

Physical Properties, Stability, and Biological Activity of a Combination Sunscreen Emulgel Formulation Containing Octyl Methoxycinnamate and Hexagamavunon-5: An In Vitro and In Vivo Evaluation

Purbandari Ajeng Sarweningtyas¹, Abdul Karim Zulkarnain^{1*}, Ritmaleni²

¹ Department of Pharmaceutics, Faculty of Pharmacy, Gadjah Mada University, Sekip Utara, 55281, Yogyakarta 55281, Indonesia

² Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Gadjah Mada University, Sekip Utara, 55281, Yogyakarta Indonesia

Article Info

Submitted: 30-12-2024

Revised: 20-05-2025

Accepted: 20-05-2025

*Corresponding author
Abdul Karim Zulkarnain

Email:
akarimzk@ugm.ac.id

ABSTRACT

OMC (Octyl Methoxycinnamate) has intense sunscreen activity, but susceptible to photodegradation upon exposure to UV light, leading to the formation of free radicals. The incorporation of antioxidants can mitigate UV-induced degradation and preserve OMC in its trans configuration, thereby maintaining its photoprotective efficacy. Hexagamavunon-5 (HGV-5) contains phenolic hydroxyl groups and conjugated double bonds, which are key to its antioxidant activity. In this study, we develop a sunscreen emulgel formulation combining OMC and HGV-5 to improve activity and stability. The Simplex Lattice Design (SLD) method was applied to optimize emulsion (Tween 80, Span 80, and Paraffin Liquid) using Design Expert (DE). The DE obtained 14 runs and testing the responses to determine the optimum formula. The optimum formula of the emulsion was then made into five(5) emulgel preparation. The emulgel were tested in vitro to determine percent transmission of erythema (%TE), percent transmission of pigmentation (%TP), and Sun Protection Factor (SPF) values as presenting of photostability test. The best formula of emulgel determines the in vivo irritation test, physical characterization, and stability test. HGV-5 has an IC₅₀ value of 8,46 ppm (strong antioxidant activity), indicating potential as a stabilizer agent for UV filters. The DE chosen as the optimum formula of emulsion were Tween 80 3.15% (v/v), Span 80 3.75% (v/v), and Paraffin Liquid 3.1% (v/v). F4 showed good photostability and obtained SPF values in the ultra protection category and %TE and %TP in the sunblock category. Referring to the storage results, the optimum formula was stable for a month. The irritation test of F4 showed that the PII value was 0 in the treatment group compared to the control group. F4 revealed that does not cause irritation, so it can be concluded that F4 is safe.

Keywords: Emulgel, OMC, GV-5, Sunscreen, Irritation Test.

INTRODUCTION

The depletion of the ozone layer has led to increased exposure to UV radiation in recent decades. It is reported that 1.5 million people experience Disability-Adjusted Life Years (DALYs) due to this radiation exposure (Owusu & Sarkodie, 2020). In Indonesia, a tropical country located on the equator, there is a potential for high exposure to solar radiation (Mumtazah et al., 2020). Three types of UV radiation that can reach the Earth's surface are UVA, UVB, and UVC. UVB radiation exposure has side effects such as melanoma,

photoaging, skin pigmentation, sunburn, and prolonged exposure, which can lead to skin damage or cancer (Bhalke et al., 2020). The harmful effects of ultraviolet rays can be prevented with sunscreen. Octyl Methoxycinnamate (OMC) is a cinnamate derivative commonly used as a sunscreen agent. OMC is often chosen because it has low toxicity, does not cause irritation or sensitization in animals, and rarely causes contact dermatitis allergy in humans (Tampucci et al., 2018). However, OMC is light-sensitive, and its protective activity against UV exposure can

decrease (Gunia-Krzyżak et al., 2018). In the study, the OMC formula with added antioxidants only degraded by 15%, whereas the OMC formula without antioxidants decreased by up to 45% (Vilela et al., 2016). The instability of OMC poses a risk of endocrine disruption and its effectiveness as a sunscreen will decrease. Therefore, sunscreen formulations need to include stabilizers to improve protection, effectiveness and safety. As a result, using formulations with antioxidants to stabilize UV filters can reduce degradation processes (Lorigo & Cairrao, 2019). One compound known to have antioxidant activity is Hexagamavunone-5 (HGV-5), an analog of curcumin that has been proven the antioxidant activity (Sari et al, 2015). HGV-5 showed strong antioxidant activity caused by had phenolic functional group reacting with a variety of free radicals to neutralize these radicals (Sardjiman et al., 1997), thereby interrupting the chain reaction of photodegradation and improve the stability of OMC (Scalia & Mezzena, 2010). Antioxidant activity testing of HGV-5 was conducted using two methods: the DPPH radical scavenging assay and the ferric reducing antioxidant power (FRAP) assay. The results showed that HGV-5 has strong antioxidant potential, as indicated by its IC₅₀ values of 150.44 µM (DPPH assay) and 35.10 µM (FRAP assay) (Sari et al, 2015).

OMC is prone to degradation upon UV exposure. Previous studies have explored the use of stabilizing agents, however the topical application of HGV-5 particularly in combination with chemical UV filters, has not been thoroughly investigated. HGV-5 exhibits antioxidant and anti-inflammatory activities, but its potential as a stabilizing agent in sunscreen emulgel formulations has not been well explored. Therefore, this study aims to formulate and evaluate a sunscreen emulgel combining OMC and HGV-5, with the goal of assessing the potential of HGV-5 as a stabilizing agent for UV filters in topical sunscreen application. Therefore, this study aims to formulate and evaluate a sunscreen emulgel combining OMC and HGV-5, to investigate the potential of HGV-5 as a stabilizing agent for UV filters in topical applications. The formulation uses an emulgel system, which is particularly suitable due to the lipophilic nature of both OMC and HGV-5. In emulgel systems, lipophilic compounds are incorporated into the oil phase, which is then dispersed into the aqueous phase and mixed into a gel base (Light & Karboune, 2022). Emulgels are chosen for their superior stability and skin penetration compared to conventional topical

dosage forms such as creams (Butkeviciute et al., 2022). To optimize the base emulsion formulation, this study utilizes the Simplex Lattice Design (SLD) method. The OMC and HGV-5 emulgel formulation is then evaluated for its physical stability, sun protection efficacy, and safety through measurements of SPF value, %transmission erythema (%TE), %transmission pigmentation (%TP), and a primary irritation test on rabbit skin.

MATERIALS AND METHODS

Octyl Methoxycinnamate (Chemspec Chemical, India), HGV-5 (Departement of Chemistry, Faculty of Pharmacy, UGM), Carbopol 940 (Bratachem, Indonesia), TEA (Bratachem, Indonesia), Aquadest (General Labora, Indonesia), Ethanol (p.a.) (Merck, Jerman), Liquid Paraffin (Brataco, Indonesia), Tween 80 (Brataco, Indonesia), Span 80 (Brataco, Indonesia), Olive Oil (Shisam Mas, Indonesia), DMDM Hydantoin (Labora, Indonesia), Propylene Glycol (Labora, Indonesia), DPPH (Aldrich, USA), and Vitamin E (Sigma Aldrich, USA). The test animals used in this study were albino rabbits with a body weight of 1.5-2 kg. The test animals met the requirements for use and treatment and were approved by the ethics committee of the FKH, Gadjah Mada University. Number of Ethical Clearance 139/EC-FKH/int./2024.

Antioxidant Activity Test of HGV-5 using DPPH

A total of 4,26 mg of DPPH was dissolved in 20 mL of 96% ethanol. The solution was shaken until homogeneous resulting in a DPPH concentration of 0.4 mM. The HGV-5 solution was prepared with at concentrations of 20, 60, 80 and 100 µM. Vitamin E, as a comparator, was prepared with concentration at 60, 70, 80 and 100 µM. Each sample solution consisted of 1 mL sample, 1 mL of the DPPH solution and ethanol 96% added to a total volume of 5 mL. The blank solution was prepared by mixing 1 mL of the DPPH solution with 4 mL of 96% ethanol in a test tube. After that, the tubes sample were kept in complete darkness for 25 min for HGV-5 and 20 min for Vitamin E (Novita Sari et.al, 2015). The absorbance was therefore determined at 517 nm (Kholifah et al., 2023). The following formula was used to compute the percentage of antioxidant :

$$\% \text{ of antioxidant activity} : \frac{(A \text{ blank} - A \text{ sample})}{A \text{ blank}} \times 100\%$$

A blank= DPPH radical absorption of 0.4mM; A Sample = DPPH radical absorption of 0.4mM after sample treatment.

Tabel I. Design Formulation of Emulgel

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14
A OMC	6	6	6	6	6	6	6	6	6	6	6	6	6	6
HGV-5	0.1 – 0.2													
Tween 80	2.2	3.15	2.2	2.2	1.25	2.52	3.15	3.15	2.2	2.2	2.2	3.15	3.15	3.15
Span 80	2.8	2.8	2.8	2.8	3.75	3.11	2.8	3.75	3.75	3.75	3.75	1.85	3.75	2.8
B Liquid Paraffin	5	4.05	5	5	5	4.37	4.05	3.1	4.05	4.05	4.05	5	3.1	4.05
Olive Oil	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
DMDM Hydantoin	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Propylen Glycol	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Carbopol 940	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
C TEA	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Aquadest	ad 100													

Phase: A (Active Ingredient); B (Emulsion); C (Gel)

After obtaining % antioxidant activity, the Inhibition Concentration 50% (IC50) was analyzed using a calibration curve using $y=ax+b$, then the IC50 value was classified (Kholifah et al., 2023).

Emulgel Formula Design for OMC and HGV-5

The emulgel formulation was developed based on a previously established emulgel formula, with modifications to the emulsifiers and oil base, specifically Tween 80, Span 80, and Liquid Paraffin. The base emulgel formula was determined with the help of Design Expert 13 software using the SLD method. The emulgel run design based on the reference formula (Table I).

Orientation of the Emulsion Formula Base for OMC and HGV-5

The formulation design was using Tween 80 at concentrations ranging from 1.25% (v/v) to 3.15% (v/v), Span 80 from 1.85% (v/v) to 3.75% (v/v), and Liquid Paraffin from 3.1% (v/v) to 5% (v/v). Determination of Tween 80 and Span 80 concentrations based on HLB calculation. The Design Expert software determined 14 formula runs of emulsion formula.

Determination and verify the Optimum Emulsion Formula

The optimum base formula was determined based on the responses obtained from each formula using the SLD method. The response categories for emulsion are droplet size, phase separation volume ratio, and emulsion viscosity. The optimum base formula was selected based on the degree of importance and target responses for each criterion. One optimal formula obtained was then subjected

to a verification test by preparing and evaluating the recommended optimal formula. Verification of the optimum formula was conducted using a one-sample t-test statistical analysis with a 95% confidence level to determine whether the data generated by the software significantly differed from the experimental results.

Formulation of Emulgel OMC and HGV-5

The selected optimum formula emulsion was then used to prepare the sunscreen emulgel with 5 different variation groups: F1 (OMC 6% w/v); F2 (OMC 6% w/v and HGV-5 0.1 % w/v); F3 (OMC 6% w/v and HGV-5 0.15% w/v); F4 (OMC 6% w/v and HGV-5 0.2% w/v); and F5 (HGV-5 0.1% w/v). The emulgel formula was prepared by incorporating the emulsion into the gel base. The preparation of the emulgel was carried out in three main stages as follows:

Preparation of Emulsion

The oil phase was mixed in one beaker, and the liquid phase was mixed in another beaker glass. In the oil phase, liquid paraffin was combined with OMC and Span 80. Next, HGV-5 was dissolved in Tween 80 using a sonicator, added to the oil phase, and stirred for 15 minutes with a magnetic stirrer until homogeneous. Distilled water and propylene glycol were mixed by stirring for 15 minutes using a magnetic stirrer to form the water phase. Both phases were separately heated to 70°C. After heating, the two phases were homogenized using an Ultraturrax to form the emulsion (Ritmaleni et al., 2023).

Preparation of Gelling Agent

Carbopol 940 was mixed with distilled water and left for 24 hours. Then, TEA was added

gradually until the pH reached 6-7 (Sah et al., 2017). The gel mixture was then added to DMDM Hydantoin and stirred for 15 minutes at 300 rpm.

Incorporation of Emulsion into Gel

The emulsion was then added gradually into the gel base and mixed until homogeneous to form the emulgel (Ritmaleni et al., 2023).

Determination of Emulgel Effectiveness

The optimum formula of the emulsion was then made into five (5) emulgel preparation, OMC 6% (w/v) addition of concentration HGV-5 (w/v), F1 (without the addition of HGV-5); F2 0.1%; F3 0.2%; F4 0.3% and F5 0.1 % (without the addition of OMC). The five formulations were then evaluated for their effectiveness through photostability and mechanical tests. The photostability test determined the Sun Protection Factor (SPF), percent transmission of erythema (%TE), and percent transmission of pigmentation (%TP).

Photostability Test of OMC and HGV-5 Emulgel

The photostability test was conducted using UV light at a wavelength of 366 nm. A sample of 0.3 g of the emulgel was applied onto a transparent glass slide, which was then exposed to UV light for 1, 2, 4, and 6 hours. For comparison, control groups were left without UV exposure (0 hours). Absorbance measurements of the emulgel samples were taken before and after UV exposure using UV spectrophotometry.

In Vitro Sunscreen Activity Test

A 0.3 g sample of the emulgel, both UV-exposed and non-UV-exposed, was weighed and placed in a 3 mL volumetric flask, to which ethanol p.a. was added. The mixture was then sonicated for 15 minutes and filtered using filter paper. An aliquot of the filtrate was taken, and its absorbance was measured using a UV-Vis spectrophotometer at 5 nm intervals within the 290–320 nm wavelength range, with three repetitions. Ethanol p.a. was used as the blank (Nugrahaeni et al., 2021). Absorbance data for SPF determination were processed using the Mansur method with the following equation:

$$SPF = CF \times \sum_{290}^{320} EE(\lambda) \times I(\lambda) \times \text{Absorbansi}(\lambda)$$

EE: Erythema Effect Spectrum; I: Solar Intensity Spectrum; Abs: Absorbance of the sunscreen sample; CF: Correction Factor is stated with a value 10.

Then SPF values was obtained then set sunscreen activity categories (Ritmaleni et al., 2023).

Determination of %TE and %TP

1g sample of the emulgel was weighed, diluted with 10 mL of ethanol p.a., and sonicated for 15 min until dissolved. The solution was filtered with filter paper moistened with ethanol p.a. Absorbance was measured in the wavelength range of 292.5–372.5 nm at 5 nm intervals (Taupik et al., 2022). Absorbance data for the calculation of percent transmission of erythema (%TE) were obtained within the wavelength range of 292.5–317.5 nm, and calculated using the following equation:

$$\%TE = \frac{\sum(\%T \times Fe)}{\sum Fe}$$

Where T: percent transmission of erythema; Fe: Erythema flux constant; $\sum Fe$: Total erythema flux from sunlight; $\sum(T \cdot Fe)$: Erythema flux transmitted by the sunscreen at erythema spectrum wavelengths.

The calculation of percent transmission of pigmentation (%TP) was performed at the wavelength range of 322.5–372.5 nm using the equation:

$$\%TP = \frac{\sum(T \times Fp)}{\sum Fp}$$

Where T: percent transmission of pigmentation; Fp: Pigmentation flux constant; $\sum Fp$: Total pigmentation flux from sunlight; $\sum(T \cdot Fp)$: Pigmentation flux transmitted by the sunscreen at pigmentation spectrum wavelengths.

Mechanical Test

The emulgel formulation was transferred into a conical tube and subjected to centrifugation at 3800 rpm for 30 minutes. Then, any physical changes in the emulgel were observed (Zulfaidah et al., 2023).

Evaluation of Physical Stability of OMC and HGV-5 Emulgel

The optimal formula is selected based on good and stable SPF values, %TE, %TP, and mechanical tests. After selecting the optimal formula, further testing is conducted to evaluate the physical properties of the emulgel for 4 weeks (organoleptic, homogeneity, pH value, viscosity, spread ability, and adhesiveness testing). Additionally, stability testing is performed (thermal cycling test).

Organoleptic Test

The organoleptic test involved the observation of the color, form, and odor of the emulgel. The observations were made 4 weeks storage period (Zulfaidah et al., 2023).

Homogeneity Test

Homogeneity was tested by applying the emulgel onto the surface of a transparent glass slide. The formulation was considered homogeneous if no particles were present, indicating that the components were uniformly mixed (Zulfaidah et al., 2023).

pH Test

The pH of the formulation was determined using a pH meter at room temperature. The pH meter was first calibrated with a neutral pH buffer solution (pH 7.01) and an acidic pH buffer solution (pH 4.01) until it displayed the appropriate pH values. The electrode was then immersed in the sample emulgel, and the pH meter was allowed to stabilize (Meliala et al., 2020).

Viscosity Test

Viscosity was measured using a Brookfield viscometer at room temperature. The procedure involved preparing the instrument and positioning the rotor horizontally. 50 grams of the emulgel was placed in the container, ensuring the rotor did not exceed the limit. The viscometer was then activated, and the rotor began to move. The measurement will display a consistent value (Elcistia & Zulkarnain, 2019).

Spreadability Test

A 0.5 g sample of the emulgel was placed at the center of a transparent glass slide, beneath which graph paper was placed. The second transparent glass slide was placed on top, and various weights (50 g, 100 g, 150 g, 200 g, and 250 g) were applied sequentially, with each weight for 1 minute. The diameter of the spreading area of the emulgel was then measured. This test was performed three times for each formula (Shovyana & Zulkarnain, 2013). An ideal spreadability range is 5-7 cm (Ratnapuri et al., 2019).

Adhesiveness Test

The adhesive properties were evaluated using the TA1 Texture Analyzer (Ametek LLOYD, AMETEK, United States) in texture profile analysis mode. A cylindrical analytical probe with a diameter of 35 mm was pressed into the sample

twice at a speed of 1 mm/s to a depth of 10 mm. The parameters were determined based on the force-time plot (Nadia et al., 2023).

Thermal Cycling Test

This study aimed to evaluate the stability under varying temperature conditions. Samples are stored at temperatures of $4^{\circ}\text{C} \pm 2^{\circ}\text{C}$ and $40^{\circ}\text{C} \pm 2^{\circ}\text{C}$, and physical changes (color and separation of emulgel) are observed (Nurfita et al., 2021).

Acute Dermal Irritation Test of Emulgel

This test is conducted in accordance with BPOM Regulation No. 7 of 2014 on Guidelines for Non-Clinical Toxicity Testing In Vivo and Regulation 139/EC-FKH/int./12024. The irritation test was conducted using adult white rabbits, the health criteria with a body weight of 1.5-2 kg, and 3 animals were used. The emulgel formulation was applied topically, with 0.5 grams of the formula and control base prepared for testing. The test was performed by leaving the application on the skin for 4 hours. Emulgel residue was immediately cleaned with distilled water and checked for erythema and edema. Follow-up observations were conducted at 1, 24, 48, and 72 hours. The primary irritation index (PII) was determined using an equation based on the Indonesian FDA guidelines. The equation PII :

$$\text{Primary Irritation Index} = \frac{A - B}{C}$$

Where A: The total erythema and edema scores at the 24, 48, and 72-hour observation points, divided by the number of observations; B: The total erythema and edema scores from the control group at the 24, 48, and 72-hour observation points, divided by the number of observations; C: The number of observations. The PII calculation was conducted after scoring the acute dermal irritation response. The test results were evaluated based on the hazard criteria of the Globally Harmonized System (GHS) for The Classification of Chemicals (Peraturan BPOM No 32 Tahun 2019 Tentang Persyaratan Keamanan Dan Mutu Obat Tradisional, 2021).

Data Analysis

The emulgel formulation was tested in three replicates, followed by data processing. The response data for the DE variables including separation ratio, viscosity, and globule size were analyzed to determine the optimal base formulation. The experimental results were then

verified by comparing them with the predicted DE responses. Data were subjected to normality testing and further analyzed using a one-sample t-test. Physical stability testing, SPF, %TE and %TP were analyzed using the Shapiro–Wilk test to assess data normality. If the data were normally distributed, two-way ANOVA was used for further analysis, otherwise, non-parametric tests were applied.

RESULT AND DISCUSSION

Antioxidant Activity

Testing of antioxidants using the DPPH method to determine the sample to be tested by looking at its ability to ward off DPPH free radicals. HGV-5 and Vitamin E (positive control) were measured at 4 series concentrations. Antioxidant activity is indicated by the IC_{50} (Inhibition Concentration 50%). The IC_{50} value is the antioxidant concentration value to reduce 50% of DPPH to lose its radical activity. The smaller the IC_{50} is the higher the antioxidant activity will be (Kholifah et al., 2023). In this research, the antioxidant test utilized a comparison of vitamin E since the compounds contained in vitamin E could reduce or ward off free radicals. The test results showing the antioxidant activity of HGV-5 had a linear regression curve of $y = 0.4106x + 41.859$ with an R-value of 0.9973. For Vitamin E, the linear regression curve was $y = 0.443x - 17.517$ with an R-value of 0.9886. Based on data analysis, the IC_{50} value of HGV-5 was 19,827 μ M or 8,46 ppm, while the Vitamin E, used as a comparator, was 72, 780 μ M or 31,35 ppm. These test showed that HGV-5 has better antioxidant activity than Vitamin E. HGV-5 showed strong antioxidant activity caused by had phenolic compound reacting with a variety of free radicals, HGV-5 can be a potential stabilizer agent for OMC when it is completely mixed into the sunscreen formula. Antioxidant activity increases due to two ortho-methoxy groups, which help stabilize the phenolic hydroxyl group and facilitate hydrogen release, thereby enhancing its effectiveness in neutralizing free radicals (Sardjiman et al., 1997). HGV-5 exhibits antioxidant activity, indicating its potential as a stabilizer for UV filters.

Optimization of Emulsion by Using Design Expert® Software

Design expert software suggested 14 formulations for the evaluation of optimal emulsion (Table I). A base formula was formulated

and analyzed for each response (volume separation ratio, emulsion droplet size, and viscosity). The normal curve plot of the residual analysis on Software Design Expert indicated that the data for three responses followed a normal distribution, as they were dispersed around and aligned with the diagonal line. Therefore, an ANOVA analysis was performed (Nahdhia et al., 2024).

The statistical analysis includes p-value, lack of fit value, R-Square (R^2), adjusted R^2 , and predicted R^2 . Based on the data below (Table II.), it can be stated that all parameters meet the required criteria. The data demonstrate a strong relationship between the mixture results and the response variables, as indicated by a significant model p-value ($p < 0.05$) and a lack of fit value showing no significant difference. Additionally, the difference between adjusted R^2 and predicted R^2 must be ≤ 0.2 .

The Response Categories of SLD

Volume Separation Ratio

The volume separation ratio is calculated by dividing the volume of the emulsifying layer by the total volume of the emulsion. The measurement aims to determine whether the emulsion shows phase separation. To assess the accelerated stability of the emulsion, the method is determined by centrifugation (Ermawati, 2017). The centrifugation test operates on the principle of utilizing centrifugal force to separate substances with different densities, such as two immiscible liquid or a liquid and a solid (El-Sayed, 2014). The emulsion separation volume ratio ranged from 0.9216 to 0.9608. The best stability emulsion is characterized by a volume separation ratio of 1, indicating that no phase separation occurs (Table II). Tween 80 and Span 80 have a positive influence with similar value and improve the emulsion stability (Figure 1A).

Improving the stability because this intermolecular interaction of the surfactants leads to decrease in interfacial tension when using a mixture of surfactants compared to using single surfactants at the same concentration (Posocco et al., 2016). Decreasing interfacial tension tend to reduce the difference in properties between the oil and water phases, so it can help increase the stability (Xiong et al., 2023). The ANOVA results show the p-value is 0.0133, indicating that the phase separation ratio is significantly affected by the variation of concentration span 80, tween 80 and paraffin liquid.

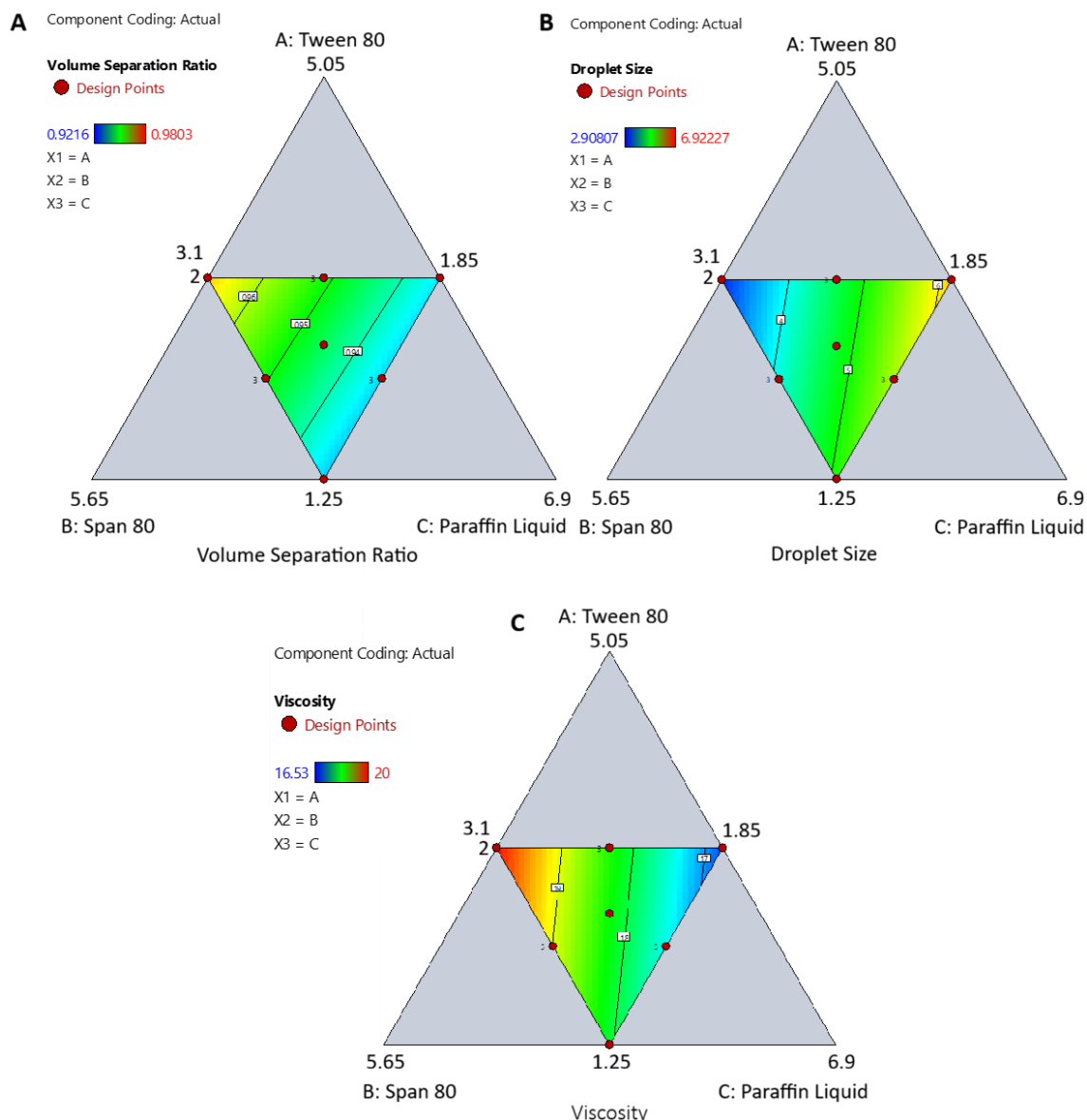


Figure 1. model graph of emulsion characteristics: (A) volume separation ratio, (B) droplet size, and (C) viscosity Analysis of Variance (ANOVA) of The Responses Emulsion content is increased, the droplets in the emulsion become larger due to their expansion. Whereas, increasing the concentration of Tween 80 and Span 80 decreases the droplet size by lowering

Table. II. Analysis of variance (ANOVA) for the responses model linear

Responses	Regression Equation	p-value	Lack of fit	Adjusted R ²	Predicted R ²
Volume Separation Ratio	Y= 0.102869A + 0.101937B + 0.084403C	0.0133	Significant 0.4614	Not significant 0.4614	0.3025
Droplet Size	Y = 0.201910A - 0.363153B + 1.23813C	0.0006	Significant 0.6924	Not significant 0.6924	0.5601
Viscosity	Y = 2.03850A + 2.72121B + 1.06131C	0.0004	Significant 0.7112	Not significant 0.7112	0.5520

Droplet Size Emulsion

Droplet size is a crucial factor in determining the stability of emulsions, with smaller droplets generally contributing to greater stability. The droplet size of an emulsion affects the rate of sedimentation. Reducing droplet size typically leads to improved emulsion stability, as long as flocculation, coalescence, or droplet growth caused by Ostwald ripening is prevented. Moreover, smaller droplets may enhance the formulation's effectiveness by improving its spreading ability (El-Sayed, 2014).

The droplet size of the emulsion ranges from 0.5 to 50 μm . The measured droplet sizes fall within this range, ranging from 2.90 to 5.24 μm . Based on the regression equation (Table II), Paraffin Liquid was the most dominant factor affecting droplet size. When the Paraffin Liquid the interfacial tension between oil and water, thus facilitating the formation of smaller droplets (Figure 1B) (Nahdhia et al., 2024). The ANOVA analysis results show that the p-value was found to be 0.0006, indicating that the model is significant.

Viscosity

Viscosity was used as a stability parameter for emulsion because higher emulsion viscosity can inhibit gravitational separation and the Brownian motion of oil droplets, which can reduce the frequency and efficiency of droplet collisions to ensure the physical stability of the emulsion against creaming, flocculation, and coalescence (Zhang et al., 2024). The viscosity test results ranged from 16.53 to 19.73 mPas, influenced by differences in the concentration of the emulsifier and the oil phase used (Table II). The highest influence was given by Span 80 with a coefficient value is + 2.72121. When the proportion of Span 80 increases, viscosity also increases because of an increasing the interfacial layer of an emulsion (Figure 1C) (Mohammed & Jaber, 2022). The p-value was found 0.0004 which is less than 0.05 indicating the model is significant.

Determination and verify the optimal formula

The optimal formula was determined using the SLD method based on acceptance criteria (Table II). The optimum formula was obtained with the proportion of Tween 80 at 3.15% (v/v), Span 80 at 3.75% (v/v), and Paraffin Liquid at 3.1% (v/v) (Table III). This formula was chosen by a Design Expert with a desirability value of 0.901. The predicted and observed values were analyzed using a one-sample t-test with a 95% confidence level.

The verification results of the optimal formula show no significant difference (p-value <0.05) between the predicted and observed values. The statistical test showed a high p-value, indicating that the experimental data did not differ significantly from the predicted values. These results indicate the validity of the proposed model.

Determination of Emulgel Effectiveness Photostability Test

The SPF value indicates the activity of the sunscreen to protect the skin from sunlight. The SPF, %TE, and %TP of five formulations were evaluated. Based on the research findings (Figure 2) F1 exhibited an SPF value in the maximum category but gradually decreased to the minimal category, while F2 remained in the maximal category, and F3 and F4 fell into the Ultra category. In contrast, F5 was classified in the minimal category. The %TE and %TP values indicate that F1 belonged to the suntan category at 0 hours and shifted to the fast tanning, while F2 and F3 were classified under the ultra protection category, F4 in the sunblock category, and F5 in the fast tanning category.

SPF Value then analyzed using two way anova shows a significant difference ($p < 0.05$), the two-way ANOVA results demonstrated a significant effect of UV exposure time, differences among formulations, and the interaction between these two factors on the SPF values. This analysis was followed by a post-hoc Tukey HSD test, which confirmed that the differences between formulations were significant, particularly between F1 and F4. These results indicate that the addition of HGV-5 to the sunscreen emulgel formulation helps maintain its effectiveness after UV exposure, as evidenced by the more stable SPF values compared to formulations containing OMC alone or HGV-5 alone. The F4 demonstrates good stability and effectiveness both before and after irradiation, F4 remains in the Ultra category for SPF and Sunblock category for %TE and %TP (Figure 2). A higher concentration of HGV-5 leads to a greater SPF value and lower erythema and pigmentation transmission percentages (Figure 2). These percentages indicate the amount of sunlight penetrating the skin after sunscreen application, where lower values indicate better skin protection (Taupik et al., 2022). This aligns with the structure of HGV-5, which contains hydroxyl groups attached to the aromatic ring, allowing the compound to absorb both UV-A and UV-B rays and reduce sun exposure to the skin (D'Orazio et al., 2013).

Table III. Verify the optimal formula

Response	Predicted Value	Observed Value	P-value	Desirability
Volume Separation Ratio	0.967	0.968	0.000	
Droplet Size	3.112	3.112	0.049	0.901 (Selected)
Viscosity	19.915	19.916	0.000	

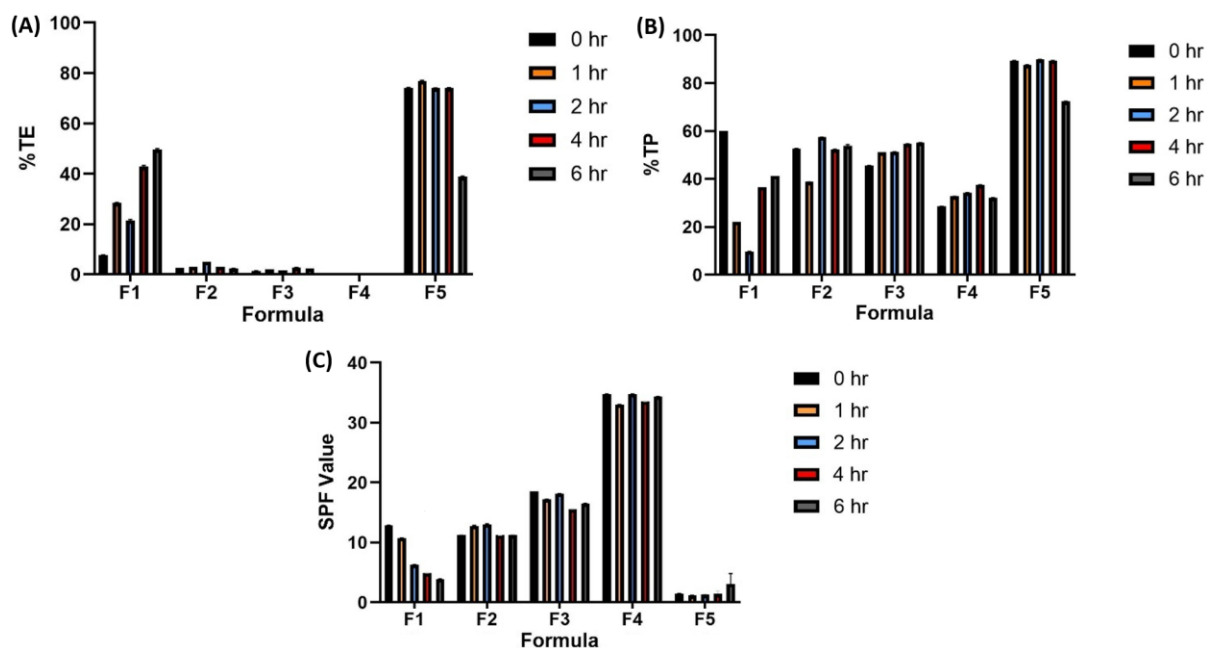


Figure 2. Photostability Test: (A) %TE, (B) %TP, (C) SPF Value

OMC is a well-known UVB-absorbing sunscreen agent with good lipophilicity but poor photostability (Xu et al., 2021). Upon UV exposure, OMC undergoes a structural change, reducing its absorption capacity due to isomerization (transitioning from the trans- to the cis-form). This instability diminishes its effectiveness, as the compound becomes rigid and susceptible to further degradation. OMC is an aromatic compound with conjugated para and ortho groups, that facilitates electron delocalization between electron-donating and electron-accepting groups due to UVA and UVB radiation energy (Kockler et al., 2012). After 1 hour of UV exposure, OMC exhibited poor photostability, it can be seen from the SPF value that the SPF value continues to decrease until the 6th hour. Therefore, to achieve optimal stability and sunscreen effectiveness, antioxidants are added as photoprotectants (Kockler et al., 2012). In the emulgel formulation, OMC is combined with HGV-5 as its antioxidant. The addition of HGV-5 improves the sunscreen emulgel.

Stability of the trans-octyl methoxycinnamate form, which has a higher extinction value compared to the cis form. This is demonstrated in F4 have good stability from the first hour through the sixth hour of exposure. The presence of HGV-5 facilitates a synergistic effect with OMC.

Mechanical Test Emulgel

Mechanical testing is a commonly used method to evaluate the stability of a product by assessing whether phase separation occurs when pressure is applied to the formulation (Smaoui et al., 2017). The test results indicate that no separation was observed in any of the formulations, this was likely a result of the appropriate homogenization speed used during emulsion preparation. This evaluation can assess and simulate resistance to shocks during distribution, and provide insight into the product's stability during storage (Erwiyani et al., 2021).

Based on photostability test and mechanical test of emulgel, the best formula showed on F4 with concentration of OMC 6% (w/v) and HGV-5 0.2% (w/v).

Evaluation of Physical Stability of OMC and HGV-5 Emulgel

A well-formulated sunscreen emulgel must fulfill key physical property criteria. In this study, the evaluation of optimal emulgel parameters for physical properties plays a vital role in determining the quality of the emulgel, as they significantly influence consumer acceptance of the sunscreen product.

Organoleptic and homogeneity test

The samples were stored at room temperature for four weeks and evaluated for odor, color, texture stability, and homogeneity. The results showed that from week 1 to week 4, the emulgel did not exhibit any organoleptic or homogeneity changes, indicating that the formula was organoleptically stable. The homogeneity test results confirmed that the emulgel was homogeneous, with no visible coarse particles, and indicated that all ingredients were well blended during the mixing process (Nurfita et al., 2021).

pH test

The testing of the emulgel formulation aims to determine the stability of the pH after formulation, ensuring its safety and stability during use. Maintaining a skin-compatible pH is essential for sunscreen emulgel, as an overly acidic formulation may irritate, while an excessively alkaline one can result in dryness and itching. The normal skin pH range is between 4.5 and 7.0. The pH test results of the emulgel showed a value range of 5.73 – 5.77, aligning with safety standards and confirming its non-irritating properties (Tanjung et al., 2022). The analysis revealed a significance value ($p > 0.05$), indicating that the weekly change in pH is not statistically meaningful. This suggests that no significant variation, and the pH value remains relatively consistent over time.

Viscosity test

The viscosity test is conducted to assess the flow properties of emulgel. Viscosity and spreadability are inversely related, meaning that as viscosity increases, the ability to spread decreases. If the viscous is too thin, its ability to adhere and

spread on the skin surface will decrease contact with the skin, so the effectiveness of sunscreen is not optimal. Conversely, if it is too thick, it may affect its ease of application when taken out of the container (Zulfaidah et al., 2023). According to SNI 16-4399-1996, the ideal viscosity value of a sunscreen emulgel is 6000-50000 cps, and the viscosity results from 21120 to 21306 cPs, fall within the acceptable range for a well-formulated emulgel (Purwanti et al., 2022).

The viscosity results (Figure 3B) show an increase, which is attributed to the rise in the emulgel's pH during storage. The gelling agent used, Carbopol 940, tends to increase viscosity as the pH rises (Maslii et al., 2021). Additionally, this increase is influenced by the flow behavior of Carbopol 940, which exhibits a shear thinning system, leading to a gradual rise in viscosity over the storage period (Dahlizar et al., 2022). The one way anova analysis indicated a significance value ($p > 0.05$), suggesting that the weekly increase in viscosity is not statistically significant. In other words, there is no notable difference, and the viscosity remains relatively stable.

Spreadability Test

Evaluating the spreadability of a emulgel formulation is a crucial aspect of its assessment, as it determines how effectively the product can be distributed over the skin surface. Optimal spreadability ensures ease of application and improves the overall experience when using the emulgel (Thomas et al., 2023). The results of the kruskal wallis statistical analysis indicate not significant difference (p -value > 0.05). Variations in spreadability values influenced by viscosity. A higher viscosity results in reducing spreadability, making the application more challenging (Tsabitah et al., 2020).

Adhesiveness Test

An adhesion test was conducted to evaluate the emulgel's ability to adhere to the skin. A higher stickiness of the emulgel formulation is expected to enhance the absorption of active ingredients due to prolonged contact time with the skin (Rahman et al., 2023). The emulgel adhesive property increased until the second week and decreased in the third until the fourth week of storage. Decreasing adhesiveness may happen when the emulgel loses water, leading to increased viscosity and reduced adhesion to the skin surface.

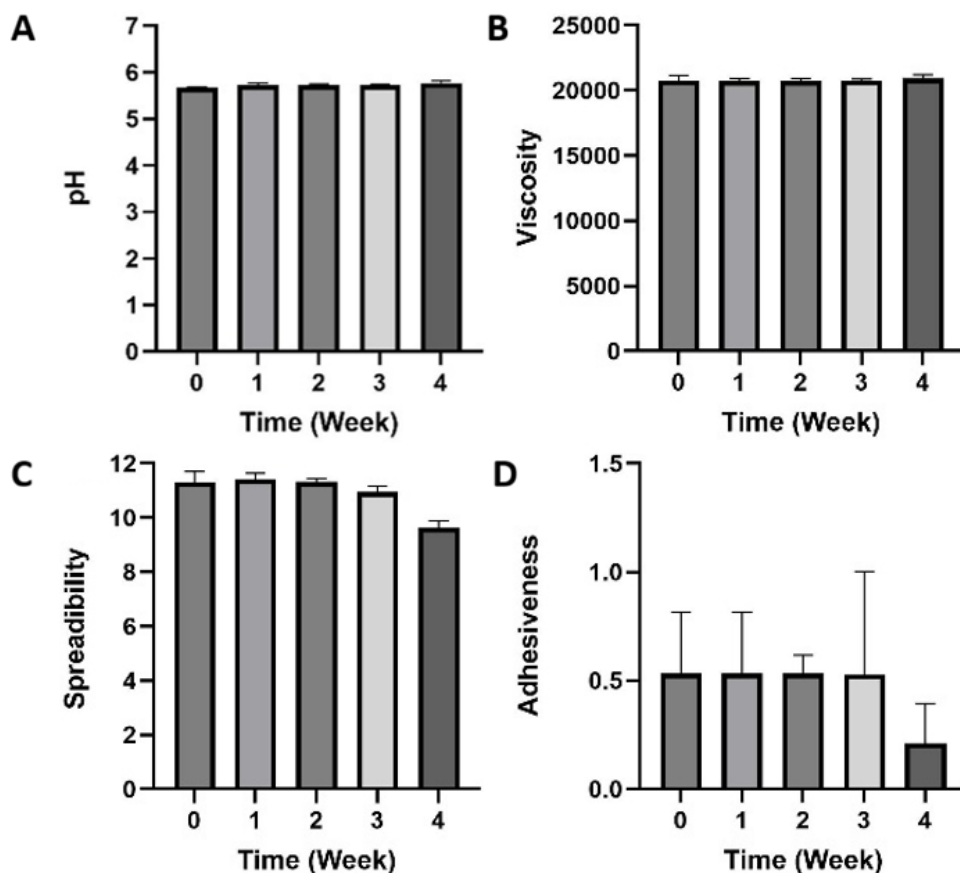


Figure 3. Physical properties of emulgel at room temperature: (A)pH values, (B) viscosity value (Cp), (C) spreadability, and (D) Adhesiveness

The results of the one-way ANOVA statistical analysis indicate no significant difference (p -value > 0.05), suggesting that the stability over 4 weeks of storage can be considered statistically insignificant and stable.

Thermal Cycling Test

Comprehensive stability testing under various storage conditions was meticulously performed to confirm the product's quality, safety, and efficacy. This testing was vital in the formulation's development and improvement, as it assessed its validity and tracked its physical and chemical properties (Nadia et al., 2023). The stability of the formulation can be seen by conducting a thermal test. This test is carried out using 4 cycles, the results formulation showed good stability if there are no signs of separation between the oil phase and the water phase (Zulfaidah et al., 2023). The results

indicate that the F4 emulgel remains stable at 4°C and 40°C during testing and no phase separation.

Acute Dermal Irritation Test of Emulgel

Irritation response testing is essential before a formulation can be used by consumers. This test is needed to determine the safety and suitability of a product for daily use, toxicity testing on the skin is required (Cursino et al., 2013). Sunscreen is a cosmetic product intended for regular use. The test was conducted following BPOM guidelines for non-clinical in vivo toxicity testing on rabbit test animals. Three test animals were used, as preliminary testing on a single animal showed no irritation response, such as erythema or edema after the formulation was applied for 4 hours. The results demonstrated that all test animals showed no signs of skin irritation, either with the no treatment group, during observations from 1 hour to 72 hours. The PII value was 0,

indicating that the F4 formulation is safe for use on the skin.

CONCLUSION

Emulgel was formulated with five concentration variations, and the fourth formula (F4), containing 6% (w/v) OMC and 0.2% (w/v) HGV-5, exhibited the highest effectiveness and stability on the skin. Based on the physical properties test of the sunscreen emulgel, including organoleptic characteristics, pH, viscosity, spreadability, and adhesion, the formulation was assessed over four weeks at room temperature. All physical attributes remained within the specified range for a well-formulated emulgel, and statistical analysis indicated no significant differences during storage. Further testing, including a primary irritation test, revealed that F4 produced an irritation and edema index of 0, indicating no irritation to the skin of the test animals. In conclusion, the F4 emulgel demonstrates potential as a physically stable sunscreen that provides optimal protection and safe for use on the skin. The investigation of HGV-5's potential as a photoprotective agent and stabilizer for UV filters can be further developed by focusing on *in vivo* studies to evaluate its effectiveness as a sunscreen, particularly in assessing its UV protection capability and dermal safety under real skin conditions. HGV-5 has also been shown to possess anti-inflammatory effects. This effect is particularly important for cosmetic purpose, especially in topical product to offer inflammatory injury from environmental factors like pollution.

ACKNOWLEDGEMENT

This research was supported by the Faculty of Pharmacy, Gadjah Mada University, through the "Hibah BIMA Kemdikbud-saintek" scheme.

CONFLICT OF INTEREST

The author reports no conflicts of interest in this work.

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