

Antiseptic activity assay of ethanolic extract of Aceh's rambutan rind (*Nephelium lappaceum* L.) against *Staphylococcus aureus* and its formulation as hand sanitizer gel

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Abstract The hands are one of the most susceptible parts of the human body to bacterial infection. One way to maintain health is to maintain hand hygiene. Ethanolic rambutan rind extract from Aceh province has been studied in order to determine if it can inhibit bacterial growth. This research was conducted to determine the antiseptic activity of the ethanol extract of rambutan rind against *Staphylococcus aureus* by determining the phenol coefficient and determining whether the ethanolic extract of Aceh's rambutan rind can be formulated into a hand sanitizer gel. Antiseptic activity testing was performed using the Rideal-Walker method which was carried out in 5 dilutions (1:100, 1:150, 1:200, 1:250 and 1:300). The absorbance measurement showed that the extract could act as an antiseptic, at a concentration of 1% and at a dilution of 1:200 which has phenol coefficient of 1.67. The ethanolic extract of Aceh's rambutan rind can be formulated in the form of a hand sanitizer gel using 1% Carbopol as gelling agent. The results showed that the gel was brown with a distinctive menthol odor and changed into a dark brown color after a cycling test. The evaluation results of all formulas appropriated the requirements except for adhesion parameter. The results of the irritation test showed that the volunteers did not experience any signs of irritation. The results of the preference test showed that the respondents liked the shape and aroma parameters but not the color parameter.

Keywords: Antiseptic activity, ethanolic extract of Aceh's rambutan rind, *Nephelium lappaceum* L, hand sanitizer gel, Carbopol

INTRODUCTION

The skin is the outermost layer of the human body, which functions as the main barrier in blocking the entry of pathogens into the body. The hands are one part of the human body that is most susceptible to various kinds of microorganisms such as bacteria, and mainly because they are always in direct contact with various objects, both dirty and clean. However, on our own hands there are normal flora that colonize the superficial parts of the skin. These normal flora do not always multiply on the skin, but they are alive and multiply sporadically on the skin surface [1]. It was reported that the most common bacteria on the hands is *Staphylococcus aureus* (*S. aureus*) [2]. The spread of *S. aureus* bacteria can be transmitted from hand to hand. These bacteria can cause diseases such as boils, acne, infection of the hair follicles, infection of

wounds, meningitis and pneumonia [3]. The World Health Organization (WHO) reported that the most pathogenic contamination in the palms is caused by *S. aureus*, *Enterococci*, or *Clostridium difficile* especially in health workers who interact with patients [1].

One of the simplest ways to prevent the spread of bacteria is to wash hands with the soap. However, along with the increasing activity of the community, soap is not easy to carry, so an innovative product such as hand sanitizer gel is required. Hand sanitizer gel is often used by dropping it on the palm of the hand, then rubbing it on the surface of the hand without rinsing it with water. One of the advantages of hand sanitizer is that it can kill microorganisms in a relatively fast time, because it contains an active alcohol compound with concentrations between 60 and 80%. The concentration of alcohol contained in hand sanitizers can kill microorganisms by denaturing and coagulating its proteins. However, a continuous use of alcohol will cause dryness and irritation of the skin [4].

One of the attempts to reduce the use of alcohol in hand sanitizer gel is to use a natural product as an active ingredient. *Rambutan* (*Nephelium lappaceum* L.) is one of the natural products that has antibacterial

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Table 1. Hand Sanitizer Formula

Materials	Concentration (%)	
	F0 (%)	F1 (%)
Rambutan rind ethanolic extract	-	1
Carbopol 940	1	1
TEA	2,5	2,5
Nipagin	0,2	0,2
Glycerin	10,25	10,25
Menthol	0,5	0,5
Aquadest	Ad 100 mL	Ad 100 ml

Note: F0 = formula without extract, F1 = formula with EERR

activity. Parts of the *rambutan* (further *N. lappaceum*) plant such as leaves, bark, fruit, roots, and seeds can be used as a medicinal plant [5]. Several studies have shown that *N. lappaceum*, L. has anti-inflammatory activity, antibacterial activity, antiviral activity, antioxidant activity, and antiproliferative activity [6].

It has been reported that the ethanolic extract of the *rambutan* rind can inhibit the bacterial of *S. aureus* with the MIC₅₀ and MBC₅₀ values were 50 mg/mL and 60 mg/mL respectively [7,8]. The ethanolic extract of *rambutan* rind and peels were reported contains some secondary metabolites mainly are ellagitannins, such as geraniin, corilagin, and ellagic acid. It also contains phenolic compound, but each plant has different concentration depending on the cultivars, cultivable soil, and method of extraction [8]. Therefore, the aim of this study was to determine the potential of the ethanolic extract of Aceh's rambutan rind (*Nephelium lappaceum* L.) into an antiseptic preparation. In this study, the antiseptic activity of the ethanolic extract of the rambutan rind was determined and then formulated it into a hand sanitizer preparation.

METHODOLOGY

Plant material preparation

Rambutan fruits were obtained from the *Lhoong sub-district area, Aceh Besar* using purposive sampling technique. The characteristics of the rambutan fruits obtained were fresh, red in color and free from pests. As much as 15 kg of rambutan fruits were obtained, then cleaned with running water and sorted to separate the fruit from the rind. Furthermore, the rambutan rind was chopped and then dried for 4 weeks or until brittle at room temperature (direct sunlight was avoided). After drying process, the dried sample was dry sorted, then weighed and powdered using a blender to obtain coarse powder. The yield of dried *Rambutan* rind obtained was 44%, respectively.

Extraction

The extraction was carried out using the maceration method with a ratio 1:10. Five hundred grams of powdered sample were mixed with 3.75 L of 96% ethanol solvent and stood for 5 days with occasional stirring. After the initial extraction, the dregs were immersed in remainder of the solvent for another 5 days. The mixture was then filtered to obtain a macerate, and then the residue was macerated for another day. All the macerates were mixed and concentrated using a vacuum rotary evaporator to obtain a crude ethanolic extract of rambutan rind (EERR). The percentage yield value of extract obtained from this procedure was 20.33%.

Antiseptic Activity Test

All the material used in this assay were sterilized using the appropriate method. The antiseptic activity assay was performed using Rideal–Walker method. The Rideal–Walker coefficient, is a figure expressing the disinfecting power of any disinfectant that kills a microorganism in the same time under identical conditions. The Rideal–Walker coefficient determines the phenol coefficient. Briefly, 0.6 mL of incubated bacterial culture were added into 15 mL of series EERR dilutions (1:100, 1:150, 1:200, 1:250 and 1:300). The dilutions then stirred and taken as much as 0.5 mL for subcultures at intervals time of 2.5; 5; 7.5, and 10 minutes. Each subculture was added to 0.5 mL of nutrient broth (NB) medium and incubated for 72 hours at 37 °C (9). The incubated subculture then measured the absorption at $\lambda = 600$

Phenol coefficient

$$= \frac{\text{Highest dilution of extract that kill bacteria in 10 minutes but not kill bacteria in 5 minutes}}{\text{Highest dilution of phenol that kill bacteria in 10 minutes but not kill bacteria in 5 minutes}}$$

Hand sanitizer formulation

Hand sanitizer formulation was carried out according to formula showed in Table 1. Formula obtained in this research is a modification [10].

Hand Sanitizer evaluation

The evaluation of the formulas was determined on several parameters including organoleptic, homogeneity, spreadability, adhesion, pH, stability (using cycling test), viscosity, irritation, and preference test.

RESULTS AND DISCUSSION

Antiseptic Activity

Antiseptic activity against *Staphylococcus aureus* ATCC 25923 was carried out using Rideal-Walker method. The test was carried out with 5 dilutions (1:100, 1:150, 1:200, 1:250 and 1:300) to determine which dilution has antiseptic activity. In this method, 2% phenol was used as a positive control. Phenol works by denaturing cell proteins and damaging

Table 2. Evaluation of EERR antiseptic activity

Test Solution	Dilution	Average Absorbance Value $\pm$ SD			
		Minute			
		2.5	5	7.5	10
Phenol 2%	100	0.0113 $\pm$ 0.0005	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0
	150	0.0467 $\pm$ 0.0011	0.0073 $\pm$ 0.0005	0 $\pm$ 0	0 $\pm$ 0
	200	0.0693 $\pm$ 0.0005	0.023 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0
	250	0.088 $\pm$ 0.002	0.047 $\pm$ 0.0017	0.0076 $\pm$ 0.0005	0 $\pm$ 0
	300	0.137 $\pm$ 0.001	0.053 $\pm$ 0	0.0133 $\pm$ 0.011	0 $\pm$ 0
EERR 0.5%	100	0.0153 $\pm$ 0.0005	0.008 $\pm$ 0	0.0006 $\pm$ 0.0005	0 $\pm$ 0
	150	0.024 $\pm$ 0	0.016 $\pm$ 0	0.0106 $\pm$ 0.0005	0.003 $\pm$ 0
	200	0.0373 $\pm$ 0.0005	0.028 $\pm$ 0	0.020 $\pm$ 0	0.0103 $\pm$ 0.0005
	250	0.0453 $\pm$ 0.0005	0.0363 $\pm$ 0.0005	0.0283 $\pm$ 0.0011	0.019 $\pm$ 0.001
	300	0.0556 $\pm$ 0.0005	0.0476 $\pm$ 0.0005	0.0373 $\pm$ 0.0005	0.0293 $\pm$ 0.0005
EERR 1%	100	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0
	150	0.0053 $\pm$ 0.0005	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0
	200	0.0166 $\pm$ 0.0005	0.0086 $\pm$ 0.0005	0.001 $\pm$ 0	0 $\pm$ 0
	250	0.0263 $\pm$ 0.0005	0.0183 $\pm$ 0.0011	0.0106 $\pm$ 0.0005	0.0033 $\pm$ 0.0005
	300	0.036 $\pm$ 0.001	0.0273 $\pm$ 0.0020	0.0193 $\pm$ 0.0005	0.0096 $\pm$ 0.0005

membranes. The phenol concentration used in this study was 2%. The results for phenol and extract antiseptic activity assay against *S. aureus* bacteria can be seen in Table 2.

The principle of antiseptic activity assay is the comparison of the concentration of extract that kills bacteria within 10 minutes but does not kill bacteria within 5 minutes [11]. The result of absorbance measurement in this research showed that phenol as positive control has antiseptic activity at 2% (dilution at 1:150). Meanwhile, the extract has antiseptic activity at 0.5% and 1% (dilution at 1:100 and 1:200 respectively)

Phenol coefficient then calculated using calculation formula below:

$$\text{Phenol coefficient for 0.5\% EERR} = \frac{100}{150} = 0,67$$

$$\text{Phenol coefficient for 1\% EERR} = \frac{200}{150} = 1,67$$

The results showed that the phenol coefficient for 0.5% of EERR was 0.67, while phenol coefficient for 1% of EERR was 1.67. These results indicated that the phenol coefficient for 1% EERR more effective than 0.5% EERR.

The antiseptic and antibacterial activity of the extract were influenced by the secondary metabolite in the extract. Secondary metabolites such as alkaloids, flavonoids, triterpenoids, saponins, and tannins have

potential as antibacterial and antiseptic agents. The mechanism of action of alkaloids as antibacterial is by inhibiting the synthesis of peptidoglycan. Peptidoglycan is the main component of the bacterial cell wall which serves to maintain its shape. The disruption of peptidoglycan synthesis causes the cell wall layer not to form completely which results in cell death [12, 13].

After examining the antiseptic activity of the EERR, the best concentration (EERR 1%) was formulated into hand sanitizer gel and the formula produced was evaluated. Evaluation results from the formula is presented on Table 3.

Stability Test

A cycling test was performed to determine the stability of the hand sanitizer. The cycling test was performed at 6 cycles (or in 12 days). One cycles (or for 2 days) was carried out at 24 hours at 45 °C, and at -3 °C for another 24 hours. The results of the cycling test were displayed in Table 3.

The spreadability test was performed to determine the dispersibility of the preparation when applied to the skin. If the solution has better spreadability, then the gel preparation will spread more easily when rubbed on the skin. The preparation is considered to have good dispersibility if the results obtained are 5-7 cm [14]. The results of the observation of the dispersibility before the cycling test showed that F0 and F1 met the dispersion requirements of topical preparations where the results obtained were 5.76 and 5.88 cm. F1 with the

Table 3. Evaluation Result of EERR hand sanitizer gel

Parameters Cycle	Homogeneity		Spreadability		Adhesiveness		pH		Shape		Color		Aroma	
	F0	F1	F0 (cm)	F1 (cm)	F0 (s)	F1 (s)	F0	F1	F0	F1	F0	F1	F0	F1
0	Homogen	Homogen	5.76	5.88	2.78	2.35	6.5	5.23	Gel	Gel	Transparent	Light brown	Menthol	Menthol
1	Homogen	Homogen	5.80	5.94	2.71	2.22	6.43	4.8	Gel	Gel	Transparent	Light Brown (+)	Menthol	Menthol
2	Homogen	Homogen	5.86	6.17	2.6	1.79	6.36	4.76	Gel	Gel	Transparent	Blackish brown (++)	Menthol	Menthol
3	Homogen	Homogen	6.03	6.41	2.38	1.69	6.3	4.76	Gel	Gel	Transparent	Blackish brown (++)	Menthol	Menthol
4	Homogen	Homogen	6.14	6.55	2.24	1.52	6.3	4.7	Gel	Gel	Transparent	Blackish Brown (+++)	Menthol	Menthol
5	Homogen	Homogen	6.29	6.67	1.98	1.47	6.3	4.66	Gel	Gel	Transparent	Blackish Brown (+++)	Menthol	Menthol
6	Homogen	Homogen	6.36	6.81	1.91	1.43	6.13	4.63	Gel	Gel	Transparent	Blackish brown (+++)	Menthol	Menthol

Note: F0 = Formula without extract; F1 = Formula with EERR

Table 4. Viscosity evaluation result of EERR hand sanitizer gel

Cycling Test	F0	F1
Before Cycling test (cPs)	20,768	19,395
After Cycling test (cPs)	13,867	15,784

Note: Viscosity test was performed using no.4 spindle at speed 20 rpm

Table 5. Irritation evaluation result

Formula	Respondent number	Observation		
		Redness	Itchiness	Edema
F0	20 people	-	-	-
F1	20 people	-	-	-

Note:(-): no reaction occurred

addition of the extract makes the preparation slightly thinner, so that the resulting dispersion is slightly greater than F0.

A pH analysis was performed to determine the acidity of the preparation and the suitability of the pH of the preparation with the pH of the skin, which must meet pH criteria of 4.5-6.5 [15]. The preparation made will be used on the skin of the hands, so the pH of the preparation must meet the requirements for safety when it is used. Preparations that are too acidic will irritate the skin while preparations that are too alkaline can cause dry skin. The pH test observations indicated that the pH of the preparation before the cycling test of F0 and F1 were 6.5 and 5.23 and still met the pH requirements of the topical preparation. Based on the observations, the difference between F0 and F1 was the addition of the extract that can affect the pH of the preparation. This was because the pH of the extract

itself was 3.7, which indicated that the extract is acidic, so that when excipients were added into the formula, it resulted in lower pH compared to the F0 which did not contain extract as one of the ingredients.

The viscosity study aims to determine the thickness of the preparation and the resistance of the preparation to flow. The higher the viscosity of a preparation, the more difficult it is to flow [16]. A good viscosity of semi-solid preparations is 4,000-40,000 cPs [17]. The results of viscosity observation before the cycling test showed that F0 and F1 met the requirements for semi-solid preparations where the results obtained were 20,768 and 19,395 cPs (Table 4). F1, with the addition of extract, made the preparation slightly thinner, so that the resulting viscosity is slightly smaller than F0. The 1% carbopol concentration used in the preparation resulted in high viscosity of the preparation, due to its function as viscosity enhancing agent. The higher the carbopol concentration used, the higher the viscosity of the preparation [18].

Organoleptic observations before and after the cycling test (Table 3) showed that the shape and aroma of F0 and F1 did not change and there was no syneresis. Meanwhile F0 did not change color, while F1 changed color to slightly blackish brown. The color change was caused by the degradation process of the materials used such as the extract used in the formulation.

The results of homogeneity observations before and after the cycling test showed that for both formula the homogeneity remains the same. The results of the spreadability test between before and after the cycling test at both F0 and F1 showed an increase in spreadability value from 5.76 to 6.81 cm (Table 3). The increase in the spreadability rate after cycling test can be caused by decreasing viscosity of the preparation after cycling test so that the ability of the preparation

to spread has increased but still meets the requirements. The spreadability is inversely proportional to the viscosity, where the greater the dispersive power, the smaller the resulting viscosity [19]. The increase in spreadability after the cycling test was thought to be due to a decrease in viscosity due to the stretching of bonds between atoms during the cycling test.

The results of the adhesion test between before and after the cycling test for both F0 and F1 showed a slight decrease from 1.43 to 2.78 seconds (Table 3). The decrease in adhesion time after cycling test can be caused by decreasing viscosity of the preparation after cycling test, so that the adhesion of the preparation also decreases, which results in the sample not meeting the requirements. The adhesion of the dosage form in each cycle decreased, presumably because the viscosity of the preparation for each cycle also decreased due to the stretching of bonds between atoms during the cycling test. However, due to the purpose of using this hand sanitizer gel, we think there is no significant problem if the adhesive test result did not meet the requirement. One of the reasons of this is to reduce the stickiness effect after applying the hand sanitizer on the palms.

The pH analysis results between before and after the cycling test at both F0 and F1 showed a decrease in number (Table 3). The pH results obtained ranged from 4.63 to 6.5 but still met the pH requirements of topical preparations. The decrease in pH that occurs during and after the cycling test is thought to occur due to the hydrolysis reaction that occurs in the preparation [20].

The results of the viscosity test between before and after the cycling test of both F0 and F1 showed a decrease (Table 4). The viscosity results obtained ranged from 13,867 to 20,768 but still met the requirements for semi-solid preparations. The decrease in viscosity after the cycling test was thought to be due to the extreme temperatures of the storage. Temperature greatly affects viscosity. The presence of heat during the storage period will increase the distance between atoms so that the forces between the atoms are reduced, the distance is stretched, and the viscosity will decrease [21]. Storage time also affects viscosity, the longer the storage time, the lower the viscosity of the preparation [18].

The irritation test was performed to observe if there was an irritating effect on the skin due to a substance. The irritation test was conducted on 20 respondents. The results of the irritation test for the hand sanitizer gel formulation showed no signs of irritation which typically including redness, itching and swelling (Table 5).

CONCLUSION

From the result of this study, it can be concluded that the 1% ethanol extract of rambutan rind (*Nephelium lappaceum* L.) possesses antiseptic properties against *S. aureus* using the Rideal-Walker method and it can

be formulated into hand sanitizer gel with 1% Carbopol as gelling agent. It also met the requirement as a pharmaceutical preparation, such as for homogeneity, spreadability, adhesiveness, pH, shape, color, aroma, and viscosity. Upon evaluating its irritative effect to healthy human, the result showed that it did not result in irritation to the test subject. Based on those result, 1% ethanol extract of *rambutan* rind (*Nephelium lappaceum* L.) has potential to be further developed into a pharmaceutical preparation.

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