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OPTIMIZATION OF CARBOPOL 940 AND PROPYLENE GLYCOL CONCENTRATION ON THE CHARACTERISTIC AND INHIBITORY EFFECT OF ETHANOL EXTRACT GEL OF PAPAYA (*Carica papaya* L.) SEEDS AGAINST *Staphylococcus aureus*

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ABSTRACT

Papaya (*Carica papaya* L.) seeds contain alkaloids, flavonoids, tannins, phenolic compounds and saponins have been proven its synergistic effect in inhibiting the growth of *Staphylococcus aureus*. In this research, ethanol extract of papaya seeds was formulated in gel preparations. Optimization of the composition of the gelling agent and humectant was carried out to obtain the gel preparation of papaya seed ethanol extract with good physical properties and stability. The parameters used to determine the stability of the preparation are Physical properties which include viscosity, spreadability, and percentage of viscosity shift. Data analysis was performed using Design-Expert software version 12 and SPSS. The inhibitory activity test was carried out by the disk-diffusion agar method with *Staphylococcus aureus* ATCC 25923 as the test bacteria. The results of the inhibitory activity test of papaya seed ethanol extract at a concentration of 20% had moderate activity and at concentrations of 40%, 60%, 80% and 100% classified as strong against the *Staphylococcus aureus*. Carbopol 940 is dominant factor in influencing the response of viscosity (92.504%) and spreadability (59.539%). Preparations with good physical properties andstability were obtained on the use of carbopol 940 and propylene glycol as much as 1.06604 grams and 13.2146 grams respectively.

Keywords: antibacterial; factorial design; papaya seeds; *Staphylococcus aureus*.

INTRODUCTION

Staphylococcus aureus is a Gram-positive bacteria found in a healthy human skin surface of about 20%. The *Staphylococcus aureus* is a major bacterial human pathogen that causes a wide variety of clinical manifestations such as skin and tissue infections, skin abscesses, purulent cellulitis, acne, impetigo, and wound infections (Nismawati *et al.,* 2018). Amoxicillin, a penicillin derivative, is an antibacterial group of β-lactams that is often used to overcome the *Staphylococcus aureus* infection. The penicillin is very effective in dealing with *Staphylococcus* infections and has been used in medicine since the 1940s, but in 1942 cases of *Staphylococcus aureus* resistance were discovered in hospitals. The *Staphylococcus aureus* resistances to penicillin derivatives occur in more than 86% of cases and lead to therapeutic failure (Setiawati, 2015).

Based on the factors causing this infection problem, it becomes a potential target for the development of research related to natural materials that have antibacterial activity and will be used as natural antibacterials. The antibacterial from

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natural materials is expected to overcome *Staphylococcus aureus* infection as effective as synthetic antibacterial without increasing the risk of bacterial resistance to synthetic antibacterial. Papaya seeds that become waste are still rarely used, whereas based on research conducted by Torar *et al*. (2017) states that ethanol extract of papaya seed contains secondary metabolites such as alkaloids, flavonoids, tannins, phenolic compounds and saponins which have been shown to have antibacterial activity at 20%, 40%, 60% and 80% concentration with classified as moderate potency against *Staphylococcus aureus*.

In this research the pepeya seed ethanol extract was formulated as a gel, which has never been reported before. Gels aresemisolid systems that consist of eithersuspension of small inorganic particles or large organic molecules interpenetrated by a liquid (Dirjen POM RI, 2013). Part of the preparations that greatly affect physical quality and stability of the gel preparations are gelling agents and humectants. The gelling agent will form a structural system which is a very important factor in the gel. The humectants maintain the stability of the gel preparation by absorbing moisture andreducing water evaporation from the gel preparation (Sayuti, 2015). Carbopol is a synthetic polymer of acrylic acid which has ahigh molecular weight and acts as a gelling agent in the concentration range of 0.5% - 2% (Rowe *et al*., 2009). The use of carbopol 940 as a gelling agent is consideredbecause of its high stability, resistance to microbial attack and widely used in the pharmaceutical and cosmetic industries. The efficiency of carbopol 940 is very good, so that low levels can provide a significant viscosity response (Allen and Ansel, 2002). The propylene glycol is a humectant in the form of clear liquid, colorless, thick, practically odorless, with a sweet taste, rathersharp like glycerin. The propylene glycol is acommon solvent that is better than glycerin and dissolves various ingredients, such as phenols, sulfa drugs, vitamins (A and D) and most alkaloids.

The propylene glycol is used in various pharmaceutical dosage form and generally considered as a relatively non-toxicingredient (Rowe *et al*., 2009). The use of gelling agents and humectants with different compositions in the gel preparationformulations can have an effect on the physical properties and stability of the gel preparations, therefore it is necessary to optimize the composition of the gelling agent and humectants to obtain the optimum compositions range of carbopol 940 and propylene glycol to obtain the gel preparations which has good physical properties and stability. Factorial design isone of methods that can be used for determining the composition of gelling agents and humectants to obtain gel preparations with good physical properties and stability. Factorial design is widely used in experiments, especially in industry,because it can determine the influence of main factors and interactions on responsesand observe the simultaneous effects ofseveral factors and their interactions (Tantri *et al*., 2015).

METHODS

Instrumentations and materials

The instrumentations used in this research were analytical balance (Nagata), oven (memert UF 260 and WTC Binder), Viscometer (Rheosys Micra Merlyn VR), rotatory evaporator (BUCHI Rotavator R-300), whatman filter paper no. 1, freezer (Samsung), hotplate (IKA C-MAG HS 7), micropipette (Pipetman Kit), spreader, paper disc, Biological Safety Cabinet/BSC (Model LA2-3A1-E; Series 95067; Brand ESCO Class II type A2); Biological Safety Cabinet used to protect personnel against biohazardous or infectious agents and to help maintain quality control of the material being worked with as it filters both the inflow and exhaust air., autoclave (KT-40; ALP), magnetic stirrer, homogenizer, vortex, Laminar Air Flow Biolus CLB-201S, nephelometer (Phoenix Spec Ref 440910), Vacuum (Gast DOA-P504 BN) and pH meter (pH 3310 SET 2 inc. SenTix 41). The materials used in this research were California variety papaya seeds, ethanol 95%, mayer reagent, aquadest, $FeCl_3$ 1%, NaOH 10%, Nutrient Agar (Merck 105450) and Nutrient Broth media (Merck 105443), Mc Farland II standard solution, Buffered Peptone Water, ethanol 70% and 10% Dimethyl Sulfoxide solution (*pharmaceutical grade*), Carbopol 940 (*pharmaceutical grade*), Propylene glycol (*pharmaceutical grade*), methylparaben and triethanolamine / TEA (*pharmaceutical grade*).

The collecting and determination ofpapaya plants (*Carica papaya* L.)

The purpose of plant determination is to match the morphological characteristics that exist in plants used in this research with comparison to the book *Flora of Java* so that there is no mistake in taking plants used for the research (Andriyani *et al*., 2010). The California (variety) papaya plants were obtained from the Educational Tourist Village plantations of Pandowoharjo, Sleman, Yogyakarta. Determination of papaya plants was carried out at the Department of Pharmacy Biology, Faculty of Pharmacy, Gadjah Mada University, Yogyakarta.

The pollination of papaya seeds (*Carica papaya* L.)

Papaya seeds were washed clean and discarded seed coatings, after that weigh and record the results. Papaya seeds drying is done using the oven with 50 °C of temperature for 24 hours. Papaya seeds that have been dried are pulverized using a blender and then sieved to obtain a powder with the same size (Torar *et al*., 2017).

The measurement of water content of papaya seed powder

The measurement of the water content of papaya seed powder was performed using moisture balance instrument, by inserting 5 grams of papaya seed powder into the instrument at temperature of 120 ° C and wait for the value of the water content appears constant number (%). The water content in simplicia powder must not exceed 10%, this is intended to avoid the rapid growth of fungi in extracts (Kartikasari *et al*., 2014).

Production of the papaya seed ethanol extract

Extracts were made by weighing 85 grams of dried papaya seed powder, then macerated using 95% ethanol as much as 500 mL in an erlenmeyer and covered with aluminium foil then left for 4 days while stirring occasionally, next filtered with filter paper to produce filtrate (1) and residue. The residue was then macerated again (remaceration) with 250 mL of 95% ethanol, then the erlenmeyer was covered with aluminium foil and left for 2 days while occasionally stirring. After 2 days, the sample was filtered to produce filtrate (2).The filtrate (1) and the filtrate (2) were mixed together and then evaporated using a rotary evaporator until a thick extract wasobtained (Torar *et al*., 2017).

Qualitative phytochemical screening

Test for Flavonoids: about 1 mL extract was added with a few drops of 10% NaOH. The appearance of orange showed the presence of flavonoids (Ikalinus *et al*., 2015).

Test for Tannins: the extract was boiled with 20 mL of water and then filtered. A few drops of $FeCl_3$ were added to the sample. Positive reaction for tannin was claimed if greenish-brown or black-blue color appearance (Patel *et al*., 2014).

Test for Saponin: the extract was boiled with 20 mL of water in a water bath. The extract was shaken and allowed to stand for 15 minutes. The formation of a stable foam showed positive samples containing saponins (Ikalinus *et al*., 2015).

Test for Alkaloids: about 1 mL of extract was added 2 drops of Mayer's reagent solution. The formation of white or yellow lumpy deposits showed the presence of alkaloids (Ikalinus *et al*., 2015).

Test for Phenolic: the extract is diluted to 5 ml with distilled water. Then add a few drops of neutral 5% $FeCl_3$ solution. The dark green color indicates the presence of phenolic compounds (Lohidas *et al*., 2015).

The antibacterial activity test

Antibacterial activity test was carried out by the diffusion method to using paper discs (6 mm diameter) and the test bacterial *Staphylococcus aureus* ATCC 25923. The bacterial suspension was made by mixing the bacterial culture into the Buffer PeptonWater, then measured on a nephelometer to equalize the number of bacteria equivalent to 6 x 10^8 CFU / mL (Mc Farland II standard solution). The concentration series of papaya seed ethanol extract was prepared by dissolving the extract into DMSO with a percentage of w/v, for example the ethanol extract of papaya seeds with a concentration of 20% was prepared by weighing 1 gram of the extract and dissolving it in 5 mL of DMSO.

The paper disc was dipped in 1 mL of the papaya seed ethanol extract and then placed on the surface of NA media inoculated with 0.2 mL of *Staphylococcusaureus* ATCC 25923 with a concentration of 6 x 10^8 CFU / mL. Incubation was carriedout at 37°C for 1 x 24 hours. 1% ampicillin and 10% DMSO solution was use as positive control and negative control respectively. 3 times replications were applied fot the tests. Observations were made on the irradical inhibition zone formed around the paper disc (Muharni *et al*., 2017).

Formulation of gel of papaya seed ethanol extract

Aseptic preparation of gel preparations was carried out in Laminar Air Flow (LAF). The gel formulation process began by dispersing carbopol 940 over 50 mL of aquadest heated to a temperature of 70 °C, the carbopol was allowed to expand and then stirred using a stamper until homogeneous.

Then triethanolamine and propylene glycol were added, stirred until homogeneous and a clear gel mass was obtained. 15 mL methylparaben was added and stirred until homogeneous. The last step was addition ethanol extracts of papaya seed and remaining aquadest while continuing stirred until the gel was homogeneous (Sarlina *et al*., 2017).

The evaluation of the physical properties and stability of gel preparations

Organoleptic and homogeneity

Organoleptic tests of the gel were carried out by observations of shapes, colors and odors visually (Salman *et al*., 2012). Homogeneity test was carried out by weighing gel preparations as much as 0.1 g and then smeared on glass objects or other suitable transparent material, the composition was observed (Salman *et al*., 2012).

pH

The pH test was carried out using a pH meter. Calibration of the pH meter was done with 2 standard buffers with pH 4.01 and 7.00. The electrodes were rinsed withdistilled water and dried. Measurement of thepH of the gel was done by weighing as much as 1 g of the gel preparation and then diluted with distilled water to 10 ml. The electrodes were dipped in the gel solution, allowed to a constant number. The number shown by the pH meter was the pH value of the preparation (Salman *et al*., 2012).

Spreadability

The gel spreadability test was carried out by weighing the gel as much as 0.5 gram and then placed in the middle of a scaledglass. On top of the gel was placed another glass or other transparent material and added a load of 150 grams, allowed to stand for 1 minute, then measured the distribution diameter (Sayuti, 2015).

Viscosity

Viscosity measurements in this research were carried out using the Rheosys instrument and done by placing the gel preparation in a viscometer container untilthe spindle is submerged (Sayuti, 2015). The use of Rheosys instrument also aimed to determine the flow properties of papaya seed ethanol extract gel.

Freeze-Thaw Cycling

The physical stability test of the gel preparation was carried out by the Freeze and Thaw cycle test by storing the gel preparation at 4 ± 2 ° C for 24 hours, and thencontinued by storing the gel preparation at 45 ± 2 ° C for 24 hours (1 cycle), testing was carried out in 3 cycles and physical changes were observed at the beginning and end of the cycle which included organoleptic, viscosity, spreadability, and pH (Warnida et al., 2016). The stability was to be good if there was no change in physical properties and shifts in viscosity (Salman et al., 2012).

RESULTS AND DISCUSSION

The rendemen of *Carica papaya* L. ethanol extract

The fixed weight of the extract was 94.7119 grams. Extract yield was the ratio of extract to simplicia weight. Determination of the yield aimed to determine the amount of approximately simplicia needed for the manufacture of a certain amount of thick extract (Farmakope Herbal Indonesia, 2008).

The extract yield was 23.33% obtained from the calculation of 94.7119 grams of extract and 405.95 grams of dried papaya seed powder. The extract yield was in accordance with research conducted by Hayatie et al. (2015) which states that the content of secondary metabolites in papaya seeds is classified as small, namely alkaloids by 14.54%, flavonoids, 0.9% and tannin 0.78%.

The qualitative phytochemical screening

In this research, the phytochemical screening results showed that the ethanol extract of papaya (*Carica papaya* L.) seeds contained alkaloids,flavonoids, tannins, phenolic compounds and saponins (presented in Table 1). The results of the phytochemical screening were in accordance with research conducted by Lohidas et al. (2015) which states that papaya seed ethanol extract contains secondary metabolites such as alkaloids, flavonoids, tannins, phenolic compounds and saponins.

Table 1. Phytochemical screening results

Test		Observations Result
Flavonoid		(+) Orange color
Alkaloid		(+) White lumpy deposits
Saponin		(+) Foam
Phenolic		(+) Dark green
Tannin		(+) Greenish brown

(+) = Proven to Contain Related Compounds

The antibacterial activity results

Measurement of the inhibition zone (irradical zone) refers to Hudzicki (2016), where the value of the measured inhibition zone is immediately recorded without reducing the diameter value of the paper disc.

Table 2. Inhibitory activity against *Staphylococcus aureus*

Extract Concentration	Average of the Irradical Inhibition Zone (mm)
20%	9.67
40%	11.33
60%	12.67
80%	14.33
100%	16.33
Positive Control	14.33
Negative Control	0
Growth Control	Good bacterial growth
Contamination Control	No Contamination

Positive Control = 1% Ampicillin
Negative Control = 10% DMSO

In this research, the results of the test for the inhibitory activity of the ethanol extract of papaya seeds that has been presented in Table 2, which at a concentration of 20% had moderate activity against *Staphylococcus aureus* bacteria, while the papaya seed ethanol extract with a concentration of 40%, 60%, 80%, and 100% had activity classified as strong against *Staphylococcus aureus* bacteria according to Davis and Stout criteria.

The gel formulation

The gel formula in this research refers to research from Arikumalasari *et al.* (2013). The difference in the formula in this research with the reference formula was found in the extract used, the type of gelling agent and the number of preservatives used. In this research papaya seed ethanol extract gel preparations has not activity against *Staphylococcus aureus* because the antibacterial activity test was only carried outon the extract, not on the gel preparation. In the gel formula, a 20% concentration of ethanol extract was used because at aconcentration of 20% it already had moderate activity in inhibiting the activity of *Staphylococcus aureus.* In addition, the use of a concentration of 20% is also in order to increase the concentration slowly over time. The formulas have been presented in Table 3.

Table 3. Formulas of gel of papaya seed ethanol extract

Ingredients	**F1** (g)	**FA** (g)	**FAB** (g)
20% Papaya seeds ethanol extract	5 mL	5 mL	5 mL
Carbopol 940	**0.75**	**1.75**	**1.75**
Propylene glycol	**10**	**10**	**15**
TEA	4	4	4
Methylparaben	0.05	0.05	0.05
Aquadest	*add* 100	*add* 100	*add* 100

The evaluation of the physical properties

Organoleptic test results and homogeneity of papaya seed ethanol extract gel preparations for the four formulas fulfilled good gel preparation criteria in terms of organoleptic aspects and homogeneity, which were clear yellowish- brown, the typical odor of extract, homogeneous and no syneresis occurred.

Figure 1. The physical appearance of antibacterial gel of papaya seed ethanol extract

The pH test is carried out to see the acidity level of the gel preparation to ensure the gel preparation does not irritate the skin due to pH that is too low or too high. The pH of the preparation according to skin pH criteria is in the interval 4.5 - 6.5 (Sayuti, 2015). The results of the pH test of papaya seed ethanol extract gel after storage cycle 0 to after 3 cycles of freeze and thaw showed that the pH of the preparation was stable (Table 4).

Table 4. The pH value of gel of papaya seed ethanol extract

Formula	pH				
	C0	C1	C2	C3	SD
F1	4.9	4	4.9	4.9	0.009
FA	5	5	5	5	0.012
FB	5.3	5.3	5.3	5.2	0.029
FAB	5.5	5.5	5.5	5.5	0.017

*C0 = Cycle 0, C1 = Cycle 1, C2 = Cycle 2, C3 = Cycle 3, SD = Standard Deviation

The resistance of a liquid to flow is expressed by viscosity. The higher the viscosity value, the higher the resistance of a liquid to flow (Sinko, 2011). Good viscosity of gel preparations is 2 – 4 Pa.s. The viscosity of the gel is too high (thick) will cause the gel preparation is difficult to remove from the container, whereas if theviscosity of the gel preparation is too low then the duration of the gel preparation staying on the skin is getting shorter.

Table 6. The results of viscosity test for gel of papaya seed ethanol extract

F	C0 (Pa.s)	C3 (Pa.S)	VS (%)
F1	2.42 ± 0.02	2.43 ± 0.01	0.76 ± 0.6
FA	3.43 ± 0.02	3.44 ± 0.02	0.62 ± 0.1
FB	2.40 ± 0.01	2.38 ± 0.01	0.63 ± 0.5
FAB	3.09 ± 0.05	3.05 ± 0.04	1.12 ± 0.7

*C0 = Cycle 0, C3 = Cycle 3, F = Formula
VS = Viscosity Shift

Formula A has the composition of carbopol 940 at a high level (1.75 grams) and propylene glycol at a low level (10 grams) so that the resulting viscosity value is high. In all four formulas it is known that formula B has the lowest viscosity value. This is because formula B contains the composition of propylene glycol at a highlevel (15 grams) and has a carbopol 940 content at a low level (0.75 gram), causing the viscosity value of the gel preparation to be low (Table 5). In this research after analyzing the data using Design-Expert software, it is known that carbopol 940 provides the greatest effect on influencing the viscosity response and has a contribution to the viscosity response of 92.509%. The effect of carbopol 940 showed that it has an influence in increasing the viscosity of papaya seed ethanol extract gel.

Table 5. Effects of both factors and their interactions on viscosity response

Factor	Effect	%Contribution	*p-value*
X_1	2.901	92.5094	<0.001
X_2	0.134	4.27182	<0.001
X_1X_2	0.101	3.21874	<0.001

*X_1=Carbopol 940 Factor, X_2 =Propylene glycol Factor, X_1X_2 =Interaction of carbopol 940 and propylene glycol Factor

The spreadability test was carried out to ensure the equal distribution of the gel when applied to the skin. Good gel dispersion is in the range of 5-7 cm (Sayuti, 2015). Based on the results of the spreadability test the spread value for formula 1, formula B and formula AB are in the desired spread range for a gel preparation that is 5–7 cm (Table 7).

Table 7. The results of spreadability test for gel of papaya seed ethanol extract

F	C0 (cm)	C3 (cm)	SS (%)
F1	5.41 ± 0.04	5.42 ± 0.04	0.90 ± 0.4
FA	4.50 ± 0.03	4.43 ± 0.04	1.55 ± 0.6
FB	6.23 ± 0.03	6.2 ± 0.1	0.53 ± 0.2
FAB	5.25 ± 0.03	5.23 ± 0.03	0.79 ± 0.6

*C0 = Cycle 0, C3 = Cycle 3, SS = Spreadability Shift**,** F = Formula

The spreadability of formula A gel was not included in the criteria of good gel dispersion accordance with the theory that the higher the viscosity value, the lower the spread power value, therefore formula A has the lowest spread value due to viscosity formula A was the highest viscosity of all formulas. The composition of Carbopol 940 in formula A is at a high level (1.75 gram) while the composition of propylene glycol at a low level (10 grams) so that the effects caused by Carbopol 940 were more dominant by which high viscosity and low value of the spread of formula A were obtained (Table 5). In this research after analyzing the data using Design-Expert software, it was found that carbopol 940 provided the greatest effect in influencing the spreadability response and has a contribution to the spreadability response of 59.5387% (Table 8). The effect caused by carbopol 940 showed that carbopol 940 has an effect in reducing the spreadability of papaya seed ethanol extract gel.

Table 8. Effects of both factors and their interactions on spreadability response

Factor	Effect	%Contribution	*p-value*
X_1	-0.946	59.5387	0.0028
X_2	0.779	40.4046	0.0344
X_1X_2	-0.029	0.0566	0.8947

*X_1=Carbopol 940 Factor, X_2 =Propylene glycol Factor, X_1X_2 =Interaction of Carbopol 940 and Propylene glycol Factor

The parameter of gel stability

Based on the data presented in Table 9, it can be concluded that there was no significant change in the viscosity value after cycle 0 and cycle 3 of the freeze and thaw treatment for the four gel preparation formulas, thus the gel was stable.

Table 9. Statistical test results (*T-test*) for viscosity of papaya seed ethanol extract gel

Formula	*P - value*
F1	0.706
FA	0.695
FB	0.096
FAB	0.406

In addition, based on the results of the viscosity and spreadability test that has been presented in Table 6 and 7, it can be seen that the four formulas have good viscosity and spreadability shift values where the expected percentage shift in viscosity and spreadability was <10%, thus the gel preparation was claimed stable (Yuliani, 2010).

Effects of both factors and their interactions on viscosity shifts after 3 cycles of freeze and thaw.

In the Design-Expert software it can be directly known percentage of the two factors contribution and their interactions with the resulting shift in the viscosity.

Table 10. Effects of both factors and their interactions on viscosity shifts

Factor	Effect	%Contribution	*p-value*
X_1	0.174	18.5090	0.0049
X_2	0.185	21.0450	0.0020
X_1X_2	0.314	60.4464	<0.001

*X_1=Carbopol 940 Factor, X_2 =Propylene glycol Factor, X_1X_2 =Interaction of Carbopol 940 and Propylene glycol Factor

Based on the data presented in Table 10 it is known that carbopol 940 can increase the viscosity shift response with a contribution of 18,509% and propylene glycol increases the viscosity shift response with a contribution of 21,045% while the interaction of both can increase the viscosity shift response with a contribution of 60.446%. Carbopol 940 and propylene glycol factors and their interactions were stated to significantly influence the shift in viscosity produced during the research because they had a p-value <0.05.

Determination of optimum area

In this research the determination of the optimum area was carried out using Design-Expert software by plotting the contour plot viscosity response and the scattered power response obtained so that the overlay plot was found as the optimum area in this research. The yellow color in the overlay plot indicates that the formula is within the desired range or research parameters, while the grey color states that the formula is not within the desired research range.

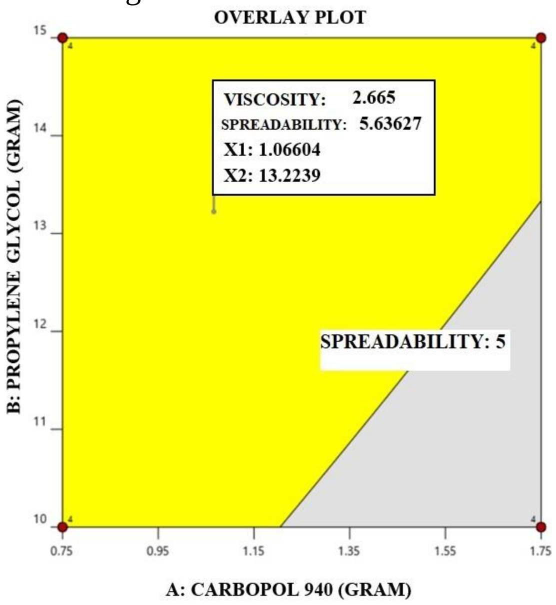

Figure 2. Overlay plots response of viscosity and spreadability of papaya seed ethanol extract gel

Figure 2 shows the plot overlays obtained from the results of the viscosity response and spreadability response plots. Grey areas indicate that there is a formula which has a spreadability value that is not included in the criteria for good spreadability or below 5 cm, namely formula A because the composition of carbopol 940 used in the formula is at a high level (1.75 gram) while propylene glycol composition at a low level (10 grams) which causes the effect of the carbopol 940 factor is more dominant and produces a low dispersion value. to find out the composition of carbopol 940 and propylene glycol which can produce gel preparations with good physical properties and stability can be done by right clicking then selecting the add flag option in the yellow area. In this research, 1.04060 grams of carbopol 940 and 13.2146 grams of propylene glycol are known to produce gel preparations with good physical properties and stability.

CONCLUSION

The gel of papaya (*Carica papaya* L.) seed ethanol extract with good physical properties and stability were obtained on the use of carbopol 940 and propylene glycol as much as 1.0660 grams and 13.2146 grams respectively. In addition, it was found that the carbopol 940 was the dominant factor in influencing the viscosity and spreadability response with contributed 92.509% in influencing the viscosity response and 59.539% in influencing the spreadability response, while the dominant factor in determining the viscosity shift response was the interaction the two factors were carbopol 940 and propylene glycol which the contribution was 60.446%.

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