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Optimization of Papaya (*Carica papaya L.*) Leaf Extract Emulgel Formulation using Simplex Lattice Design for Topical Application

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ABSTRACT. Papaya (*Carica papaya* L.) leaf extract is rich in bioactive compounds with antioxidant, anti-inflammatory, and wound healing effects, making it a promising candidate for topical applications. However, there are challenges in formulating an effective and stable system. This study aimed to optimize the formulation of Papaya leaf extract emulgel using the simolex lattice design (SLD) method with various concentrations of Carbopol 940, Olive oil, and Tween 80. Eight formulations were evaluated for pH, viscosity, spreadability, and physical stability. This study showed that the optimal formulation of 1.0% Carbopol 940, 15% olive oil, and 10% Tween 80, which produced an emulgel with pH 6.1, viscosity of 4.580 cP, and spreadability of 6.8 cm, which are acceptable according to pharmaceutical standards. The above formulation showed good physical stability over 28 days of storage. In conclusion, the SLD method can be applied to developing typical herbal-based products and standardized for better effectiveness and stability.

INTRODUCTION

Papaya (*Carica papaya L.*) is a tropical plant found in Indonesia, valued not only for its nutritious fruit but also for its leaves, which possess numerous medicinal properties. Papaya leaves, commonly found, inexpensive, and often considered agricultural waste, offer a strong foundation for becoming an economical and sustainable pharmaceutical raw material. Papaya leaves have also been traditionally used in ethnomedicinal treatments for fever, skin inflammation, and wounds, thus enhancing their relevance as a topical therapy. These leaves contain several bioactive compounds, including flavonoids, alkaloids, tannins, and saponins, which have been identified for their therapeutic potential (Dwivedi et al., 2020). These compounds are extracted using ethanol as a solvent to isolate polar and semi-polar compounds (Dagne et al., 2021). After extraction, these bioactive compounds can be formulated into topical delivery systems such as emulgels, which offer various functional and cosmetic benefits (Wibowo et al., 2023).

Emulgel is a semi-solid dosage form that combines gel and emulsion, ideal for topical application. This form can provide stability, ease of application, skin penetration, and improve patient compliance (Talat et al., 2021). The selection and concentration of thickening agents, hydroxypropyl methylcellulose (HPMC) and Carbopol 940, significantly influence emulgel formulation. These ingredients contribute to key physical properties, including viscosity, pH, spreadability, and adhesion, which determine product performance and customer acceptance (Apriani *et al*., 2024).

The Simplex Lattice Design (SLD) is a statistical approach that enables researchers to evaluate the effects of different formulation components efficiently (Pratiwi *et al*., 2023). This method allows identifying the optimal ratios of HPMC and Carbopol that yield the desired physical characteristics in the emulgel (Samodra *et al*., 2023). This approach streamlines the formulation process but also enhances the reproducibility of results, making it a valuable tool in pharmaceutical development (Mahfuz *et al*., 2023).

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Several studies have explored topical product formulations using Papaya (*C. papaya* L.) extract and other fruit extracts. For example, Alfaridz and Amalia (2016) examined the use of Papaya leaf extract in a topical antioxidant gel. Khairunnisa *et al.*(2023) successfully identified alkaloids, flavonoids, and saponins in *C. papaya* L. and their formulation into a stable topical gel. Pratiwi *et al*. (2023) developed a guava leaf-based emulgel with significant anti-inflammatory effects. Samodra *et al*. (2023) optimized a topical formulation containing mangosteen peel extract using the SLD method. Meanwhile, Dagne *et al*. (2021) demonstrated that rambutan peel extract can be effectively incorporated into gel formulations for antibacterial activity. These studies highlight the feasibility and therapeutic potential of fruit-derived phytochemicals in emulgel systems.

In this study, the emulgel formulation will undergo rigorous physical testing, including pH measurement, viscosity determination, adhesion tests, and spreadability assessments (Dhal *et al*., 2023). These parameters are crucial in determining the suitability of the emulgel as a topical preparation and ensuring its efficacy and safety for consumers (Lakshmi *et al*., 2021). The findings of this study will contribute to the development of knowledge regarding herbal-based topical product formulations and their potential benefits (Olayemi and David, 2023).

RESEARCH METHODS

The materials used in this study were Papaya (*C. papaya* L.) leaf extract, Carbopol 940 (Lubrizol, USA), hydroxypropyl methylcellulose (HPMC; Dow Chemical, USA), propylene glycol, methyl paraben, propyl paraben, liquid Paraffin, Tween 80, Span 80, Triethanolamine (TEA), and distilled water; all sourced from Brataco, Indonesia.

The equipment used in this study were analytical balances (A&D, Japan), a rotary evaporator (Heidolph, Germany), maceration equipment, a mortar, a stamper, a beaker glass, a stirring rod, a water bath, a Brookfield viscometer (Brookfield, USA) to determine viscosity, a digital pH meter (Mettler Toledo, Switzerland) for pH analysis, spreadability and adhesion test equipment based on standardized pharmaceutical procedures, silica gel GF254 plates, and UV light at 254 and 366 nm.

Experiment

Papaya leaf was extracted by maceration using the aforementioned equipment. Emulgels were prepared in eight different formulation compositions designed using the SLD, as detailed in Table 1. Physical characterization of each formulation was conducted using a Brookfield viscometer (Brookfield, USA) to determine viscosity, a digital pH meter (Mettler Toledo, Switzerland) for pH analysis, and spreadability and adhesion test equipment based on standardized pharmaceutical procedures. Phytochemical screening was performed to detect flavonoids, alkaloids, saponins, and tannins, using both tube test reactions and thin-layer chromatography (TLC) with silica gel GF254 plates and visualized under UV light at 254 and 366 nm. Observational results such as color change, precipitation, or foam persistence were recorded manually and interpreted based on standard phytochemical references. All measurements were carried out in triplicate. Data were analyzed using descriptive statistics and, where applicable, one-way ANOVA to evaluate significant differences across formulations. The methodology was designed to ensure reproducibility and clarity in process and result interpretation.

Table 1. Papaya leaf emulgel formula design

Materials (%)	**Run**							
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Papaya leaf extract	6	6	6	6	6	6	6	6
Carbopol 940	1.25	2	2	1.5	0.875	1.625	1	0.5
HPMC	3.25	2.5	2.5	3	3.625	2.875	3.5	4
Propylene glycol	5	5	5	5	5	5	5	5
Methyl paraben	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Propyl paraben	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Liquid paraffin	5	5	5	5	5	5	5	5
TEA	2	2	2	2	2	2	2	2
Tween 80	3.12	3.12	3.12	3.12	3.12	3.12	3.12	3.12
Span 80	5.88	5.88	5.88	5.88	5.88	5.88	5.88	5.88
Distilled water	ad 100	ad 100	ad 100	ad 100	ad 100	ad 100	ad 100	ad 100

The overall experimental process is summarized in Figure 1 to provide a clearer understanding of the sequence and interconnection between each methodological step.

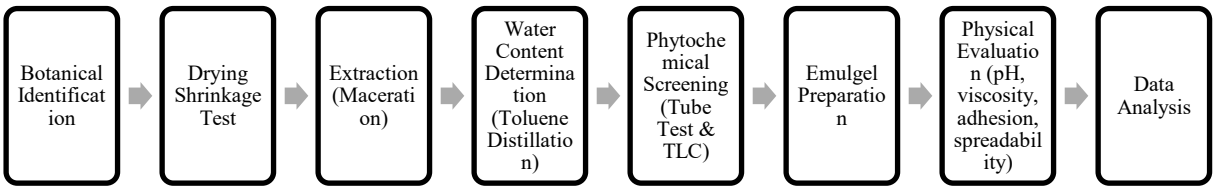

Figure 1. Methodological flow of emulgel formulation and characterization based on Papaya (*Carica papaya* L.) leaf extract.

Botanical Identification and Drying Shrinkage Test

The experimental setup began with the botanical identification of the Papaya leaves (*C. papaya* L.) to ensure the authenticity of the plant material used. The leaves were collected from the Center for Research and Development of Medicinal Plants and Traditional (B2P2TOOT), Tawangmangu, Central Java, Indonesia (GPS coordinates: -7.6635957, 111.1344777). This identification was conducted at UPF Yankestrad, RSUP Dr. Sardjito, Yogyakarta, following standard taxonomic procedures, including macroscopic observation of leaf morphology in accordance with established botanical references (Nurdin *et al*., 2024; Yap *et al*., 2022). For the drying shrinkage test, 2 grams of powdered Papaya leaves were weighed and placed in a moisture balance set at 105 °C. The process continued until a constant weight was achieved, indicating moisture loss not exceeding 10% (Artanti *et al*., 2021; Yilmaz *et al*., 2021).

Extraction

Extraction of the Papaya leaves was carried out using the maceration method. The powdered plant material was soaked in 96% ethanol for six hours with periodic shaking, followed by an additional soaking period of 18 hours. The mixture was then filtered using filter paper and flannel to separate the residue and filtrate. The remaining residue was re-macerated to maximize compound extraction. The resulting filtrate was evaporated using a rotary evaporator at 50 °C until a thick extract (Khor *et al*., 2021).

Water Content Determination

Water content was determined using the toluene distillation method. Five g of Papaya leaf extract was placed in a Bidwell-Sterling distillation apparatus with 200 mL of water-saturated toluene, then heated slowly using a Bunsen burner for 15 minutes until no water separated in the receiving tube. Water content was measured using a separate volume of water (Kamilla *et al*., 2021).

Phytochemical Screening

Phytochemical screening of the extract was carried out using tube tests and Thin Layer Chromatography (TLC) to detect the presence of secondary metabolites such as flavonoids, saponins, alkaloids, and tannins.

Emulgel Preparation

The emulgel was prepared by first dispersing Carbopol 940 and HPMC in distilled water and stirring the mixture until homogeneous. Triethanolamine was gradually added to form the gel base. Methyl- and propyl-paraben were dissolved in propylene glycol and incorporated into the gel. Meanwhile, the oleaginous phase, composed of liquid paraffin and Span 80, and the aqueous phase, consisting of Tween 80 and distilled water, were separately heated to 70°C. Both phases were combined and stirred to form an emulsion, which was subsequently added to the gel base and stirred to obtain the final emulgel (Shah, 2021).

Physical Evaluation

The data collection focused on assessing the physical properties of the emulgel formulation. The organoleptic observations were conducted to assess odor, color, and consistency. A digital pH meter was used to measure pH levels, while viscosity was determined using a Brookfield viscometer. Adhesion was evaluated using a glass slide apparatus, and spreadability was assessed using a standardized plate method. These tests were conducted to ensure the stability, safety, and usability of the topical formulation.

Data Analysis

Data analysis involved summarizing the results through descriptive statistics, and where necessary, applying statistical tests such as ANOVA to evaluate significant differences across the eight formulation runs as outlined in Table 1.

RESULTS AND DISCUSSION

Botanical Authentication and Raw Material Quality

The Papaya leaves used in this study were authenticated at UPF Yankestrad Tawangmangu RSUP Dr. Sardjito Yogyakarta, as confirmed by evaluation letter number TL.02.04/D.XI.6/19292.1016/2024. The species was identified as *C. papaya* L. The drying shrinkage test of the powdered Papaya leaves showed an average loss of 5.5%, indicating compliance with the Indonesian Ministry of Health standard, which allows a maximum of 10% (Farmakope Herbal Indonesia, 2017). This relatively low moisture loss may be attributed to the proper drying technique, optimal environmental conditions during sample collection and storage, and the inherent low water content of mature Papaya leaves at the time of harvest.

Extraction Yield

Extraction was carried out using a rotary evaporator at 60 °C, yielding a thick extract of 205.29 grams, equivalent to 18.67%, which satisfies the yield requirement of not less than 18.2% according to the Indonesian Herbal Pharmacopoeia standard (Farmakope Herbal Indonesia, 2017).

Physical Evaluation of Emulgel

After extraction, the emulgel formula was then evaluated for its physical properties related to its pharmaceutical properties. The parameters measured were pH, viscosity, spreadability, and adhesion. Spreadability and adhesion were measured and calculated using the following Equations 1 and 2, respectively:

$$S = \frac{M \times L}{T} \quad (1)$$

where S is spreadability (g·cm/s), M is the applied load (g), L is the distance spread (cm), T is the time required (s).

$$A = W \times T \quad (2)$$

where A is adhesion (g·s), W is weight (g), T is time (s).

Water Content of Extract

The average water content of the extract, determined using the distillation toluene method with the Bidwell Sterling apparatus, was 13.33%. This value also meets the required threshold of ≤20% (Farmakope Herbal Indonesia, 2017). The relatively moderate water content may be influenced by several factors, including the hygroscopic nature of certain phytochemical constituents such as flavonoids and saponins, which tend to retain moisture. Incomplete removal of residual water during rotary evaporation, possibly due to limited evaporation time, suboptimal vacuum pressure, or moderate temperature settings. Furthermore, high environmental humidity during concentration may result in reabsorption of water by the extract, especially if cooling and storage conditions are not fully controlled.

Phytochemical Screening

Phytochemical screening showed the presence of flavonoids, alkaloids, saponins, and tannins, supported by both test tube observations and thin-layer chromatography (TLC), as shown in Tables 2 and 3. The TLC results showed appropriate Rf values and corresponding colors under UV at λ (nm) 254 and 366 for each phytochemical component, validating the presence of target compounds.

Table 2. Phytochemical screening of Papaya leaf extract.

Phytochemical Compound	Reagent Tes	Observed Results	References
Flavonoids	Amyl alcohol + Mg + HCl (Shinoda test)	Orange color in the amyl alcohol layer	There is an orange color in the amyl alcohol layer (Alfaridz and Amalia, 2016).
Alkaloids	Mayer's and Dragendorff's reagents	Yellowish-white precipitate (Mayer's), orange precipitate (Dragendorff's)	Positive for containing alkaloids if there is an orange precipitate in the Dragendroff reagent and a yellowish white precipitate in the Mayer reagent (Khairunnisa *et al*., 2023).
Saponin	Foam test with HCl	Persistent foam after the addition of 1 drop of 2N HCl	Foam 1-10 cm high forms for no less than 10 minutes, and by adding one drop of 2 N HCl the foam does not disappear (Khairunnisa *et al*., 2023).
Tannin	$FeCl_3$ 1% solution	Formation of blackish-green color	Shows a blackish green color (Khairunnisa *et al*., 2023).

Table 3. Rf values from TLC analysis.

Testing	Color of test results							
	Comparative standard	Mobile phase	Spray reagent	UV 254 nm	UV 366 nm	Standard Rf	Rf extract	Note
Flavonoids	Quercetin	n-butanol: distilled water: acetic acid (2.8:3.5:0.7)	Cytorborate	Gray	Blackish grey	0.50	0.36; 0.43; 0.50	+
Alkaloids	Caffeine	Chloroform : methanol (6.3:0.7)	Dragendorf	Yellowish green	Brownish red	0.87	0.63; 0.7; 0.8	+
Saponin	Sapogenin	Chloroform: methanol: aquadest (4.2:2.1:0.7)	Anisaldehyde -sulfuric acid	Gray green	Blackish red	0.8	0.2; 0.45; 0.6	+
Tannin	Gallic acid	n-butanol: distilled water: acetic acid (2.8:3.5:0.7)	$FeCl_3$ 1%	Blackish green	Blackish red	0.8	0.45; 0.6; 0.8	+

Physical Characterization

Physical characterization of the emulgel showed that all eight formulations had consistent organoleptic properties with a blackish-green semi-solid consistency and distinctive odor. The homogeneity test indicated no visible lumps when spread between glass plates. Table 4 details the pH, viscosity, spreadability, and stickiness test results for each formulation. The pH ranged from 6.24 to 8.94, viscosity from 32.066 to 49.533 cP, spreadability from 5.2 to 6.18 cm, and stickiness from 4.02 to 9.7 seconds.

Effect of Polymer Composition

The drying shrinkage and water content values indicate that the raw and extracted materials are within the acceptable limits for pharmaceutical preparations. The presence of key phytochemicals such as flavonoids and alkaloids is essential for the therapeutic potential of the emulgel. As shown in formulation studies on Table 4, increasing HPMC content across formulations (e.g., F3 to F8) correlated with higher viscosity and adhesion values,

suggesting that HPMC plays a key role in modifying these physical properties. Conversely, higher Carbopol content tends to lower pH and improve spreadability, as observed in Carbopol-based systems. These outcomes align with the chemical characteristics of the polymers HPMC, being a non-ionic cellulose derivative, enhances gel structure and viscosity, whereas Carbopol, a synthetic acidic polymer, contributes to increased spreadability (Hashemi-Afzal *et al*., 2025; Alburyhi *et al*., 2025). HPMC improves structure and viscosity because its cellulose chains can form a three-dimensional network through hydrogen bonding with water molecules. As the HPMC concentration increases, the number of hydroxyl groups interacting with water increases, resulting in a thicker and more stable solution. Conversely, Carbopol is an acrylic acid polymer that ionizes at a neutral or slightly alkaline pH. Under these conditions, the polymer chains repel each other, swell, and produce a gel that spreads easily. However, its acidic nature lowers the pH of the system, so formulations with higher Carbopol content tend to have a lower pH and better spreadability.

Table 4. Physical characteristics of emulgel formulations.

Testing	Results							
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
Test pH	7.36 ± 0.005	6.68 ± 0.45	6.24 ± 0.02	6.81 ± 0.08	8.49 ± 0	6.24 ± 0.02	8.14 ± 0.04	8.94 ± 0.04
Viscosity	41.800 ± 200	37.200 ± 1928	32.066 ± 3239	45.800 ± 1311	48.933 ± 2003	43.600 ± 916	46.066 ± 986	49.533 ± 2042
Spreadability	5.93 ± 0.20	5.9 ± 0.05	6.18 ± 0.07	5.66 ± 0.02	5.43 ± 0.15	5.7 ± 0.17	5.66 ± 0.23	5.2 ± 0.1
Stickiness	5.45 ± 0.98	5.26 ± 0.31	4.02 ± 0.48	8.02 ± 1.66	9.03 ± 1.82	5.09 ± 0.74	6.68 ± 1.06	9.7 ± 1.18

Optimization Using Simplex Lattice Design (SLD)

The optimization of the emulgel formulation was conducted using the SLD approach. The model used for prediction is as in Equation 3.

$$Y = \beta_1 X_1 + \beta_2 X_2 + \beta_{12} X_1 X_2 \quad (3)$$

Where Y is the response (e.g., viscosity, spreadability), X_1 is the proportion of HPMC, X_2 is the proportion of Carbopol, and β is the regression coefficient. The predicted, actual experimental, and validation values for the responses are shown in Tables 5, 6, and 7. The number of plus signs (+) in the "Importance" column reflects the relative weight assigned to each response during optimization: +++++ indicates very high importance, and +++ denotes moderate importance, as determined by the formulation goals and critical product requirements. The results obtained are derived from the calculation of the SLD regression equation built from the experimental data of eight formulations.

Table 5. Predicted responses based on the SLD model.

Critical point	Goal	Limits		Importance
		Lower	**Upper**	
pH test	*In range*	4.5	6.5	+++++
Viscosity test	*In range*	6.000	50.000	+++++
Adhesion test	*Maximize*	1	15	+++
Spreadability test	*Maximize*	5	7	+++

Table 6. Experimental results of emulgel formulations.

Carbopol 940 (%)	HPMC (%)
1.658	2.842

Optimization results using the SLD method yielded the best composition for the emulgel formulation, namely Carbopol 940 at 1.658% and HPMC at 2.842%. These percentages were obtained from Response Surface Methodology (RSM) calculations, which combine experimental data from various concentration combinations with a quadratic equation model to meet the desired response criteria.

Table 7. Validation of the statistical model.

pH	Viscosity (cP)	Adhesive Strength (second)	Spreadability (cm)	*Desirability*
6.346	40083.755	5.656	5.860	0.913

The formulation with these compositions was then realistically prepared in the laboratory and tested to ensure the model's predictions met. Validation results showed a pH of 6.346, a viscosity of 40,083.755 cP, an adhesive strength of 5.656 seconds, and a spreadability of 5.860 cm. The desirability value of 0.913 indicates that this optimum formula has a very high level of conformity to the established target criteria.

The results of the optimization tests using the SLD method are displayed in Figure 2. In the pH response surface (Figure 2a), higher concentrations of HPMC increased the pH value, while increasing carbopol concentrations had the opposite effect. The viscosity response graph (Figure 2b) demonstrated a positive correlation with increasing HPMC levels. Similar trends were seen in the adhesion test (Figure 2c), where higher HPMC led to increased adhesion time. In contrast, the spreadability graph (Figure 2d) showed better results with higher carbopol concentrations, producing a more easily spreadable formulation.

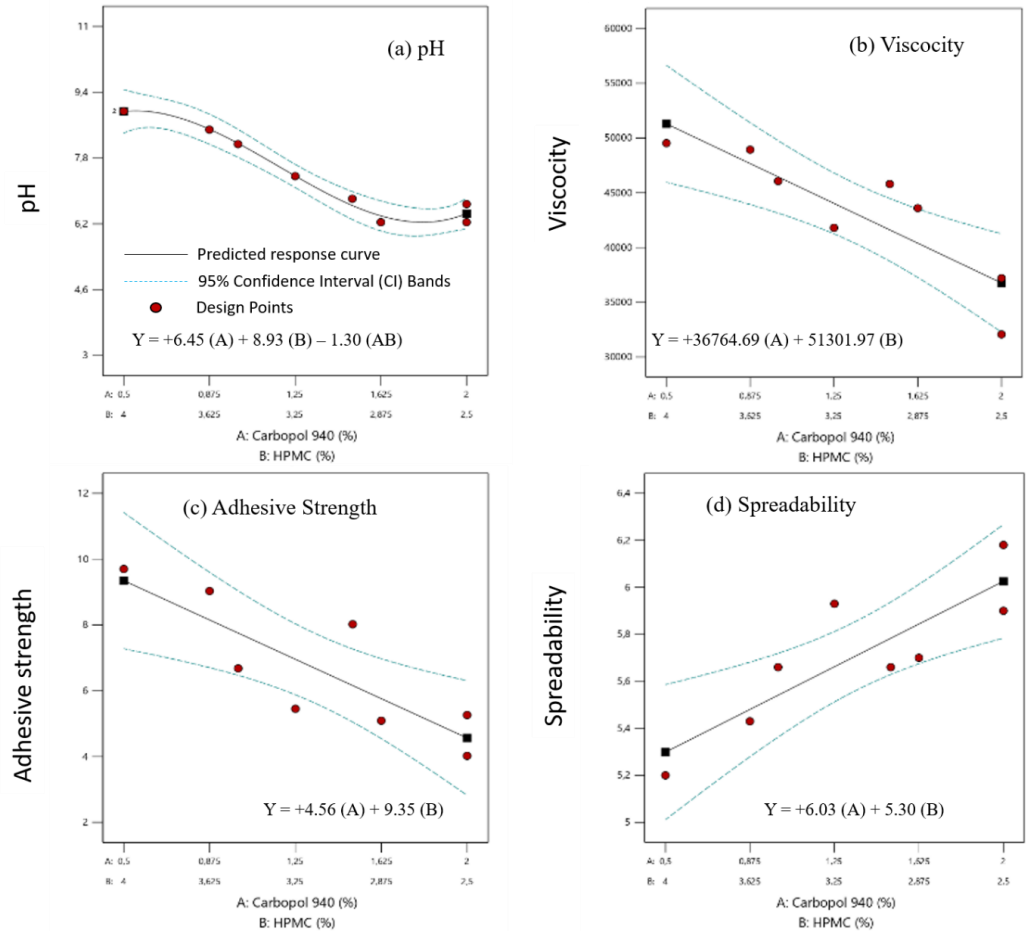

Figure 2. Effect of Carbopol 940 and HPMC composition on emulgel characteristics.

This trend occurs due to the differences in the chemical properties of the two polymers. HPMC, as a non-ionic polymer, increases the density of the gel network, thereby increasing the pH, viscosity, and adhesion time. Conversely, the acidic Carbopol 940 lowers the pH and, upon neutralization, produces a softer, more spreadable gel, thus improving spreadability. In the pH response, higher HPMC concentrations increased the pH value, while increasing carbopol concentrations had the opposite effect. The viscosity response showed a positive correlation with increasing HPMC concentration, and a similar trend was observed in the adhesion test, where higher HPMC concentrations resulted in longer adhesion times. Conversely, the spreadability response showed better results at higher carbopol concentrations, resulting in more spreadable formulations. This pattern reflects the intrinsic properties of each polymer. As a non-ionic cellulose derivative, HPMC slightly increases the pH and strengthens

the three-dimensional gel network, thus increasing viscosity and adhesion. Meanwhile, Carbopol, a polyacrylic acid polymer, contributes acidic groups that lower the pH and, at high concentrations, reduce gel stiffness, thus increasing spreadability.

Model Validation

Table 8 compares the average values of the physical test results (pH, viscosity, spreadability, and adhesion) and the predicted values of the SLD software. All parameters showed $p > 0.05$, indicating no significant difference between the experimental results and the predicted values. The "Experiment results" value is the average (± SD) of three tests, while the "Prediction software" was obtained from the SLD model calculation based on the formula selected from the response surface graph in Figure 2. This insignificance ($p > 0.05$) indicates that the SLD model can predict the physical characteristics of the formula well, making it useful in the optimization process, as it allows the selection of the optimum composition without many additional laboratory experiments. Based on the prediction analysis, the optimum formula is Carbopol 940 at 1.658% and HPMC at 2.842%.

The physical and chemical characteristics of the Papaya leaf extract and its emulgel formulation align well with findings reported in previous studies. Alburyhi *et al*. (2025) also noted that HPMC significantly increases pH and viscosity in topical formulations. Donthi *et al*. (2023) emphasized that optimal gel agent combinations influence the efficacy of active compound delivery. The presence of major phytochemicals corresponds with observations by Khairunnisa *et al*. (2023) and Alfaridz and Amalia (2016). Alfaridz and Amalia (2016) identified similar components in *C. papaya* L. using comparable test methods. Furthermore, the validation of the Simplex Lattice Design predictions against experimental data (Table 8) with no significant differences ($p > 0.05$) supports the reliability of using such statistical approaches in formulation optimization. The optimum formula Carbopol 940 at 1.658 % and HPMC at 2.842 % matches the SLD prediction results, consistent with findings by Pérez-González *et al*. (2023) and Elsewedy *et al*. (2021).

Table 8. Physical quality test values of the optimum formula for Papaya leaf extract emulgel preparations.

Testing	Experiment results	Prediction software	Significance (p-value)	Information
pH test	6.34 ± 0.015	6.34	>0.05	Not significantly different
Viscosity Test	41066 ± 2928	40078	>0.05	Not significantly different
Spreadability Test	5.93 ± 0.25	5.85	>0.05	Not significantly different
Adhesion Test	5.35 ± 0.15	5.65	>0.05	Not significantly different

Study Limitations and Future Directions

Although the formulation process successfully produced stable and compliant emulgel products, there are some limitations to consider. The influence of environmental conditions, such as temperature fluctuations during weighing and mixing, may have contributed to minor inconsistencies in some runs. Furthermore, this study was conducted in a controlled laboratory setting and did not evaluate long-term stability, bioactivity on human skin, or microbial contamination. These factors may impact the formulation's real-world implementation and require further study. Future research should explore optimized emulgel shelf life, long-term stability, and in vivo testing to assess skin compatibility and pharmacological efficacy. Studies on microbial stability and adding preservatives are also essential to ensure the formulation's safety during long-term use. Furthermore, comparing the scope of active compounds from *C. papaya* L. with other botanical extracts could enhance the product's therapeutic potential and competitiveness.

CONCLUSION

This study successfully created a topical emulgel using Papaya (*C. papaya* L.) leaf extract, optimized using hydroxypropyl methylcellulose (HPMC) and Carbopol 940 through the Simplex Lattice Design method. Eight formulations demonstrated physical characteristics suitable for topical application, including stable pH (6.24 – 8.94), viscosities (32.066 – 49.533 cP), spreadability (5.2 – 6.18 cm), and adhesion (4.02 – 9.7 seconds). Phytochemical analysis revealed the presence of important bioactive compounds such as flavonoids, alkaloids, saponins, and tannins, which enhance the therapeutic potential of the extracts. The optimized formulation demonstrated good homogeneity and met general quality standards for herbal-based semi-solid products. While the results are promising, this study is limited by the lack of in vivo and in vitro biological testing to confirm

pharmacological activity or skin suitability. Future investigations should include such biological evaluations to strengthen the therapeutic claims and assess safety in clinical contexts. Additionally, stability testing over time and under various storage conditions is necessary to ensure long-term usability and commercial viability. These findings are particularly relevant in the context of increasing global interest in herbal-based pharmaceutical innovation and the regulatory encouragement of evidence-based traditional medicine. The successful use of the Simplex Lattice Design further highlights the value of statistical modeling in modern formulation science, supporting the advancement of standardized, effective, and scalable topical therapies derived from locally sourced botanical ingredients.

CONFLICT OF INTEREST

There is no conflict of interest in this article.

AUTHOR CONTRIBUTION

NR: Data Colection, Data Analysis; SA: Conceptualization, Methodology; MN: Manuscript Drafting; DM: Conceptualization, Data Analysis, Manuscript Review and Editing

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