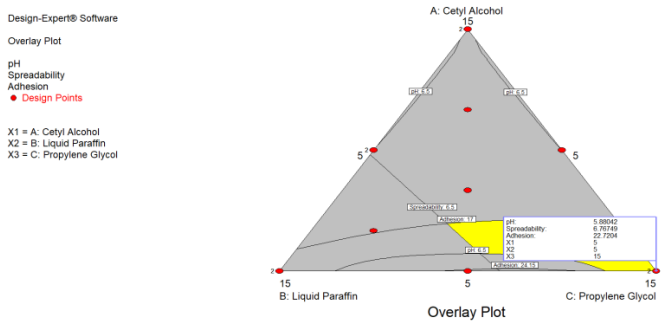

Fig. 5: Superimposed of NFMM optimal formula (Design Expert® Ver. 7.0.0.)

The simplex lattice design in the Design-Expert version 7.0.0 software produced the optimal formula. Fig. 5 describes the resulting superimposed contour plot of the pH response, dispersion, and adhesion. The superimposed contour plot provides a yellow area that gives optimal response. This area offers an optimal formula prediction with a desirability of 0.654. The optimal nanocream formula was obtained using a combination of nanocream bases, namely cetyl alcohol, liquid paraffin, and propylene glycol, which was designed using the simplex lattice design method in the Design-Expert software. Cetyl alcohol was used in oil-in-water emulsions to form a viscoelastic continuous phase in combination with an aqueous emulsifying solution, which imparts semisolid properties to the emulsion and prevents coalescence of droplets and increases stability [22]. The use of cetyl alcohol in oil in water-type creams increased viscosity and decreased drug release [23]. Cetyl alcoholism is a hardening agent that affects the viscosity and ability of the active compound to be released from the dosage form. The hydrophilic active compounds in the preparation were expected to be quickly released from base lipophilic creams such as cetyl alcohol to increase the diffusion rate [24]. The viscosity of mono-dispersion and poly-dispersion systems is enhanced by decreasing particle size and increasing interactions [25, 26]. Various types of liquid paraffin influence the viscosity of the formulation. The viscosity factor was influenced by the pre-hydration of the lipophilic gel–soft paraffin, and this procedure could affect the particle size of the dispersed phase. In this study, the particles were 15 to 90 m long [27]. Propylene glycol could increase trans-epidermal water loss by increasing water absorption from the dermis to the epidermis [28]. Moisturizer was a significant component of primary daily skin care, especially in the presence of a barrier to epidermal changes and a decrease in the moisture content of the epidermis [29].

Characterization and verification of optimal formula NFMM

Verification is done by making the optimal nanocream foundation experimental results, which are compared with predictive software. Table 1 shows the results of the verification of the optimal formula.

Based on the probability value of each response, the obtained p-value is more significant than 0.05, so it can be concluded that there is no significant difference between the prediction results of the simplex lattice design in the Design-Expert software and the results of experimental observations. The observations results of the nano cream foundation were compared with the results of the predicted responses generated by the optimal formula in the simplex lattice design. The verification was carried out using the one-sample t-test in the Open Stat software. The data were analyzed with SPSS using the one-sample t-test. In the pH test, the obtained p-value was 0.401>0.05, showing no difference between the predictions of the simplex lattice design method in the Design-Expert software and the experimental results of the optimal nanocream foundation formula. In the dispersion test, the obtained p-value was 0.939>0.05, indicating that there is no difference between software predictions and experimental results. Furthermore, the adhesion test's p-value was 0.678>0.05, meaning that a significant difference between software predictions and experimental results is not found.

Table 1: Test results for optimal formula NFMM

Sample	pH	Spreadability (cm)	Adhesion (min)
Nanocream foundation from software prediction	5.88	6.76	22.72
Nanocream foundation from research	6.1±0.36	6.57±0.06	22.20±0.03

(Prediction from software Design Expert, n=1, from software, values from research are mean±SD; n=3)

Based on the physical characteristics test results, the optimal nanocream formula has met the pH, spreadability, and adhesion requirements. The formulation of cream met the required standard of physical characteristics and could provide active compounds to penetrate the membrane by using 2% cetyl alcohol as a stiffening agent [30]. A topical vehicle is a 'carrier system' for an active pharmaceutical (or cosmetic) substance, which can be used as an emollient to improve dry skin. Vehicles played an essential role in determining the bioavailability of a given drug at its final target in the skin [31]. Propylene glycol in the optimum formula, has the most significant proportion of composition, which is 15 parts. Propylene glycol is an aliphatic alcohol that functions as a skin conditioning agent, viscosity-reducing agent, solvent, fragrance, and an ingredient in cosmetics. Polypropylene glycol functions primarily as a skin conditioning agent, with some use of solvents. Propylene glycol is generally non-toxic and non-carcinogenic. Clinical testing has shown no dermal sensitization at the concentrations used. Dermal absorption of propylene glycol, a highly water-soluble substance, through intact skin was estimated to be very limited [32].

Propylene glycol (PG) has been used in formulations as a co-solvent and to enhance drug absorption through the skin in topical preparations. PG modulates permeability by increasing or decreasing it in compounds with poor permeability. Percutaneous absorption, using pig skin on Franz diffusion cells, reported in the evaluated formulations, tend to have lower permeability than PG solutions. The results showed the enhancing properties of PG for all compounds, especially for the hydrophilic ones. The results showed an increase in the area under the curve, indicating a higher amount of lipid in the deeper layers and changing the lipid sequence from a bilayer structure to a more disordered lipid structure [33]. Propylene glycol was a co-surfactant that is often used in cosmetic preparations where the use of co-surfactants can reduce the flexibility of the surface tension so that it has sufficient flexibility to form nanoemulsions with large compositions [31]. Propylene glycol was a co-surfactant that was included in category A in forming nanoemulsions, taking less than 1 min, and it gave a positive interaction with oil in increasing the emulsification time [16]. The use of a combination of non-ionic surfactants could produce a very stable nano-cream preparation [34].

Based on the test results, the average size of nanocream is 47 nm, less than 300 nm. This proves that the prepared nanocream can produce particles in the nanometer range [35]. This shows that the nanocream made by the High-Pressure Homogenizers (HPH) method with a homogenizer produces a nanocream according to the particle size. Low and high-energy use differs in the energy used, and at the critical point, it affects the formation of nano-sized droplets. Energy plays a role in forming the nano-sized droplets. The type of equipment used determines the flow that involves the mixing process, which involves both laminar and turbulent flow. When stirring occurs, the oil and water phases form unstable droplets. Surface-free energy in the emulsion system is affected by area and surface tension. The tool affected the droplet and emulsion dispersion that occurs, namely by breaking up and dispersing the internal phase to the external phase to produce smaller droplet sizes to prevent coalescence and maintain the emulsion stability [36]. This study used a homogenizer: the dispersion of two liquid phases was achieved by passing the mixture through high pressure. When the pressure was increased, the stirrer was compressed, some of the dispersion would be free between the valves, and the energy stored in the liquid, namely the pressure, would be released spontaneously, resulting in turbulence and hydraulic shear [37].

Nanocream is made using a co-surfactant with a voltage reduction mechanism between phases, namely the oil phase and the water phase and fluidizes the film layer. The value of the Polydispersity Index (PI) indicates the homogeneity of the nanocream particles. The PI value obtained from testing is 0.296. The PI value varies from 0.0 to 1.0, and the closer to 0, the more homogeneous the particles [40]. The PI of less than 0.5 indicates a uniform globule size distribution [38, 39]. So it can be concluded that the nanoemulsion particle size distribution is uniform, and that the method of making nanocream has good reliability.

A **γ**-oryzanol nanocream using high stirring time at high speed resulted in a particle size of 48.1 12.1 nm [40], as well as in the manufacture of kenikir extract nanocream with a mixer, the particle size was less than 300 nm. The particle size of cinnamon leaf oil nanocream was 286 nm with an ultra turrax homogenizer and was stable for 6 mo of storage [41]. The use of a homogenizer at a speed of 2000-4000 rpm for 10-60 min on *Eichhornia crassipes* extracts resulted in a particle size of 100-400 nm [42].

The NFMM stability

Organoleptic test is a test which is carried out based on the sensing process, and it is a physical test of organic soap preparations, including color, odor and shape or texture. Organoleptic tests were performed to see the physical appearance of the preparations produced by observing their color, aroma and shape or texture. Based on the organoleptic test results, the optimum preparation of the nanocream foundation has shown a light green color, distinctive aroma with a homogeneous texture (+++).

Based on fig. 6, the pH value and spreadability of the nanocream foundation increase on storage while the adhesion decreases. Based on the stability test data analyses for testing pH, dispersibility, and adhesion, a significant difference between the storage and the one-way ANOVA test has yet to be found. In the pH, dispersion, and adhesion tests, a p-value>0.05 is obtained, so there is no significant difference in storage for the 28 d. Emulsion stability is the stability of a material where the emulsion contained in the material does not tend to combine with other particles and form separate particles. The stability of the nanocream emulsion was higher due to its more homogeneous and fused particles. The emulsion stability increased from 88% to 97% when stirring at one and three hours, respectively [43].

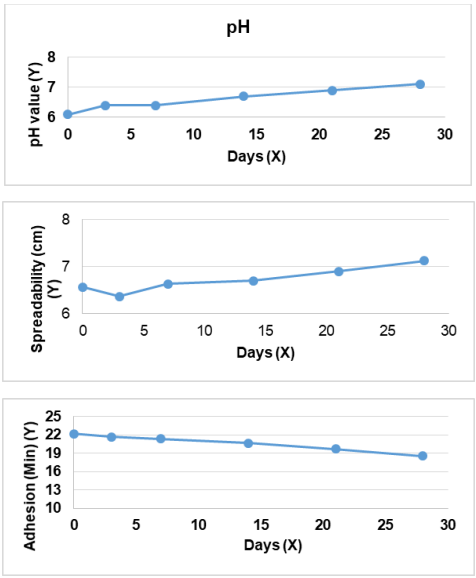

Fig. 6: Real-time stability for pH, spreadability, and adhesion (All values are mean, n=3)

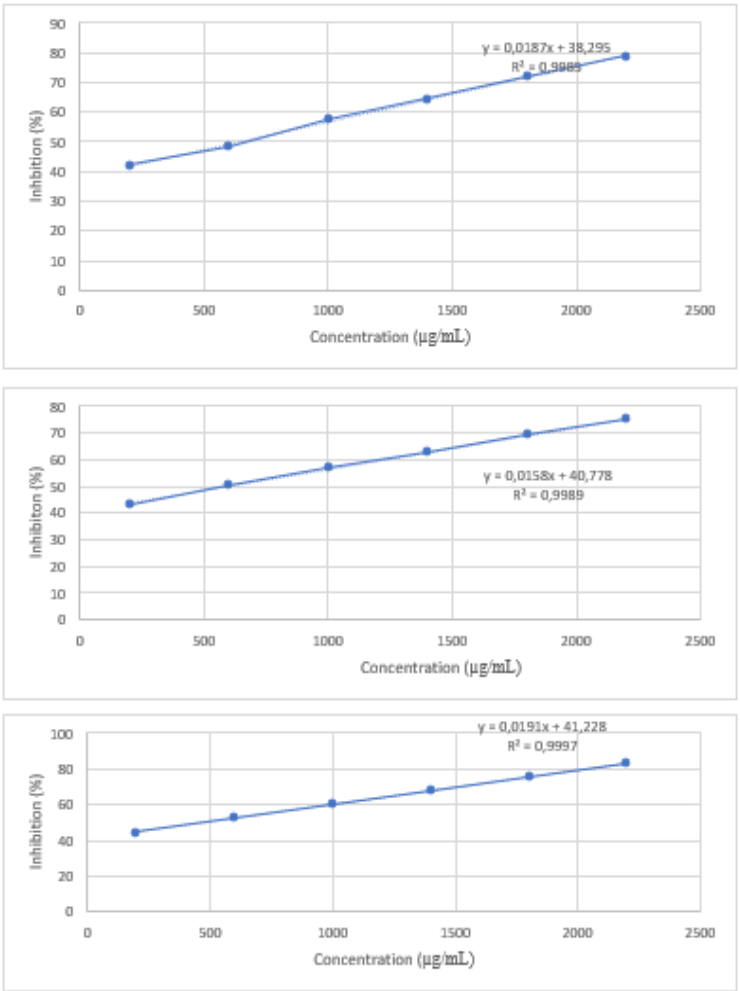

Fig. 7: Antioxidant activity from NFMM, (All values are mean; n=3)

Optimal formula NFMM antioxidant activity

The antioxidant activity of *Melastoma malabathricum* was assessed using the DPPH method with UV-Vis spectrophotometry at a maximum wavelength of 515.5 nm. The IC_{50} value, which represents the concentration of the sample solution needed to inhibit 50% of DPPH free radicals, was determined using a linear regression equation from the relationship curve of the sample concentration to the percent inhibition (Y= ax+b), with sample concentration (ppm) as the X-axis and percentage inhibition as the Y-axis. Based on the linear regression equation (fig. 7), the obtained IC_{50} values were 556.29 ppm, 583.67 ppm, and 459.27 ppm. The IC_{50} values categorize the antioxidant activity as strong, potent, moderate, or weak, with values less than 50 ppm indicating powerful antioxidants, 50 to 100 ppm as potent, 100 to 150 ppm as moderate, and 150 to 200 ppm as weak. Antioxidants with IC_{50} values exceeding 200 ppm are considered fragile. The nanocream preparation showed weak antioxidant activity due to the low content of *Melastoma malabathricum* in the nanocream foundation (0.1%). Additionally, previous research indicated that the antioxidant ability of extracts in preparations is generally lower than in extracts without preparations [44-51].

CONCLUSION

The optimal nanocream foundation can be formulated using the Design-Expert software with Melastoma malabathricum l. The simplex lattice design method allows for the prediction of the ideal nanocream foundation. This nanocream foundation technology exhibits physical characteristics that meet the necessary requirements and remains stable during 28 d of real-time testing. Additionally, the nanocream foundation derived from Melastoma malabathricum demonstrates antioxidant activity, which is assessed using the DPPH method.

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AUTHORS CONTRIBUTIONS

Liza Pratiwi: Contributed of an experiment, the designed idea of the research, conceived of the original idea, contributed of the experiment, wrote the manuscript with support from Rafika Sari, Pratiwi Apridamayanti: Editor the manuscript, contributed of the experiment, help to wrote the manuscript.

CONFLICTS OF INTERESTS

The author declares no conflicts of interest

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