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Original Paper

Optimization of The Combination of CMC-Na and Glycerin in Tobacco (*Nicotiana tabacum* L.) Hand Sanitizer Gel Using The Simplex Lattice Design

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Abstract*—Tobacco leaves have active compounds such as phenols and alkaloids that can be used as antibacterial and antiseptic because they can damage the cell components of microorganisms. Tobacco leaf extract in hand sanitizer gel has been shown to have antibacterial activity against Staphylococcus aureus and Eschericia coli bacteria at a minimum concentration of 0.25%. Hand sanitizer is an antiseptic product that is used to clean hands and is preferred because it is practical, has a cooling and dries quickly when compared to hand soap. To make hand sanitizer products that are safe for the skin, various chemical compounds are used as building blocks, including CMC-Na and glycerin. CMC-Na acts as a gelling agent and glycerin has a role as a vehicle. This study aims to obtain the optimum formula for hand sanitizer gel preparations with variations in the concentration ratio of CMC-Na and glycerin using Simplex Lattice Design (SLD) and to determine the effect of variations in the concentration ratio of CMC-Na and glycerin on physical, chemical, and microbiological characteristics of the results of the optimum formula for hand sanitizer gel preparations. The research method used in this study is a type of laboratory experiment using Completely Randomized Design (CRD). The data obtained from the research results were processed using Analysis of Variance (ANOVA) with a 95% confidence level and continued with Duncan's Multiple Range Test at a significance level of 5%. The results showed that there were 3 optimum formulas for hand sanitizer gel of tobacco leaf extract based on the desirability value, 0.912 (Formula 1), 0.457 (Formula 4) and 0.653 (Formula 5). The variation of the concentration ratio of CMC-Na and glycerin in the optimum formula showed that CMC-Na had the most dominant influence on physical (homogeneity), chemical (total flavonoid) and microbiological (antibacterial and antiseptic) characteristics. Meanwhile, glycerin has the most dominant influence on product viscosity stability. The three optimum formulas have homogeneous gel characteristics.

Keywords*—CMC-Na and glycerin, Tobacco, Hand Sanitizer Gel, Simplex Lattice Design

I. INTRODUCTION

Indonesia as an agricultural country has great potential in the plantation sector, one of which is tobacco. in 2019 Jember Regency was one of the production centers with a total of 13.11 thousand tons of dry leaves [5]. Considering the amount of production, efforts are made to diversify a product from this green gold [14]. Tobacco leaves contain active compounds that can be used as antimicrobial and antiseptic. Phenol and alkaloid compounds in tobacco leaves have the ability to denature and coagulate bacterial cell proteins, thereby reducing surface tension and causing disruption of cell membrane permeability [3][29]. Tobacco leaf extract in hand sanitizer gel preparation has been shown to have antibacterial activity against *Staphylococcus aureus* and *Eschericia col*i bacteria at a minimum concentration of 0.25% [15]. Therefore, the alkaloid and phenol group compounds in tobacco leaves can be used as natural active ingredients in the manufacture of hand sanitizer gel preparations.

Hand sanitizer is an antiseptic product that is chosen by the community to clean hands because it is practical, has a cooling sensation, and is easy to use [3][26]. One type of hand sanitizer that is currently being produced is the gel type. Commercial hand sanitizer products use synthetic active ingredients which if used in excess will cause skin irritation [27]. Efforts to minimize the use of chemicals contained in hand sanitizer products are by using plant extracts that contain active compounds as antimicrobial substances [2], for example in tobacco.

In the hand sanitizer gel formula, various chemical compounds were used as constituents, including CMC-Na and glycerin. CMC-Na acts as a gelling agent and glycerin has a role as a vehicle (aqueous) [19]. Focusing on their role, the two ingredients are considered to have the most dominant influence on the physical characteristics of hand sanitizer gel preparations. CMC-Na as a gelling agent has advantages because it is able to create more stable preparations, the appearance of the gel is clearer, and not sticky [10]. Hand

sanitizers are composed of various chemical compounds, so the role of glycerin as a vehicle in aqueous solution is needed to unite all the components in it. In the real of pharmaceutical products such as hand sanitizer, the role of the vehicle is described as an inert medium used as a solvent or diluent in formulas to create preparations that have stable conditions [24]. Therefore, this study aims to obtain the optimum formula for hand sanitizer gel preparations with variations in the concentration ratio of CMC-Na and glycerin using the Simplex Lattice Design (SLD) and to determine the effect of variations in the concentration ratio of CMC-Na and glycerin on physical, chemical characteristics, and microbiology on the results of the optimum formula for hand sanitizer gel preparations.

II. MATERIALS AND METHOD

A. Materials

The tools used include beakers, measuring cups, volume pipettes, digital balance (Sartorius), water bath (Memmert), aluminum foil, spatula, stir bar, hot plate magnetic stirrer (Medline Scientific 300HS), pH-meter, watch glass, vortex, UV-Vis spectrophotometer (Optima SP-300nano), autoclave (Hirayama HVE-50), incubator, petri dish, ose needle, bunsen, viscometer (Brookfield DV-II+Pro), caliper, stopwatch, weight.

The materials needed consist of musk tobacco, CMC-Na, nipagin, propylene glycol, glycerin, 96% ethanol, essential oil, aquades, quercetin, aluminum chloride, acetic acid, Sodium Agar (NA), Nutrient Broth (NB), *Staphylococcus aureus*.

B. Method

Preparation of Gel Hand Sanitizer

Making hand sanitizer gel begins with making a gel base with dissolved CMC-Na powder in boiling water using a ratio of 1:10 (g/ml) [28]. The solution was cooled to room temperature to form a perfect gel base. Then, gel base added nipagin which has been dissolved in a ratio of 1:10 (g/ml), glycerin, and propylene glycol was added until homogeneous. Then, heated tobacco extract, 96% ethanol, and essential oil are added. The final stage is the homogenization of all the ingredients that have been added with distilled water.

Optimization of Gel Hand Sanitizer Preparation Formula

The research method used in this study is a type of laboratory experiment using Completely Randomized Design (CRD). In this study, there were two variables, variations in the ratio of CMC-Na and glycerin. The test parameters for selecting the optimum formula were based on physical parameters, such as pH, viscosity, adhesion, and spreadability.

Concentrations for CMC-Na and glycerin were determined taking into account the upper and lower limits of their use. The limits for the use of the two ingredients are listed in Table 1, while the variations in the proportions of the formulas are listed in Table 2.

TABLE I. UPPER AND LOWER LIMITS ON THE USE OF MATERIALS [19]

Ingredient	Concentration	
	Lower limit (%)	***Upper limit (%)***
CMC-Na	3	6
Glycerin	5	15

TABLE II. VARIATIONS IN THE PROPORTION OF INGREDIENT FORMULAS

Ingredient Name	Formula (%)				
	F1	***F2***	***F3***	***F4***	***F5***
CMC-Na	1	0.25	0	0.5	0.75
Glycerin	0	0.75	1	0.5	0.25

Determination of the composition of CMC-Na and glycerin as hand sanitizer gel ingredients that have been substituted in the composition of the 5 formulas can be seen in Table 3. The formula used in determining the composition of the ingredients is as follows [8]:

$$\text{Ingredients} = f \times (A - B) + B \times V \quad (1)$$

Information :
f = the composition of the ingredients in the formula
A = upper limit
B = lower limit
V = volume of solution

TABLE III. COMPOSITION OF INGREDIENTS FOR GEL HAND SANITIZER

Ingredient Name	Formula				
	F1	***F2***	***F3***	***F4***	***F5***
Tobacco Extract (g)	1.25	1.25	1.25	1.25	1.25
CMC-Na (g)	6	3.75	3	4.5	5.25
Nipagin (g)	0.2	0.2	0.2	0.2	0.2
Propylene Glycol (ml)	15	15	15	15	15
Glycerin (ml)	5	12.5	15	10	7.5
Etanol 96% (ml)	10	10	10	10	10
Essential Oil (ml)	1	1	1	1	1
Aquades (ml)	61.55	56.3	54.55	58.05	59.8

The data obtained from the research results were processed using Analysis of Variance (ANOVA) with a 95% confidence level and continued with Duncan's Multiple Range Test at a significance level of 5%. The selection of the optimum formula was carried out based on the desirability value approach with the Simplex Lattice Design method using Design Expert Version 13 software [20]. The verification stage for the selection of the optimum formula was carried out using statistical analysis One Sample T-Test.

Optimum Formula Hand Sanitizer Gel Preparation

The testing parameters on the optimum formula hand sanitizer gel were carried out based on physical, chemical, and microbiological parameters. On the physical parameters, homogeneity test and stability test were carried out based on the viscosity shift. The chemical parameters were tested for total flavonoid content. The microbiological parameters were tested for antibacterial and antiseptic properties. The data obtained from the research results were processed using Analysis of Variance (ANOVA) with a 95% confidence level

and continued with Duncan's Multiple Range Test at a significance level of 5%.

III. Results And Discussion

A. *Optimization Characteristics of Hand Sanitizer Gel Formula*

pH Test

The pH test aims to ensure the safety of the tobacco leaf extract hand sanitizer gel when applied topically. The ideal topical preparation has a pH value that is the same as the pH of the skin so that when applied it does not cause skin irritation. The normal range of pH values ranges from 4.5 to 8 [21].

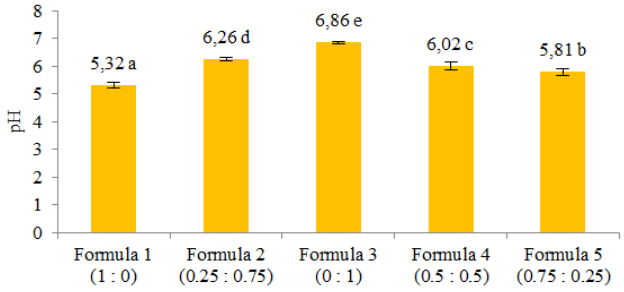

Fig. 1. pH Test Results

The results of the study on the pH parameters of the tobacco extract hand sanitizer gel obtained data in the range of values from 5.32 to 6.86 which showed the hand sanitizer gel in the entire formula was in accordance with the applicable quality standards. Therefore, herbal hand sanitizer gel can provide a sense of comfort and safety when applied to the skin. The ANOVA statistical test used at a significant level of 5% gave results if the model had a p value ≤ 0.05, which means that there was a significant difference in the variation in the ratio of CMC-Na and glycerin to the pH value of the hand sanitizer gel.

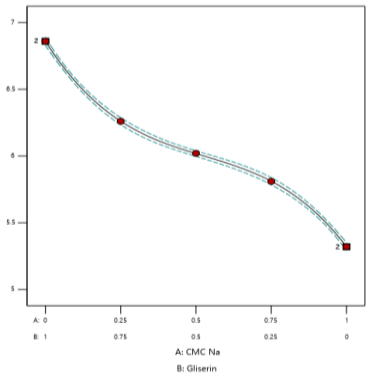

Fig. 2. pH Test Contour Plot

The Simplex Lattice Design equation for the pH response is as follows:

$$Y = 5.31971\ A + 6.85971\ B - 0.285714\ AB \quad (2)$$

In this equation Y indicates the pH response, A indicates CMC-Na, B indicates glycerin, and AB indicates the combination of CMC-Na and glycerin. The coefficient value in variable B has the greatest value, meaning that glycerin has the greatest influence on changes in pH in hand sanitizers with tobacco leaf extract. Glycerin is an alkaline compound that has a pH of > 10 [4]. The nature of glycerin causes an increase in the pH value of the tobacco leaf extract hand sanitizer gel as the concentration of glycerin in the formula increases.

Viscosity Test

Viscosity is the resistance of a fluid that indicates viscosity. The viscosity of a good gel preparation should not be too high or too low because it will affect the comfort level of the product when implemented. Good gel viscosity values are in the range of values of 2000 – 50000 cP[7].

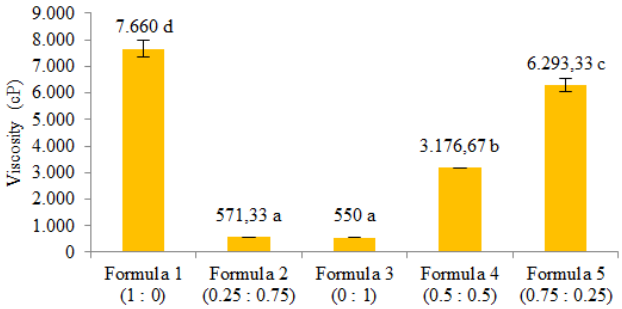

Fig. 3. Viscosity Test Results

The results of the study on the viscosity parameters of the tobacco extract hand sanitizer gel obtained data in the value range of 550 cP - 7660 cP, so it was shown that there was a hand sanitizer gel formula that did not have a good viscosity value because it was below the standard viscosity value. Formulas that do not have good viscosity values are Formula 2 and Formula 3. The ANOVA statistical test used at a significant level of 5% gives results if the model has a p value ≤ 0.05, which means that there is a significant difference in the variation of the ratio of CMC-Na and glycerin to the value hand sanitizer gel viscosity.

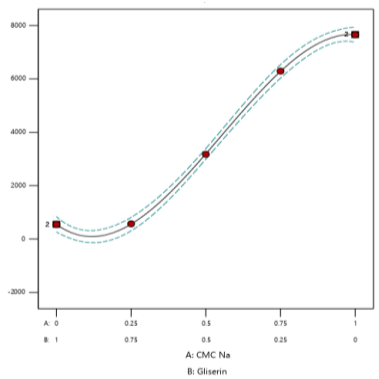

Fig. 4. Viscosity Test Contour Plot

The Simplex Lattice Design equation for the viscosity response is as follows:

$$Y = 7662.69457\ A + 552.69457\ B - 3659.42857\ A \quad (3)$$

In this equation Y indicates the viscosity response, A indicates CMC-Na, B indicates glycerin, and AB indicates the

combination of CMC-Na and glycerin. The coefficient value in variable A has the largest value, meaning that CMC-Na has the greatest influence on changes in viscosity in hand sanitizers of tobacco leaf extract. The effect of CMC-Na on viscosity cannot be separated from its role as a gelling agent [19]. The role of CMC-Na causes an increase in the viscosity value of the tobacco leaf extract hand sanitizer gel as the concentration of CMC-Na in the formula increases. CMC-Na is hydrophilic, so that when the compound is dispersed in water, it can absorb water [16]. The ability of CMC-Na causes the absorbed water cannot move freely which results in an increase in viscosity.

Adhesiveness

Adhesiveness indicates the length of time the hand sanitizer gel will stick to tobacco leaf extract when applied to the skin surface. Gel preparations with good adhesion will ensure the complete absorption of active compounds that act as antibacterial substances on the skin. Good adhesion to topical preparations is not less than 4 seconds [23].

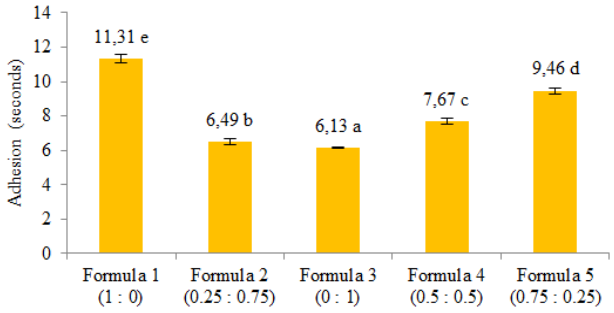

Fig. 5. Adhesion Test Results

Results research on the stickiness parameter of the tobacco extract hand sanitizer gel obtained data in the value range of 6.13 seconds - 11.31 seconds which shows the hand sanitizer gel in the whole formula has a good adhesion value. Therefore, herbal hand sanitizer gel can perform its role in absorbing active compounds that act as antimicrobials on the skin properly and not blocking the pores. The ANOVA statistical test used at a significant level of 5% gave results if the model had a p value ≤ 0.05, which means that there was a significant difference in the variation in the ratio of CMC-Na and glycerin to the stickiness of the hand sanitizer gel.

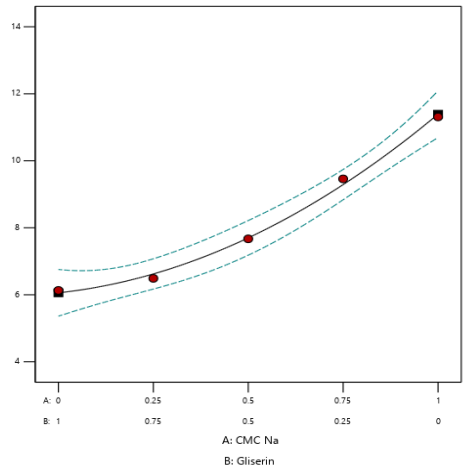

Fig. 6. Adhesion Test Contour Plot

The Simplex Lattice Design equation for the adhesive response is as follows:

$$Y = 11.39086\ A + 6.05886\ B - 4.10286\ AB \quad (4)$$

In this equation Y indicates the response of adhesion, A indicates CMC-Na, B indicates glycerin, and AB indicates the combination of CMC-Na and glycerin. The value of the coefficient on variable A has the largest value, meaning that CMC-Na has the greatest influence on changes in adhesion to hand sanitizers of tobacco leaf extract. The effect of CMC-Na on adhesion is inseparable from its role as a gelling agent [19]. The role of CMC-Na has an effect on gel consistency. Adhesion to gel preparations is directly proportional to the viscosity value. When the viscosity is higher, the higher the adhesion produced [22].

Spreadability

Spreadability aims to measure the spread of the gel when applied to the skin. The even distribution of the gel will optimize the role of the active compounds in the hand sanitizer gel. The spreadability of a good hand sanitizer is in the value range of 5-7 cm [21].

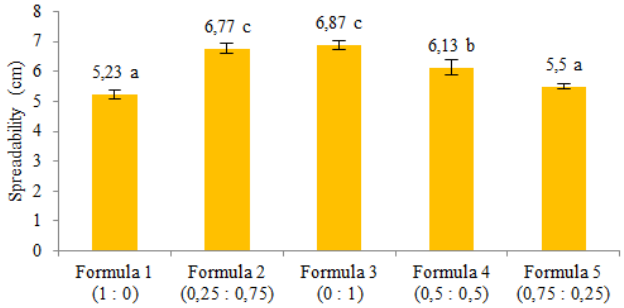

Fig. 7. Spreadability Test Results

The results of the study on the dispersion parameters of the tobacco extract hand sanitizer gel obtained data in the range of 5.23 cm - 6.87 cm which showed the hand sanitizer gel in the entire formula was in accordance with the applicable quality

standards. Therefore, herbal hand sanitizer gel can provide a sense of comfort and perform its role as a synthetic detergent optimally when implemented on the skin. The ANOVA statistical test used at a significant level of 5% gave results if the model had a p value ≤ 0.05, which means that there was a significant difference in the variation in the ratio of CMC-Na and glycerin to the spreadability of the hand sanitizer gel.

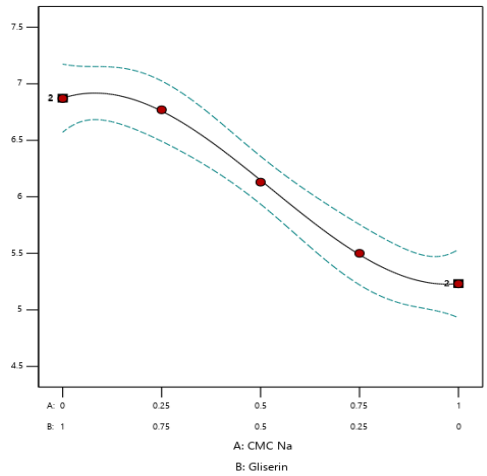

Fig. 8. Spreadability Test Contour Plot

The Simplex Lattice Design equation for the spreadability response is as follows:

$$Y = 5.23286\ A + 6.87286\ B + 0.377143\ AB \quad (5)$$

In this equation Y indicates the response of dispersion, A indicates CMC-Na, B indicates glycerin, and AB indicates the combination of CMC-Na and glycerin. The value of the coefficient on variable A has the largest value, meaning that CMC-Na has the greatest influence on changes in adhesion to hand sanitizers of tobacco leaf extract. The effect of CMC-Na on adhesion is inseparable from its role as a gelling agent [19]. The role of CMC-Na has an effect on gel consistency. The dispersion of gel preparations is inversely proportional to the viscosity value. When the viscosity is higher, the value of the resulting adhesion will be lower [22]. Changes in dispersion values are also influenced by glycerin which is hygroscopic [11]. These properties cause glycerin to be able to absorb water molecules if it is not stored in a closed container. The increase in water consistency in the preparation can provide a decrease in the viscosity value which has an effect on increasing the dispersion value.

B. Determination of The Optimum Formula for Gel Hand Sanitizer

The optimization of the formula was carried out to determine the optimal ratio of CMC-Na and glycerin. Software Design Expert V.13 was chosen to determine the optimum formula through the desirability value approach. The desirability value shows the level of closeness of the response to the target which is influenced by the number of variables used, the complexity of the variables, and the expected target. The optimum formula chosen is the formula with the composition of CMC-Na and glycerin which has a desirability value close to the maximum value (one) [17][25].

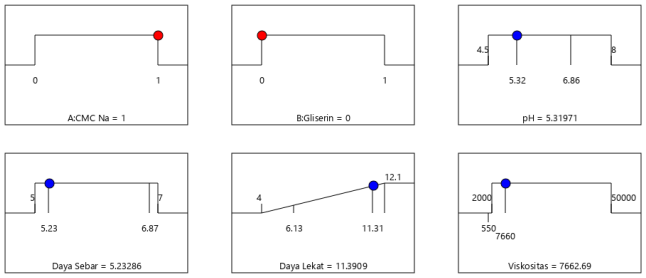

Fig. 9. Desirability Formula Optimum Gel of Hand Sanitizer

Formula 1, Formula 4, and Formula 5 are in the optimum area. The three formulas have physical parameter values that match the test response parameter criteria. The simplex lattice design method can determine the predicted response value for each parameter analysis. The predicted value generated is not always the same when compared to the test results, but the difference in the range of values owned is not too significant. This condition can be interpreted if the formula presented is in accordance with the criteria for each parameter.

TABLE IV. PHYSICAL CHARACTERISTICS OF OPTIMUM FORMULA

Parameter	Prediction	sig. 2 tailed	Test Result		
			F1	*F4*	*F5*
pH	6.01829	0.895	5.32	6.02	5.81
Viscosity	3192.84	0.769	7660	3176.67	6293.33
Adhesion	7.69914	0.624	11.31	7.67	9.46
Spreadability	6.14714	0.893	5.23	6.13	5.50
Desirability			0.912	0.457	0.653

The results of the analysis of determining the optimum formula based on the desirability value were validated using the T-Test One Sample parametric test. The four parameters indicate the value of sig. 2 tailed ≥ 0.05 which means that the value of the test results does not have a significant difference compared to the predicted value. If in the observation process there is a value that does not differ much from the predicted value, then the formula can be chosen as the optimum formula.

C. Optimum Formula Hand Sanitizer Gel Preparation

Homogeneity

Homogeneity is the ability to physically mix the preparation in the gel formulation. Good homogeneity in a preparation is indicated by the absence of particle clumps in the gel distribution.

TABLE V. HOMOGENEITY TEST RESULTS

Formula	Information
Formula 1	Homogeneous
Formula 4	Homogeneous
Formula 5	Homogeneous

The homogeneity of the hand sanitizer gel of tobacco leaf extract shows that all components of the constituent materials can be well dispersed into the gel base.The homogeneity is influenced by CMC-Na as a gelling agent which has a role in the formation of gel appearance. A good gel base can be created by mixingat high temperatures because it can encourage loose bonds in CMC-Na[28]. Gel manufacturing process using CMC-Nadone with medium rotationbecause it will produce a gel appearance that is not clear if using a high rotation speed, while agglomerates will form if homogenized with a low rotation speed.

Stability Test

Tobacco leaf extract hand sanitizer gel stability describes the gel consistency after 4 weeks of storage. The stability test was assessed by calculating the viscosity shift in the hand sanitizer gel that had just been made and after the storage period. The greater the value of the viscosity shift, the more unstable the resulting cell preparation, where the gel preparation is stable when it has a viscosity shift value of <10% [12].

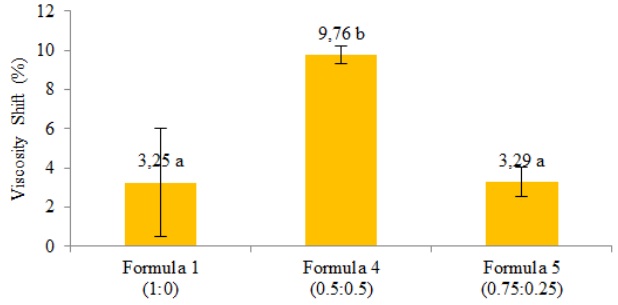

Fig. 10. Stability Test Results

The ANOVA statistical test used at a significant level of 5% gave results if the model had a p value ≤ 0.05, which means that there was a significant difference in the variation in the ratio of CMC-Na and glycerin to the shift value of the viscosity shift of the optimum hand sanitizer gel formula. The results of stability research on the viscosity shift in the hand sanitizer gel of the optimum formula tobacco extract obtained data in the range of values of 3.25% - 9.76% which showed the optimum formula hand sanitizer gel had a stable gel viscosity. Changes in viscosity values that cause a shift in viscosity during storage are influenced by glycerin because it has hygroscopic properties [11]. These properties cause glycerin to be able to absorb water molecules if it is not stored in a water and airtight container.

Total Flavonoid Level

Identification of the total flavonoid content contained in the hand sanitizer gel of tobacco leaf extract was carried out by quantitative analysis using the spectrophotometric method because flavonoid compounds could be identified through absorption waves in the ultraviolet and visible spectrum regions. The test procedure uses quercetin as a standard solution which has a linear regression of y = 0.0104x + 0.0079 with a value of R^2 = 0.9988.

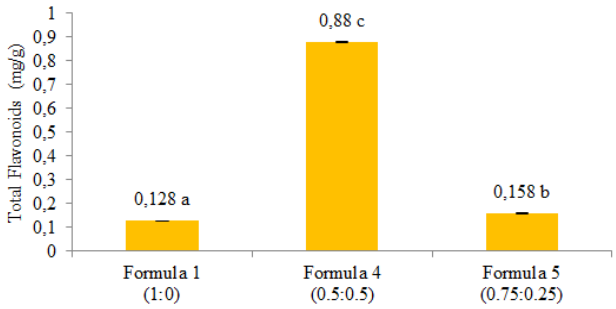

Fig. 11. Total Flavonoid Level Test Results

The ANOVA statistical test used at a significant level of 5% gave results if the model had a p value ≤ 0.05, which means that there was a significant difference in the variation in the ratio of CMC-Na and glycerin to the release of flavonoid content in the total gel hand sanitizer optimum formula. Tobacco leaves are known to contain active compounds in the form of flavonoids, saponins, steroids, and terpenoids [13]. Tobacco leaf extract contains 1.34 mg/g total flavonoid content [6]. This value is lower than the total flavonoid content contained in the hand sanitizer gel of tobacco leaf extract because there has been a mixing process with the components of the hand sanitizer making material, resulting in a decrease in concentration due to the dilution process during homogenization [1]. The increase in the release of flavonoid compounds was inversely proportional to the increase in the concentration of CMC-Na. This is related to the role of CMC-Na as a gelling agent that can increase gel viscosity, while high viscosity can prevent the release of flavonoid compounds because it can reduce the value of the diffusion coefficient of these compounds [9].

Antibacterial Test

Antibacterial test was carried out on Staphylococcus aureus bacteria using agar diffusion method. Observations were based on the clear zone after incubation at 37°C for 24 hours. The clear zone is an indication of the sensitivity of the bacteria to the antibacterial material used as the test material. There is a category of inhibitory power [18], with a diameter of 0-5 mm having a weak growth inhibitory response, a diameter of 10-20 mm having a moderate growth inhibitory response, and diameters >20 mm having a strong growth inhibitory response.

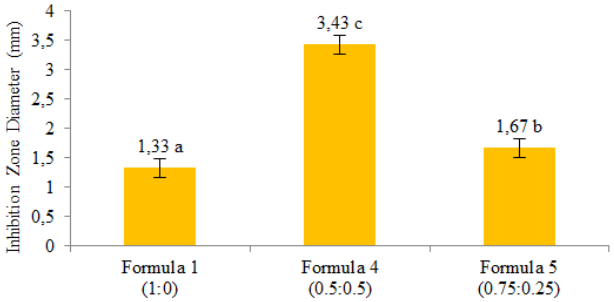

Fig. 12. Antibacterial Power Test Results

The ANOVA statistical test used at a significant level of 5% gave results if the model had a p value ≤ 0.05, which

means that there was a significant difference in the variation in the ratio of CMC-Na and glycerin to the antibacterial power of the optimum formula hand sanitizer gel. The inhibitory power of the tobacco leaf extract hand sanitizer gel is 1.33 mm – 3.43 mm, indicating that the inhibitory power is weak. The diameter of the inhibition zone formed was inversely proportional to the increase in the concentration of CMC-Na. This is related to the role of CMC-Na as a gelling agent that can increase gel viscosity, while high viscosity can hinder the release of active compounds because it can reduce the value of the diffusion coefficient of these compounds [9]. Therefore, the increase in viscosity which is proportional to the increase in the concentration of CMC-Na can reduce the effectiveness of the release of flavonoid compounds as antibacterial substances in the hand sanitizer gel of tobacco leaf extract.

The active compounds from tobacco leaf extract contained in the hand sanitizer gel play an active role in increasing the antibacterial power of the preparation. Tobacco leaf extract contains several active compounds such as flavonoids, saponins, steroids, and terpenoids. Flavonoid compounds have the ability to damage cell walls to cause cell death. Flavonoids are able to provide obstacles to the formation of proteins which result in the inhibition of microbial growth [13].

Antiseptic Power Test

The antiseptic power test aims to measure the ability of the hand sanitizer gel to inhibit contamination of the growth of flora colonies on the skin using the replica method. Antiseptic effectiveness was determined based on the decrease in the number of colonies, where the lower the number of colonies, the better the antiseptic ability. A good hand sanitizer has microbial contamination which is indicated in the Total Plate Number (ALT) a maximum of $1x10^3$ colonies/g[21].

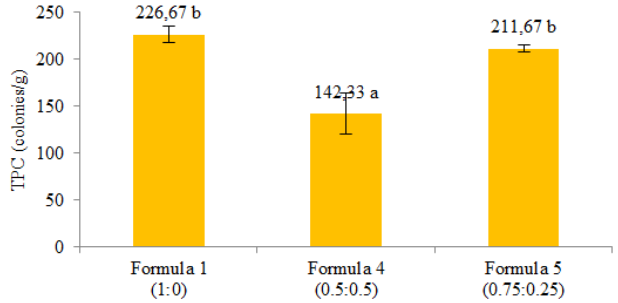

Fig. 13. Antiseptic Power Test Results

The ANOVA statistical test used at a significant level of 5% gave results if the model had a p value ≤ 0.05, which means that there was a significant difference in the variation in the ratio of CMC-Na and glycerin to the antiseptic power of the optimum hand sanitizer gel formula. The growth of microorganisms indicated by the Total Plate Count (TPC) on the tobacco leaf extract hand sanitizer gel of 142.33 colonies/g – 226.67 colonies/g indicates that the hand sanitizer is safe to use because it is able to maintain aseptic conditions by inhibiting contamination according to regulated quality standards. The distribution of colonies formed was inversely proportional to the increase in the concentration of CMC-Na. This is related to the role of CMC-Na as a gelling agent that can increase gel viscosity, while high viscosity can hinder the release of the active compound because it can reduce the value of the diffusion coefficient of the compound [9]. Therefore, the increase in viscosity which is proportional to the increase in the concentration of CMC-Na can reduce the effectiveness of the release of flavonoid compounds as antiseptic substances in the hand sanitizer gel of tobacco leaf extract.

The active compounds from tobacco leaf extract contained in the hand sanitizer gel play an active role in increasing the antibacterial power of the preparation. Tobacco leaf extract contains several active compounds such as flavonoids, saponins, steroids, and terpenoids. Flavonoid compounds have the ability to damage cell walls to cause cell death. Flavonoids are able to provide obstacles to the formation of proteins which result in the inhibition of microbial growth [13].

IV. Conclusion

There are 3 optimum formulas for hand sanitizer gel of tobacco leaf extract based on the desirability value, 0.912 (Formula 1), 0.457 (Formula 4) and 0.653 (Formula 5). The variation of the concentration ratio of CMC-Na and glycerin in the optimum formula showed that CMC-Na had the most dominant influence on physical characteristics (homogeneity), chemical (total flavonoid content) and microbiological (antibacterial and antiseptic) characteristics. Meanwhile, glycerin has the most dominant influence on product viscosity stability. The three optimum formulas have homogeneous gel characteristics.

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