JURNAL FARMASI SAINS DAN KOMUNITAS
Journal of Pharmaceutical Sciences & Community

p-ISSN 1693-5683; e-ISSN 2527-7146

Vol. 21, No. 1, May 2024, pp. 109-119

Research Article

Preparation and Characterization of Binahong (*Anredera cordifolia*) Leaf Extract Transfersome Wound-Healing Gel

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doi https://doi.org/10.24071/jpsc.007311

J. Pharm. Sci. Community, 2024, 21(1), 109-119

Article Info

Received: 05-10-2023
Revised: 09-11-2023
Accepted: 18-12-2023

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Keywords:
Binahong; Gel; Transfersome; Wound healing

ABSTRACT

Burn injuries are a significant global health concern due to their profound impact on morbidity and mortality rates. Immediate medical care is essential given the potential for bacterial infections to complicated burn injuries. Binahong leaves (*Anredera cordifolia* (Ten.) Steenis) contain vitexin compounds that demonstrate wound healing and antibacterial potential. However, vitexin has low solubility, prompting the use of ethanol for extraction and the introduction of nanoparticle technology to enhance solubility, namely transfersomes. The present study explored the development of a gel using binahong extract transfersomes with the composition of carbopol 940 and Na-CMC to determine the effect of carbopol 940, Na-CMC, and the interaction of the two on the gel's physical properties and stability as well as obtain the optimum composition of the two. This study demonstrates positive results in terms of gel physical properties, including pH, spreadability, and viscosity. A Factorial design method is used for optimization. The results showed that Na-CMC had the most effect on increasing viscosity, while carbopol 940 had the most effect on reducing spreadability. The optimal formula obtained in this research was to use 0.653 grams of Na-CMC and 4.391 grams of Carbopol as gelling agents.

INTRODUCTION

Burns are a form of injury that occurs when skin tissue is exposed to various heat sources, including hot water, fire, chemicals, electricity, and radiation (Larissa *et al*., 2017). Burn injuries represent a pressing global health concern that demands immediate attention due to their substantial impact on both morbidity and death rates on a global scale. According to the World Health Organization's report from 2018, it has been estimated that there are approximately 180,000 fatalities resulting from burn injuries annually, with the majority of these incidents transpiring in nations classified as low- and middle-income. According to Collier *et al*. (2022), a significant proportion of burn cases (approximately 46 %) occurred in Asia in 2019. Among the regions in Asia, Southeast Asia emerged as one of the most heavily affected areas regarding burn injuries. According to the survey conducted by the Indonesian Ministry of Health, in 2018, Indonesia exhibits the second-highest prevalence of burn injuries among all types of injuries, accounting for 1.3% of reported cases. Based on the frequency of these occurrences, appropriate medical care should be administered because of the susceptibility of burn injuries to bacterial infection, leading to an extended inflammatory phase that may impede the wound healing process (Larissa *et al*., 2017)

Currently, burn wound therapy using Silver Sulfadiazine is the gold standard because it has antibacterial content. According to many studies, the use of Silver Sulfadiazine creates a decent healing effect by reducing the amount of bacteria in burn wounds (Nasiri *et al*., 2015). However, further negative effects of silver sulfadiazine use include argyria, leukopenia, and liver and renal damage issues (Adhya *et al.*, 2015). Indonesia is a country that has about 30,000 kinds of plants and 940 of them are used as medicinal plants. Treatment with medicinal plants is popular because it is relatively safer and affordable (Surbakti *et al.*, 2018). One of the commonly used medicinal plants is binahong leaves (*Anredera cordifolia* (Ten.) Steenis). This plant has many benefits and one of them can be used as anti-cancer medicine (Jazilah *et al.*, 2014), has wound healing potential and promotes collagen formation in a *Staphylococcus* infected wound (Nuroini *et al.*, 2021). Binahong leaves are known to contain saponins, flavonoids, quinons, steroids, monoterpenoids, and sesquiterpenoids (Dwiastuti and Ardiyati, 2020). One of the compounds contained in binahong leaves is vitexin (Santosa *et al.*, 2020) that can treat wounds (Bektas *et al.*, 2020). However, Vitexin has low solubility, therefore ethanol was used for the extraction of binahong leaf (Bhardwaj *et al.*, 2018). In addition, the use of nanoparticle technology is needed to improve vitexin solubility. Nanoparticles are drug compounds that are encapsulated in a particular nanometer-sized carrier system. The purpose of encapsulation is to compensate for the poor bioavailability of slightly soluble and insoluble active substances (Abdassah, 2017). One of the nanoparticle technologies that can improve vitexin solubility and skin permeation is transfersomes. Transfersomes are vesicles that have elastic and ultra-flexible properties. Transfersomes contain surfactants as edge activators that are capable of destabilizing the lipids of the vesicle's bilayer so that the vesicles become ultra-deformable (Amnuaikit *et al.*, 2018). Transfersomes are one of the nano-drug delivery systems used for wound treatment and skin regeneration (Wang *et al.*, 2019)

In this study, binahong extract transfersomes were prepared in gels. Gel preparation is a semi-dense preparation that has a transparent color and a fairly high solvent. Gel preparation was chosen because it is easy to clean, easy to apply, easily absorbed by the skin, has a good drug release, and does not leave an oily layer when applied to the skin (Sani *et al.*, 2021). Carbopol and Na-CMC were used as gel bases in this study. Gelling agents can affect the spreadability and viscosity of gel preparations. (Susianti *et al.*, 2021). The higher the concentration of the gel base, the higher the resulting viscosity (Rizkia *et al.*, 2022). Carbopol is a hydrophilic gel base, and the resulting gel has good viscosity at low carbopol concentrations. Na-CMC was selected because it can provide stable viscosity for the gel. In this study, carbopol and Na-CMC were used as gel bases in the hope that carbopol can compensate for the flaw of Na-CMC, which can form a colloidal solution in water so that a clear gel preparation is formed and has good physical properties (Sari and Saryanti, 2021). Gelling agents or gel bases are important constituents of a gel that determine the quality of the dosage form. Therefore, optimization using factorial design was performed to determine which gelling agent had simultaneous effects on gel quality. Optimization was performed to obtain the optimal gel formula from the binahong leaf ethanol extract as a wound-healing gel. The optimal gel formula was demonstrated with the gelling agent that obtained positive results in terms of gel physical properties, including pH, spreadability and viscosity. Optimization was also performed to determine the interaction effect of Carbopol, Na-CMC, and both components on the physical properties. Previous studies have successfully made transfersome gel of Pandan leaf extract (Ambarwati and Yulianita, 2022) and a gel of binahong leaf extract (Hanifah *et al.*, 2019); however, transfersome gel preparations that contain binahong leaf extract have not been well studied.

METHODS

Instrumentations and materials

The tools used in this study namely HPLC (Shimadzu), blender (Philips), Ultra Turax (Ystral GmbH D-7801 Dottingen), sonicator (Elmasonic), particle size analyzer (PSA), hotplate (IKA C-MAG HS 7), magnetic stirrer, evaporating dish, Transmission Electron Microscopy (TEM) (Jeol JEM-1400), thermometer, mortar and pestle, plastic wrap, analytical balance (OHAUS), Viscometer (Rion VT-06), glassware (Pyrex), *Design Expert Version 13*. The materials used in this research are binahong leaf ethanol extract, methanol, orthophosphoric acid, acetonitrile, L-alpha-phosphatidylcholine (Sigma-Aldrich), Tween 80, Carbopol 940, Na-CMC, methyl paraben, glycerin, TEA, and redistilled water.

Binahong leaf extraction

Binahong leaves were cultivated from Klaten, Central Java. The cleaned binahong leaves are dried using direct sunlight. Dried leaves are then powdered by blending them to obtain binahong leaf simplicia powder. 20 grams of binahong leaf simplicia powder was weighed and 200 ml of 96% ethanol was added (ratio 1:10). The container used was covered with aluminium foil and heated at 50°C for 90 minutes on a magnetic stirrer hotplate, then set the speed at 200 rpm. The resulting mixture after 90 minutes was filtered using filter paper. The filtering results were evaporated using a rotary evaporator until an extract of 25% of the initial volume was obtained (Dwiastuti and Ardiyati, 2020). The extract was subsequently standardized by quantification of the vitexin content using HPLC with the method described in (Santosa *et al*., 2020).

Optimization and preparation of binahong leaf extract transfersomes

Transfersome suspension of ethanol extract from binahong leaves was prepared according to a modified method of liposome preparation (Dwiastuti *et al*., 2016), by heating 90.9 mL of redistilled water using a hot plate until it reached a temperature of 60°C. Heated redistilled water was used to dissolve 8,2 grams of l-alpha-phosphatidylcholine. Then, 1,4 grams of the surfactant was added to the mixture. The mixture was blended for 60 s. The blended mixture was transferred to a glass beaker and homogenized using an Ultra-Turrax for 60 s. The mixture was then sonicated using an ultrasonicator for 30 min at 60°C. The suspension was then tested using a particle size analyzer (PSA) at the Research Laboratory of the Faculty of Pharmacy, Muhammadiyah University, Surakarta, to determine the particle size of the transfersomes and morphologically assayed using TEM at the Chemistry Department of Gadjah Mada University, Yogyakarta.

The formulation of transfersome gel

The formula used in this study refers to that employed in the research conducted by (Mardiana *et al*., 2020) The reference formula was modified in this study by substituting the telang flower extract with binahong leaf extract transfersomes. In this research, a two-factor, two-level factorial method was utilized. Transfersome gel formulations of the ethanol extract of binahong leaves were prepared by initially placing individual bases in separate containers. The Carbopol base was incorporated into 70 parts of the transfersome suspension, whereas Na-CMC was incorporated into 30 parts of the transfersome suspension. The resulting mixture was allowed to expand and swell for 15 minutes. Both Carbopol and Na-CMC underwent simultaneous swelling in the mortar until homogeneity was achieved. Subsequently, the base was transferred to a blender. TEA, glycerin, and methylparaben were then added to the mixture. Subsequently, the mixture was homogenized at a moderate speed for 3 min (Dwiastuti and Ardiyati, 2020). The formula for transfersome gel containing the ethanol extract of binahong leaves is presented in Table 1. The quality of the gel produced using each formula was evaluated.

Stability and physical properties of gel preparations

Organoleptic

The organoleptic test is carried out by observing the physical appearance of the gel preparation. Observations were made of the smell, color, and shape of the gel preparation (Forestryana *et al*., 2022)

Homogeneity

The visual assessment of the gel's homogeneity was conducted after its application onto the object glass. The gel's homogeneity was evaluated by visually examining for the presence of undissolved particles in the gel, as described by (Rahayu *et al*., 2016).

Table 1. Binahong leaf extract transfersome gel formula

Ingredients	F1	FA	FB	FAB
Carbopol (g)	0.5	2	0.5	2
Na-CMC (g)	3	3	6	6
Methylparaben (g)	0.1	0.1	0.1	0.1
Glycerin (g)	5	5	5	5
TEA (g)	1	1	1	1
Transfersome suspension (mL)	100	100	100	100

pH

Gel pH measurements were performed using universal pH paper that was immersed in a gel sample. Color changes occurring are matched to the universal pH standard (Slamet *et al.*, 2020).

Spreadability

The spreadability test was conducted by measuring the mass of 0.5 grams of gel and positioning it at the center of a circular glass platform. An additional cylindrical glass was positioned above the gel, varying weights of 0 g, 50 g, 100 g, and 150 g. The setup was left undisturbed for 1 minute. The measurements were conducted in five replicates (Forestryana *et al.*, 2022).

Viscosity

The viscosity test was conducted utilizing a RION VT-06 viscometer. The gel preparation was made with a maximum quantity of 50 grams and then transferred into the viscometer cup. Subsequently, the rotor was introduced into the cup until it reached the discernible boundary on the rotor. The viscometer was activated and then allowed to stabilize until the needle reached a steady state (Fahrezi *et al.*, 2021). All measurements were carried out in five repetitions (Dewi, 2021; Fahrezi *et al.*, 2021).

Cycling test

The stability test was conducted utilizing the cycling test technique, wherein the gel formulation was stored at a temperature of 4±2 °C for 24 hours, followed by subsequent storage at a temperature of 40±2 °C for another 24 hours, constituting a single cycle. The stability test was conducted over three cycles, during which physical changes at the commencement and conclusion of each cycle were noted. These changes encompass organoleptic properties, homogeneity, pH levels, spreadability, and viscosity (Dwiastuti and Ardiyati, 2020).

Optimum formula determination for binahong transfersome gel

Viscosity and spreadability test results were analyzed using Design Expert software and the two-factor-two-level factorial design method to find the best formula.

RESULTS AND DISCUSSION

Vitexin Content Determination in Binahong Extract

In this study, quantitative determination of vitexin was performed to determine the amount of extract required to prepare transfersomes. From the calibration curve, the vitexin content of the extract was determined to be 2,769 ppm. The quantity of binahong extract used in the experiment was 9.1 mL, as determined by the minimum inhibitory concentration (MIC) of vitexin against *Staphylococcus aureus* bacteria, which was reported as 252 µg/mL in a study conducted by Das *et al.* (2022).

Optimization and characterization of transfersome

In this study, one of the five formulas used to prepare binahong extract transfersomes was selected. The difference in each formula is the surfactant used in the preparation and ratio of the surfactants. The transfersome formulas and the characterization are listed in Table 2. Previous studies have investigated the effect of surfactants such as Tween 80 and Span 80 on the size and polydispersity index (PDI) of transfersomes (Anggraini *et al.*, 2017; Miatmoko *et al.*, 2022). These findings indicate that the choice of surfactant affects the physical properties of the transfersomes. Tween 80, a nonionic surfactant, leads to the formation of smaller transfersomes that have enhanced skin penetration capabilities. Span 80 is a surfactant that can dissolve in oil. They can interact with the lipid chains of phospholipids and influence the characteristics of transfersomes. The choice of surfactant used in transfersomes can influence the polydispersity index (PDI), as observed in various studies, where specific surfactants have resulted in a more consistent PDI (Miatmoko *et al.*, 2022). The primary factors to consider when choosing the most suitable formula are the size of the transfersomes and the Polydispersity Index (PDI). The optimal size of transfersomes for wound-healing gels may vary depending on the application and formulation. Nevertheless, prior research has shown that the size of transfersomes ranges from 50 to 500 nm (Opatha *et al.*, 2020; Surini *et al.*, 2020; Khan *et al.*, 2021; Rasheed *et al.*, 2022). PDI is a significant measure that indicates the size distribution of the transfersomes. A decrease in PDI was associated with an increase in the homogeneity of the size distribution of the transfersomes. The optimal PDI of transfersomes utilized in wound-healing gels can differ based on their application and formulation. However, prior research has documented the polydispersity index (PDI) values of transfersomes to be within the range of 0.1 to 0.3 (Wu *et al.*, 2019; Khan *et al.*, 2021). The optimal formula identified in this study was Formula 1, which yielded transfersomes with the most desired size and PDI characteristics, namely 73,067 nm and 0,276, respectively. Formula 1 had Tween 80 as a surfactant.

The morphological assessment of the transfersome suspension was conducted using Transmission Electron Microscopy (TEM). As depicted in Figure 1, the transfersomes generated in this study exhibited a spherical morphology with a size below 100 nm. It also could be seen that the surfactant is present in the surroundings of the transfersome particle. The transfersome utilized in this investigation resembles the transfersome generated in a study conducted by (Avadhani *et al*., 2017).

Gel physical characteristics

Organoleptics and homogeneity

The organoleptic test outcomes and homogeneity of the binahong transfersome gel for F1, FA, and FB demonstrated satisfactory adherence to the standards for proper gel preparation in terms of organoleptic properties and uniformity. However, FAB did not meet these criteria because of its lack of uniformity. Formulas F1, FA, and FB exhibited a turbid, yellowish-brown appearance, and had a scent characteristic of binahong extract. These formulations were homogeneous and did not demonstrate syneresis. The physical appearance of the gel produced in this study is shown in Figure 2.

Table 2. Transfesome characterization

Formula	Tween 80 : Span 80 Ratio	Soy Phosphatidylcholine (g)	Binahong extract (mL)	Z-average (nm)	PDI
F1	1 : 0	8.2	9,1	73,067±1,274	0,276±0,01
F2	0.75 : 0.25	8.2	9,1	73,633±2,501	0,318±0,023
F3	0.5 : 0.5	8.2	9,1	81,733±1,607	0,370±0,037
F4	0.25 : 0.75	8.2	9,1	98,733±0,764	0,285±0,037
F5	0 : 1	8.2	9,1	172,367±0,306	0,261±0,044

Table 3. The physical and stability properties of the gel

Formula	Physical properties results			%change after 3 cycle			*p-value*		
	pH	Viscosity $(x \pm SD)$(dPa.s)	Spreadability $(x \pm SD)$(cm)	pH	Viscosit y	Spreadability	pH	Viscosity	Spread-ability
1	6	24±65	25±1.41	0	4.17	5.01	-	0.291	0.189
A	4.50	23.2±1.79	25.6±1.34	0	10.34	4.67	-	0.01	0.199
B	5.50	26.4±01.67	26.2±1.79	9.09	0.76	4.73	-	0.389	0.015
ab	5.50	34.60±0.89	36.40±1.95	0	5.20	10.44	-	0.04	0.116

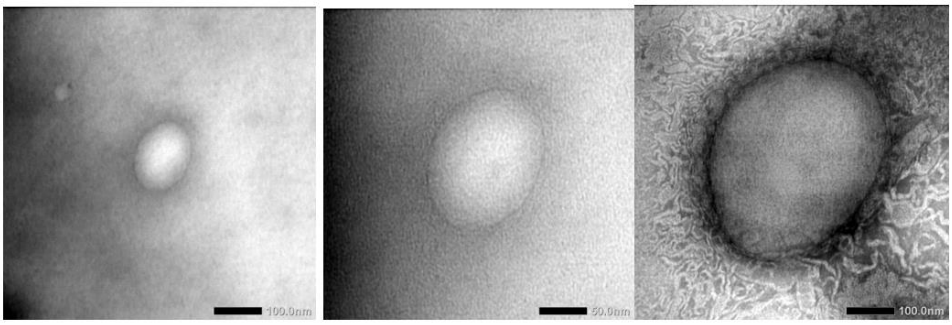

Figure 1. Transfersomes morphology

(a) (b) (c) (d)

Figure 2. The physical appearance of binahong leaf extract transfersome gel F1 (a), FA (b), FB (c), and FAB (d)

Table 4. Effects of Carbopol and Na-CMC and their interactions

Factor	Viscosity			Spreadability		
	Effect	%Contribution	*p-value*	Effect	%Contribution	*p-value*
X_1	3.700	16.797	0.0004	-1.4633	71.782	<0.0001
X_2	6.900	58.381	<0.0001	-0.8899	26.54	0.0003
X_1X_2	4.500	24.831	<0.0001	0.2235	1.674	0.257

*X_1 = Carbopol, X_2 = Na-CMC, X_1X_2 = The interaction of Carbopol and Na-CMC

Viscosity

High viscosity indicates a strong intermolecular link among the constituent molecules of the gel. It is well known that an increase in the concentration of the gelling agent leads to a corresponding increase in the viscosity. The optimal viscosity range is typically between 2000 and 50,000 centipoise (cps) (Rusli *et al.*, 2021). According to an additional reference, the optimal viscosity range for gel formulations is 2-4 Pa.s. If the viscosity of the gel is excessively high, it will result in challenges when attempting to remove the preparation from the container. Insufficient viscosity can negatively impact the adhesive properties of the gel, resulting in a reduced attachment time to the skin and increased susceptibility to removal (Yandri and Setyani, 2021). The viscosities of the gel preparations are listed in Table 3. Formula AB is composed of a high level of both carbopol and Na-CMC, specifically 2 grams and 6 grams, respectively. A higher concentration of gelling agents leads to an increased viscosity level of the gel. Formula A exhibited the lowest viscosity among the 4 tested formulas. This can be attributed to its high carbopol content (2 grams) and low Na-CMC content (3 grams), which resulted in a reduced viscosity value for the gel formulation. From the design expert results, it was found that Na-CMC had the greatest influence on the viscosity of the gel. The influence of each factor on the gel viscosity is presented in Table 4. It is shown that Na-CMC makes the greatest contribution to increasing gel viscosity. When sodium carboxymethyl cellulose (Na-CMC) is added to water, the sodium ions (Na+) are released and substituted with hydrogen ions (H+), resulting in the formation of carboxymethyl cellulose with hydrogen ions (HCMC). This process leads to an increase in viscosity (Bochek *et al.*, 2001).

Spreadability

A spreadability test was performed to assess the ease of application of the gel onto the surface of the skin. Utilizing a readily applicable gel can facilitate transdermal absorption of the medication. According to (Nurman *et al.* (2019)., the optimal spreadability range is 5–7 cm. As shown in Table 3, Formulas 1 and B have been shown to fulfil the optimal spreadability criteria, as indicated by the results of the spreadability test. Formula AB exhibits the least spreadability because of its comparatively high viscosity compared to the other formulas. The AB formula consists of carbopol and Na-CMC at high concentrations of 2 and 6 g, respectively. Analysis of the data using Design-Expert software revealed that carbopol had the most significant influence on gel spreadability. As shown in Table 4, carbopol showed a significant impact of 71.782% on the spreadability response. Carbopol decreases gel spreadability. Carbopol can form a bulk network or matrix so that it can increase the viscosity of the gel preparation thus decreasing the gel spreadability (Sumule *et al*., 2020).

pH

The gel's pH analysis was conducted to assess the gel's acidity level to ensure that it does not induce skin irritation resulting from excessively low or high pH values. According to (Chandra *et al*., 2022), it is essential that the pH value of the gel preparation is within the neutral pH range or is compatible with the skin, specifically between 4.5 and 6.5. The pH test is conducted by dipping universal pH paper into the diluted gel sample. The pH stability of the transfersome binahong gel was assessed by a series of cold and hot cycles, and the results indicated that the pH of the gel was relatively stable. The data is shown in Table 3.

The stability of the gel

In order to ascertain the stability of the gel, a cycling test was conducted. The data was then evaluated using a paired t-test. The results show that F1 shows no statistically significant change in either viscosity or spreadability, indicating gel stability. The viscosity of FA and FAB shows a statistically significant change. On the other hand, Table 3 shows that FB exhibited stability in terms of viscosity while experiencing a statistically significant change in its spreadability. The formula FA and FAB contain carbopol in high concentration which has a more rigid structure than the CMC-Na. Furthermore, FAB has a high CMC-Na concentration. The high water binding capacity of CMC-Na causes the formula to get more viscous and have low spreadability value, which is inversely correlated with viscosity. Additionally, the change in the viscosity value was caused by the hygroscopic properties of glycerine. Glycerine may attract water molecules from the air as a result of these properties, making the formula more viscous (Saryanti *et al*., 2022; Wiyono *et al*., 2023) Nevertheless, the four formulas exhibited favorable spreadability and viscosity value shifts. According to a study conducted by Putriana *et al*. (2019), the acceptable shift in values should not exceed 9% for viscosity and 10.9% for spreadability.

Optimum area determination

Based on the results of the effect analysis and ANOVA test of the viscosity response using the expert version 13 design, the equation for the viscosity response was obtained as follows:

$$y = 27.05 + 1.85\,X1 + 3.45\,X2 + 2.25\,X1X2$$

The equation obtained shows that Y is the viscosity response value, X1 is the factor level of Carbopol, X2 shows the Na-CMC factor level, and X1X2 shows the interaction between Carbopol 940 and Na-CMC. Based on this equation, Na-CMC has a greater influence in increasing the viscosity response. In addition, the equation for the spread power response is obtained as follows:

$$y = 4.90 - 0.7317\,X1 - 0.4450\,X2 + 0.1117\,X1X2$$

From the equation above, Y shows the spreadability response value, X1 is the factor level of Carbopol 940, X2 is the factor level of Na-CMC, and X1X2 is the interaction factor level between Carbopol 940 and Na-CMC. The coefficients X1 and X2 are negative which indicates that Carbopol 940 and Na-CMC reduce the viscosity response.

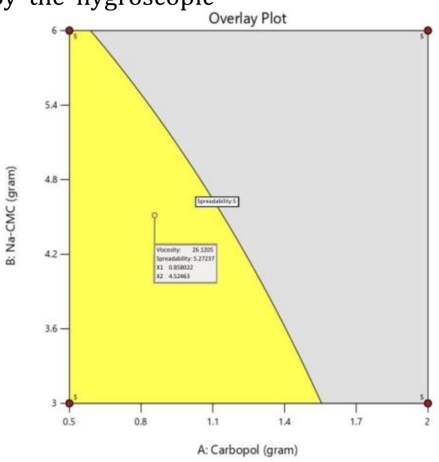

Figure 3. Overlay plot of the relationship between the viscosity and spreadability of a gel formulation containing binahong extract transfersomes.

The optimum area is an area that meets the response requirements of the analysis for each response. The optimum area will provide the amount of ingredients from Carbopol 940 and Na-CMC which will obtain a transfersome gel preparation formula for ethanol extract of binahong leaves with good and stable physical properties. Determination of the optimum area was carried out using the Design Expert Version 13 software with the requirements for a viscosity response in the range of 20 to 40 dPa.s and a spreadability in the range of 5 to 7 cm. For each response analyzed, a contour plot was obtained which was then combined to form an overlay plot to determine the optimum area. In the overlay plot, the analysis results are used which show a significant influence of the viscosity response and spreadability. The yellow color on the plot overlay indicates that the formula is within the specified research range or parameters. On the other hand, the gray color indicates that the formula does not meet the intended research criteria. The presence of a gray area indicates that there is a formula whose spreadability value does not meet the specified criteria, namely less than 5 cm, specifically referring to the FA and FAB formulas. The contour plot can be seen in Figure 3, there are 100 solutions with the amounts of Carbopol 940 and Na-CMC which are predicted to produce a gel preparation with a viscosity response and spreadability that meets the requirements. Through the results of the overlay plot, the optimum area was obtained with a range of Carbopol 940 amounts of 0.5-1.6 grams and Na-CMC of 3-6 grams. The optimum area is the range of amounts of Carbopol 940 and Propylene glycol which will produce a gel preparation with physical properties and stability that meet the specified requirements. Researchers used Carbopol 940 in the amount of 0.65 grams and Na-CMC 4.39 grams. Researchers used this amount because this amount falls within the optimum area limits and is predicted to produce a viscosity of 25 dPa.s and a spreadability of 5.5 cm and has good physical properties and physical stability.

CONCLUSIONS

Transfersome that encapsulates binahong extract was successfully made using tween 80 as a surfactant. The optimal binahong extract transfersome gel formula obtained in this study uses 0.858 grams of carbopol and 4.524 grams of NA-CMC as a gelling agent. In addition, it was found that the Na-CMC was the dominant factor in influencing the viscosity response, with a contribution value of 58.381%. In comparison, carbopol was the dominant factor influencing spreadability response, with a contribution value of 71.782%. Further investigation is necessary to determine the encapsulation efficiency of the transfersome and antibacterial activity of the gel.

ACKNOWLEDGEMENTS

The authors thanked Institute for Research and Development of Society, Sanata Dharma University for the funding of this research.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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