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Optimization of Papaya Leaf Extract Cream Using Stearic Acid and Triethanolamine via Simplex Lattice Design

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ABSTRACT: *Papaya leaves (Carica papaya* L.*) are known to contain bioactive compounds such as flavonoids, alkaloids, tannins, and saponins, which exhibit antiseptic, anti-inflammatory, antifungal, and antibacterial properties, making them promising for topical pharmaceutical preparations. However, achieving optimal physical characteristics in cream formulations requires careful selection and proportioning of emulsifiers. This study investigates the effect of varying ratios of stearic acid and triethanolamine on the physical properties of creams containing ethanol-extracted papaya leaf extract. The extract was obtained via maceration using 96% ethanol and confirmed to contain active compounds through phytochemical screening and thin-layer chromatography. Eight formulations were developed using a Simplex Lattice Design (SLD) with stearic acid concentrations ranging from 15–17% and triethanolamine from 2–4%. Physical evaluations included tests for pH, viscosity, adhesion, and spreadability. All formulations met standard of cream quality requirements, but the optimal formula was identified at 15.20% stearic acid and 3.79% triethanolamine, offering the most desirable physical characteristics. This formulation strategy demonstrates the potential for producing effective and stable papaya leaf creams, with implications for natural-based dermatological product development.*

Keywords: *cream formulation; papaya leaves (Carica papaya* L.*); simplex lattice design; streatic acid; triethanolamine*

1. Introduction

Papaya leaves (*Carica papaya* L.) are rich in flavonoids, alkaloids, papain, and vitamins C and E [1,2]. These bioactive compounds have been successfully formulated in various topical products, including facial serums and creams, due to their ability to improve skin health and combat acne-causing bacteria like *Propionibacterium acnes* [3,4]. Cream formulations are favored in such applications for their semi-solid consistency, user-friendly application, and efficient active compound delivery [5,6]. However, ensuring physical stability in cream products requires precise emulsification, typically using agents like stearic acid and triethanolamine, which improve texture, pH balance, and emulsion formation [7,8]. Research into plant-based creams has advanced with tools such as the Simplex Lattice Design (SLD), which allows for efficient optimization of ingredient ratios by analyzing critical parameters like pH, viscosity, spreadability, and adhesion [9–12]. Various natural extracts from duku leaves, naringenin, to banana corm have been optimized using SLD, demonstrating its adaptability in cosmetic research [7,13]. Despite progress, the systematic optimization of papaya leaf extract cream using SLD remains limited, especially in terms of emulsifier concentration effects [14–20]. Therefore, this study aims to fill that gap by formulating and optimizing a papaya leaf extract cream using SLD with the aid of Design Expert software, building on recent literature hile contributing a novel evidence-based approach to improve the formulation's stability and effectiveness.

2. Materials and methods

2.1. Materials

The materials used in this study included both reagents for phytochemical screening and solvents for the extraction process, as well as ingredients for the cream formulation. The reagents comprised methylene blue (molecular biology grade, MP Biomedicals®), Sudan III (practical grade, HiMedia®), toluene (ACS grade, Merck®), formic acid (reagent grade, Merck®), n-butanol (reagent grade, Merck®), acetic acid (ACS grade, Merck®), gallic acid (analytical grade, Merck®), methanol (ACS grade, Merck®), chloroform (ACS grade, Merck®), glycyrrhizin (≥95% purity, Sigma-Aldrich®), anisaldehyde sulfuric acid (reagent grade, Sigma-Aldrich®), magnesium (reagent grade, Merck®), amyl alcohol (reagent grade, Merck®), and Liebermann-Burchard reagent (ready-to-use, Sigma-Aldrich®). Distilled water (type II, in-house production) was used throughout the experiments.

The main ingredients for the formulation of the cream included papaya leaf extract (*Carica papaya* L., lab-prepared), stearic acid (cosmetic grade, Bratachem®), triethanolamine (TEA, cosmetic grade, Bratachem®), cetyl alcohol (pharmaceutical grade, Bratachem®), glycerin (USP grade, Merck®), propylene glycol (USP grade, Merck®), methyl paraben (pharmaceutical grade, Sigma-Aldrich®), propyl paraben (pharmaceutical grade, Sigma-Aldrich®), and distilled water (type II, in-house).

2.2. Instrument

The instruments used in the study included an analytical balance (OHAUS® Pioneer PX224/E), moisture balance (OHAUS® MB120), oven (Memmert® UN55), blender (Waring Laboratory Blender), mesh no. 60 sieve (Retsch®), rotary evaporator (IKA® RV8), maceration apparatus (custom glass setup), glassware (Pyrex®), water bath (Memmert® WB14), Brookfield viscometer (DV2T Touch Screen, Brookfield®), pH meter (Starter Series, OHAUS® ST3100), cream pot (generic laboratory grade), adhesion tester (YF-06 Adhesion Tester, Yihong Instruments®), and spreading tester (custom-made glass plate setup).

2.3. Methods

2.3.1. Preparation of papaya leaf extract

Fresh papaya leaves collected from Tawangmangu, Central Java, were dried, ground with a laboratory blender, and sieved using mesh

Table 1. Papaya leaf extract cream formula

Name of material	Amount (%)								Function
	F1	F2	F3	F4	F5	F6	F7	F8	
Papaya leaf extract	6	6	6	6	6	6	6	6	Active substance
Stearic acid	15.7	15	15.5	16.5	17	16.3	16	17	Cream base
Triethanolamine	3.3	4	3.5	2.5	2	2.7	3	2	Emulgator
Cetyl alcohol	4	4	4	4	4	4	4	4	Emollient
Glycerin	4	4	4	4	4	4	4	4	Humectant
Proplyene glycol	7	7	7	7	7	7	7	7	Humectant
Methyl paraben	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	Antimicrobial
Propyl paraben	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	Antimicrobial
Aquadest ad	100	100	100	100	100	100	100	100	Solvent

no. 60. Moisture content was assessed using a moisture balance at 105°C to ensure a final level below 10%, following standard protocols [21]. A total of 1.25 kg of powdered leaves was macerated in 18.75 L of 96% ethanol (technical grade, Bratachem®) for two phases (6 hours and 18 hours) under occasional stirring. The mixture was filtered through flannel cloth and Whatman No.1 filter paper, and the residue was re-macerated. All filtrates were combined and concentrated using a rotary evaporator at 50°C to obtain a thick extract.

2.3.2. Determination of water content in extract

Water content in the extract was determined using the Sterling-Bidwell method. A 5 g sample of the extract was mixed with 200 mL of toluene (ACS grade, Merck®) and heated for 15 minutes. The process was stopped once no further condensation was observed. After phase separation, the volume of water was recorded.

2.3.3. Phytochemical screening

Qualitative phytochemical screening was performed on both the powdered leaf material and the ethanol extract. Tests for flavonoids involved treatment with methanol (ACS grade, Merck®) and magnesium (reagent grade, Merck®) in the presence of hydrochloric acid (concentrated, analytical grade, Merck®). Alkaloids were identified using Dragendorff's and Mayer's reagents (analytical grade, Sigma-Aldrich®). Tannins and saponins were detected using ferric chloride (analytical grade, Merck®) and froth tests, respectively. Thin-layer chromatography (TLC) with specific spray reagents such as anisaldehyde-sulfuric acid (Sigma-Aldrich®) was also used for compound identification.

2.3.4. Cream formulation

Eight cream formulations were prepared by varying the concentrations of stearic acid (15–17%) and triethanolamine (TEA, 2–4%) using the Simplex Lattice Design, as shown in Table 1. Other components such as papaya leaf extract (6%), cetyl alcohol (4%), glycerin (4%), propylene glycol (7%), methyl paraben (0.2%), and propyl paraben (0.02%) remained constant. Distilled water was added up to 100%.

The oil phase (stearic acid, cetyl alcohol, propyl paraben) and aqueous phase (TEA, propylene glycol, glycerin, methyl paraben, and water) were heated separately. The aqueous phase was added gradually into the melted oil phase with constant stirring to form an emulsion. Once cooled to room temperature, the papaya extract was incorporated using a mortar and pestle to produce a homogeneous cream.

2.3.5. Evaluation of cream formulations

The cream formulations were evaluated for organoleptic properties (color, odor, consistency), homogeneity (microscopic observation), and type (dilution test to confirm oil-in-water emulsion). Viscosity was measured using a Brook-

Table 2. Phytochemical screening results of papaya leaf ethanol extract using thin layer chromatography method

Inspection	Reagent	Result	Library	Conclusion
Flavonoids	Extract + ethanol + Mg powder + HCl	Orange color formed on the amyl alcohol layer	Formation of red or yellow, or orange color on the amyl alcohol layer	(+)
Saponin	Extract + water	Foam formed	Formation of foam	(+)
Tannin	Extract + FeCl3	Blackish green color formed	Formation of blackish blue or blackish green color	(+)
Alkaloids (Mayer)	Extract + HCl + Mayer	White precipitate formed	Formation of white-yellow precipitate	(+)
(Dragendorff)	Extract + HCl + Dragendorff	Orange color formed	Formation of orange color	(+)
Saponin	Extract + water + HCl	Foam formed	Formation of foam	(+)

Table 3. Phytochemical screening results of papaya leaf ethanol extract using the tube method

Test result colour								
Parameter	**Comparative standard**	**Motion phase**	**Spray reagent**	**UV 254 nm**	**UV 366 nm**	**Rf standart**	**Rf extract**	**Not**
Flavonoids	Quercetin	n-butanol : aquadest : acetic acid (2.8:3.5:0.7)	Sitorborat	Gray	Blackish ash	0.50	0.36 0.43 0.50	+
Alkaloids	Caffeine	Chloroform : methanol (6.3:0.7)	Dragendorf	Yellowish green	Red brown	0.87	0.63 0.7 0.8	+
Saponin	Sapogenin	Chloroform : methanol : aquadest (4.2:2.1:0.7)	Anisaldehyde-sulfuric acid	Grayish green	Blackish red	0.8	0.2 0.45 0.6	+
Tannin	Gallic acid	n-butanol : aquadest : acetic acid (2.8:3.5:0.7)	FeCl3 1%	Blackish green	Blackish red	0.8	0.45 0.6 0.8	+

field® viscometer, and pH was assessed using a calibrated digital pHmeter. Spreadability was determined by placing a fixed amount of cream between two glass plates and measuring the diameter after applying a fixed weight. Adhesion was measured by recording the time of the cream remained adhered under applied pressure.

2.3.6. Statistical optimization

The Simplex Lattice Design was applied using Design Expert software to analyze the influence of stearic acid and TEA on cream properties. The responses evaluated included pH, viscosity, spreadability, and adhesion. Statistical significance was determined using ANOVA, and a p-value of less than 0.05 was considered significant. This enabled identification of the optimal emulsifier ratio for a stable and effective cream formulation.

3. Results and discussion

3.1. Extract preparation and characteristics

The study began by confirming that the sample used was papaya leaves, which produced a powder yield of 36.23%, an essential metric reflecting both process efficiency and material usability. The drying shrinkage test showed an average value of 5.5%, which is within the acceptable range (≤10%) as per the Indonesian Herbal Pharmacopoeia [22]. Ethanol extraction via maceration yielded 228 grams of extract with an efficiency of 18.24%, meeting the standard for ethanol extract yields (>18.2%). The water content was re-

Table 4. pH, viscosity, adhesion, and spreadability test

Parameters	Test Results							
	F1	F2	F3	F4	F5	F6	F7	F8
pH	7.61	7.90	7.89	7.15	7.12	7.89	7.54	7.15
Viscosity (cP)	31.266	26.400	30.666	36.800	39.666	35.616	33.616	37.066
Adhesion (seconds)	2.26	2.04	2.19	2.42	2.52	2.35	2.28	2.45
Spreadability (cm)	6.51	7.03	6.95	5.79	5.17	5.80	6.03	5.58

Table 5. Predictive value and trial of papaya leaf extract cream

Response	Prediction value	Mean experimental value ± SD	Conclusion
pH	7.90	7.87± 0.02	Not significantly different
Viscosity (cP)	28,514.9 cP	30,666.6 ± 1501.11cP	Not significantly different
Adhesion (seconds)	2.11 seconds	2.09 ± 0.05 seconds	Not significantly different
Spreadability (cm)	6.92 cm	6.9 ± 0.02 cm	Not significantly different

corded at 13.3%, which complied with the ≤20% requirement.

3.2. Phytochemical analysis

Phytochemical screening using both thin-layer chromatography (TLC) and tube methods confirmed the presence of flavonoids, saponins, tannins, and alkaloids. These results are summarized in Table 2 and 3, which detail the reaction outcomes, reference standards, and conclusions of each chemical test. Notably, all target secondary metabolites yielded positive results, indicating the functional potential of the papaya leaf extract in topical formulations.

3.3. Cream formulation and physical evaluation

Physical characterization of the eight formulated creams (F1–F8) revealed uniform organoleptic properties: all were semi-solid, dark green, had a distinct papaya scent, and showed good homogeneity. Emulsion testing through dilution, dye interaction, and conductivity confirmed an oil-in-water (O/W) type across all formulations, which is ideal for topical applications. Table 4 shows the results of pH (ranging from 7.12 to 7.90), viscosity (26,400 to 39,666 cP), adhesion (2.04 to 2.52 seconds), and spreadability (5.17 to 7.03 cm) all aligned with national standards (SNI 16-4399-1996), reinforcing the suitability of these formulations.

3.4. Regression analysis and component interaction

Regression analysis using the Simplex Lattice Design (SLD) allowed for the derivation of equations correlating each response (pH, viscosity, adhesion, and spreadability) to the proportions of stearic acid and triethanolamine. For example, pH was strongly influenced by triethanolamine (coefficient +7.98), while viscosity and adhesion were more affected by stearic acid (coefficients +38,994.65 and +2.50, respectively). Interestingly, spreadability showed higher sensitivity to triethanolamine (coefficient +7.11). These interactions are visualized in Figure 1, illustrating the influence of formulation components on physical outcomes. The patterns indicate interactive effects: an increase in stearic acid tends to reduce pH and spreadability but increase viscosity and adhesion.

3.5. Optimization and validation

Optimization using the Simplex Lattice Design and Design Expert software identified a formulation with 15.2025% stearic acid and 3.7975% triethanolamine, resulting desirable performance characteristics: pH of 7.9, viscosity of 28,514.9 cP, adhesion of 2.11853 seconds, and spreadability of 6.92 cm. This optimal formula achieved a desirability value of 0.905, suggesting near-ideal

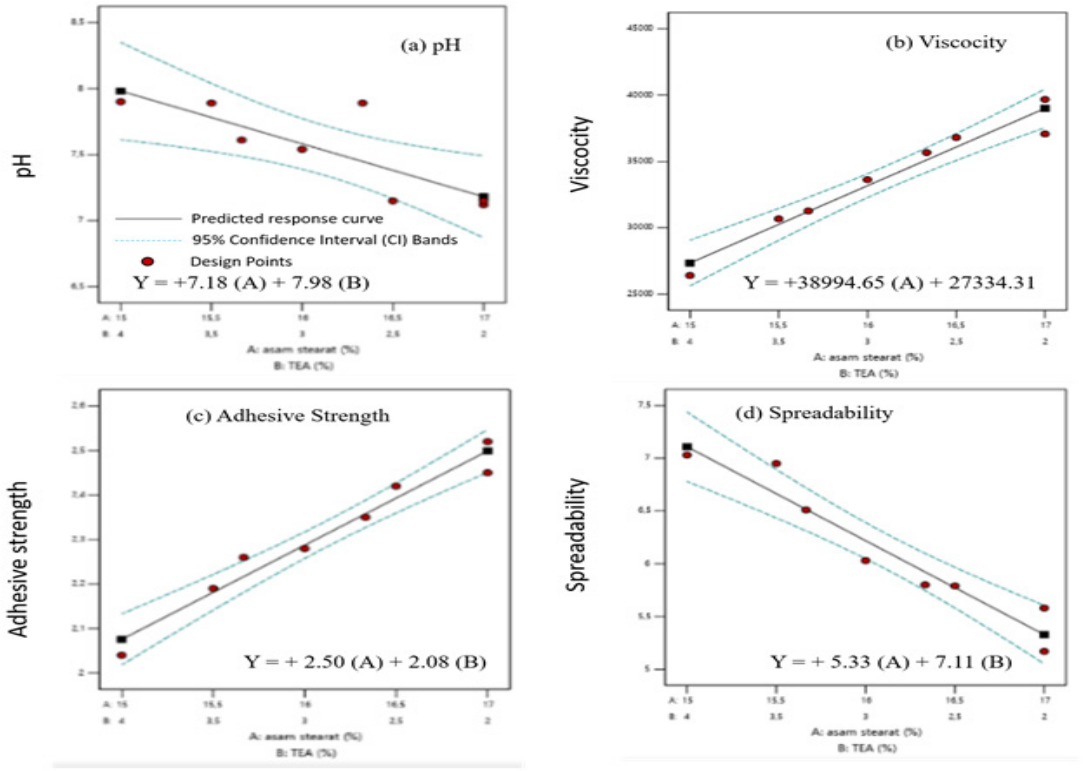

Figure 1. Influence of formulation components on physical results

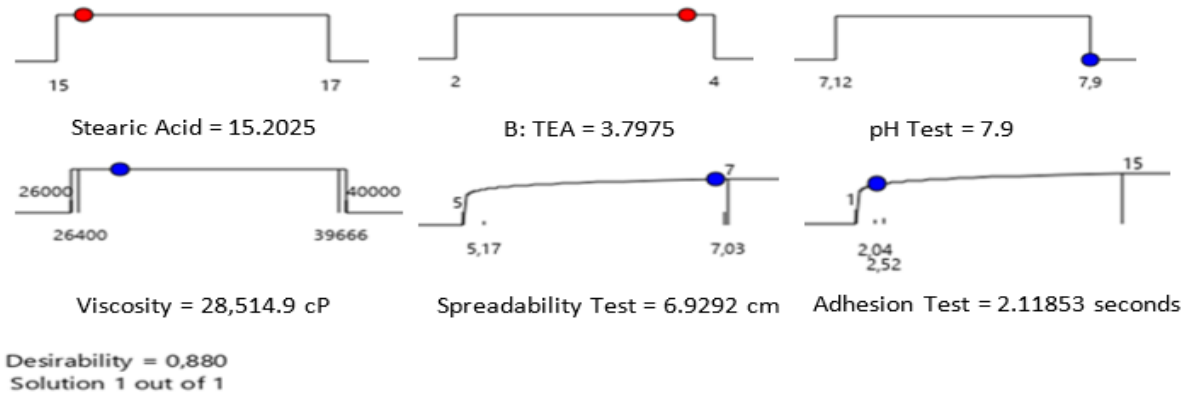

Figure 2. Optimum formula solution

conformity with the target attributes. The graphical output of this optimization is depicted in Figure 2, which presents the overlay plot indicating the optimal region in yellow, highlighting the most favorable ratio of emulsifiers to achieve the desired physical characteristics.

Validation through actual experimentation showed no significant difference from the predicted values, as detailed in Table 5. The SPSS Shapiro-Wilk test confirmed that discrepancies were statistically insignificant, reaffirming the reliability of the optimization process and the SLD modeling.

3.6. Comparison with previous studies

The results are consistent with similar findings from prior research. For example, Hartanati et al. reported comparable phytochemical contents in papaya leaf extracts, supporting the present findings [23]. The physical quality parameters are also in line with formulation standards in topical herbal preparations as discussed by Badwaik et

al. demonstrating that the formulation process effectively preserved bioactive properties while achieving desirable physical attributes [24].

3.7. Limitations and future work

While the study yielded promising results, it did not assess biological activities like anti-inflammatory or antimicrobial effects, nor did it evaluate the stability or shelf-life of the cream, which are important for therapeutic and commercial applications. Future studies should include long-term stability testing, biological efficacy evaluations (in vitro/in vivo), explore alternative emulsifiers or preservatives, and incorporate consumer sensory assessments to support product development and commercialization.

4. Conclusion

The study concluded that the combination of stearic acid and triethanolamine significantly influences the physical properties of papaya leaf extract (*Carica papaya* L.) cream, including pH, viscosity, adhesion, and spreadability. The optimal formulation was identified at 15.20% stearic acid and 3.79% triethanolamine, resulting in a stable cream with desirable characteristics. These findings underscore the importance of emulsifier balance in the development of effective topical herbal formulations and suggest that papaya leaf extract can be successfully utilized in cosmetic or pharmaceutical preparations. Future research is recommended to improve the organoleptic qualities of the cream and to explore alternative topical delivery systems, such as gels or lotions, which may further enhance the antioxidant potential and overall performance of papaya leaf extract-based products.

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