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The Effectiveness Of Hand Sanitizer N-Hexane Fraction Of Avocado Leaves (Persea americana Mill.) Against Bacteria Staphylococcus aureus and Escherichia coli

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ABSTRACT

Background; Infectious diseases are one of the main public health problems in developed and developing countries. Most infectious diseases are caused by microorganisms in the form of bacteria, including Staphylococcus aureus and Escherichia coli. Avocado leaves contain, among other things, flavonoids, polyphenols, alkaloids, saponins, quercetin which are antibacterial. Previous research stated that the flavonoid content contained in avocado leaves (Persea americana Mill.) has antifungal, antiviral and antibacterial activity. **Purpose**; to determine the formulation and effectiveness test of the n-hexane fraction of avocado leaf (Persea americana Mill.) hand sanitizer against Staphylococcus aureus and Escherichia coli bacteria. **Method**; This type of research is experimental and aims to develop a hand sanitizer gel preparation product from avocado leaf fractions and test its antibacterial activity against Staphylococcus aureus and Escherichia coli bacteria. Avocado leaf fraction gel formulations were made with fraction concentrations of 5%, 10%, 15% with CMC-Na as the base. For gel results, physical tests were carried out including: organoleptic test, homogeneity test, pH test and spreadability test. **Result**; The antibacterial activity test was carried out using the agar diffusion method and for the positive control Nuvo hand sanitizer gel was used and DMSO was used for the negative control. The results of this study indicate that the avocado leaf fraction gel has antibacterial activity with an average diameter of the inhibition zone for a gel fraction concentration of 5% (9.45mm, 9 mm), a gel fraction concentration of 10% (9.63 mm, 9.16 mm). , 15% concentration (10.3 mm, 9.8 mm), positive control (8.56 mm, 8.78 mm), and negative control (0 mm, 0 mm). A concentration of 5% is classified as a strong inhibitory power, a concentration of 10%, 15% is classified as a strong inhibitory power. The positive control was classified as moderate inhibitory and the negative control did not provide antibacterial activity. **Conclusion**; Avocado leaf fraction (Persea americana Mill.) has antibacterial activity against Staphyococcus aureus and Escherichia coli bacteria with the highest inhibition zone at a concentration of 15% and the most effective concentration based on statistical tests is 5%.

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1. Introduction

Infectious diseases are one of the main public health problems in developed and developing countries. The World Health Organization (WHO) states that this disease is the main cause of death in children (WHO, 2015). Most infectious diseases are caused by microorganisms in the form of bacteria, including Staphylococcus aureus and Escherichia coli. Staphylococcus aureus is a gram-positive bacteria that can be found anywhere, including the human body (Lutpiatina, 2017).

The staphylococcus aureus bacteria is the cause of pyogenic infections. Infections caused by this bacteria usually appear with typical signs, namely inflammation, necrosis, and abscess formation, and can cause various infections such as acne, boils, or pus (Jawetz, Melnick, & Adelbergs's , 2008).

Escherichia coli is an enteric gram-negative bacterium (Enterobactericeae), a normal flora bacterium found in the human large intestine. These bacteria are pathogenic if they are outside the intestine, namely the normal location where the bacteria are and other places where these bacteria rarely live. Escherichia coli often causes infections in the urinary tract, bile ducts, and other places in the abdominal cavity. Escherichia coli is also a cause of diarrhea and urinary tract infections (Jawetz, Melnick, & Adelbergs's, Medical Microbiology, 2005).

Clinical treatment to treat infectious diseases such as antibiotics is very necessary. The high level of inappropriate use of antibiotics in society currently causes the problem of antibiotic resistance. Resistance problems occur when bacteria change in one way or another, causing a decrease or loss of effectiveness of drugs, chemical compounds, or other substances used to prevent or treat infections (Utami, 2011).

The discovery of new antibiotic compounds that have not experienced resistance is an alternative solution to overcome this problem. These compounds can be obtained from plants that contain compounds that have the potential to act as antibacterials with new mechanisms of action and have not experienced resistance. One of the plants that has antibacterial activity is avocado leaves (Persea Americana Mill.) (Amalia, Wahdaningsih, & Untari, 2014).

Avocado leaves contain, among other things, flavonoids, polyphenols, alkaloids, saponins, and quercetin which are antibacterial (Puluh, Edy, & Siampa, 2019). Previous research stated that the flavonoid content contained in avocado leaves (Persea americana Mill.) has antifungal, antiviral, and antibacterial activity (C W, Nurwati, & Istiati, 2012).

Based on research conducted by Ayu Ulfa Sari (2016) Regarding the Antibacterial Activity Test of avocado leaf fractions (Persea Americana Mill.) against staphylococcus aureus and Escherichia coli bacteria. The results showed that there was antibacterial activity in the avocado leaf fraction as indicated by the presence of a clear zone. The largest clear zone was 10.09 mm which was obtained from the n-hexane fraction with a concentration of 10% during the growth of Escherichia coli bacteria (Sari, Annisa, Ibrahim, & Rijai, 2016).

Using hand sanitizer is said to be more effective in killing germs in a short time than washing hands with running water because running water does not contain anti-germicidal (antibacterial) substances. In addition, germs can be carried along with the airflow, causing the reduction in the number of germs to be ineffective (Nurwaini & Saputri, 2018).

2. Method

Research Tools

Glass (pyrex), parchment paper, dropper pipette, spatula, glass object, analytical scale, blender, rotary evaporator, petri dish, porcelain cup, mortar, pestle, Simplicia preparation container,

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separating funnel, Bunsen lamp, tripod stand, petri dish (pyrex), autoclave, label paper, matches, sterile cotton buds, oven (Memmert UP400), tissue, asbestos, calipers, paper discs and scales.

Material

Avocado leaf ethanol extract, 96% ethanol, glycerin, propylene glycol, distilled water, staphylococcus aureus and Escherichia coli test bacteria, NA (Sodium agar) media, 0.9% NaCl, 0.36 N H2SO4, 1.175% BaCl2H2O, hand sanitizer gel Nuvo brand.

Research Procedure

1. Sample Processing

The plant part taken is the leaves. The collection was carried out purposively, that is, without comparing with similar plants from other areas. The samples used in this research were avocado leaves. The leaves taken are the young and old leaves (not the yellow leaves), the young leaves are the leaves that are picked from the first to fourth tip leaves. Meanwhile, when the old leaves are picked from the fifth to the eighth, the leaves are picked manually one by one. Samples were taken from the Gunung Bahgie village area, Kebayakan sub-district, Central Aceh district.

2. Making Extracts

To make avocado leaf extract using the maceration method. 10 kg of avocado leaves were cleaned, chopped then dried and samples were obtained. The extraction process was carried out for 7 days, where 1500 g of avocado leaf simplicia was put into a container then soaked using 11,250 ml of 96% ethanol solvent, covered with aluminum foil for 5 days (stirred every day), then filtered using filter paper and obtained filtrate 1 and dregs 1. The dregs are soaked again using 3,700 ml of 96% ethanol solvent for 2 days (stirred every day), then filtered using filter paper and filtrate 2 and dregs are obtained. Next, filtrate 1 and 2 are combined into one, and then concentrated using a rotary evaporator until a thick extract is obtained (Kumesan, Yamlean, & Supriati, 2013).

3. Fractionation

The coarse fractionation process carried out refers to the method of Can-ake et al. (2004), namely the partition process using water and hexane. A total of 10 g of thick extract was dissolved in 100 ml of water. The solution was then partitioned by adding 100 ml of n-hexane solvent, stirring/shaking in a separator flask, leaving for 30-60 minutes, and separating the layers formed (ethanol layer at the bottom, hexane layer at the top). The process of adding n-hexane was carried out 7 times in a row until the n-hexane layer became clear (indicating that there were no compounds that could be withdrawn), and the hexane layers obtained were combined into one as a hexane fraction. The fraction obtained was separated from the solvent using a rotary evaporator at a temperature of 50°C to obtain the fraction and dried in a water bath for 24 hours to obtain the N-hexane fraction (Can-Aké, Erosa-Rejón, May-Pat, Peña-Rodríguez, & Peraza-Sánchez, 2004).

4. Gel Preparation Formula

In this research, a gel preparation will be made with a variety of different extract concentrations, namely the avocado leaf fraction gel preparation formula 5%, 10%, and 15%.

5. Making Gel Preparations

The Na-CMC was weighed and then developed in a mortar with a little hot distilled water. Next, add the avocado leaf fraction and stir until completely dispersed. Next, glycerin and propylene

glycol are added. Stir until it forms a gel. Once the gel is formed, put it in a suitable container and label it.

6. Evaluation of Inventory

Evaluation of avocado leaf fraction gel preparations (Persea Americana Mill.) includes organoleptic tests, homogeneity tests, pH tests, and spreadability tests.

7. Creation of Basic Media and Growth Media

A total of 20 grams of NA was dissolved by heating in 1 liter of distilled water on a hot plate and using a magnetic stirrer until clear, then sterilized using an autoclave at 121 C for 15 minutes. Making NA agar slants is done by placing approximately 5 ml of sterilized media into a test tube, plugging the tube with sterile cotton, and tilting it until it solidifies (Alexander, Strete, & Niles, 2007).

8. Preparation of Mc Solution Turbidity Standards. far away country

99.5 ml of 0.36 N H2SO4 solution was mixed with 0.5 ml of 1.175% BaCl2.2H2O solution in an Erlenmeyer flask. Then shake until a cloudy solution is formed. This turbidity is used as a standard for the turbidity of the test bacterial suspension (Kumesan, Yamlean, & Supriati, 2013).

9. Making Bacterial Suspensions

To make a suspension of Staphylococcus aureus and Escherichia coli bacteria, by culturing staphylococcus aureus and Escherichia coli, they are taken with sterile ase wire, then suspended in a test tube containing 10 ml of 0.9% NaCl until a turbidity is obtained that is the same as the standard turbidity of the Mc. Farland solution. (Oktasila, Nurhamidah, & Handayani, 2019).

10. Inhibitory Power Test of Avocado Leaf Fraction Antiseptic Gel Preparation

The inhibitory power test used the agar diffusion method, namely paper discs. Prepare Petri dishes that have been sterilized by autoclaving. Pour 20 ml of homogenized NA media and let sit until it solidifies. Place the paper disc using tweezers. The antibacterial activity test was carried out by dipping paper discs into the paper discs, each of which was the avocado leaf fraction gel preparation at a predetermined concentration, namely 5%, 10%, 15%, DMSO as a negative control and Nuvo brand hand sanitizer as a control. positive. Next, the paper disc was placed on the bacterial medium with tweezers and then incubated for 24 hours at a temperature of 37°C. observe bacterial growth and measure the zone of inhibition using a caliper (Yanti & Mitika, 2017).

3. Result and Discussions

Preparation of Avocado Leaf Ethanol Extract

Tabel 1. Results of Making Ethanol Extract of Avocado Leaves

Simplicia Powder Weight	Condensed Extract Weight	Yield Value
1.500 gram	226 gram	15,07%

The maceration process uses 96% ethanol solvent because ethanol is a solvent that is relatively less toxic when compared to other solvents and has the property of being a universal solvent that is able to dissolve almost all substances found in plants, both polar, semipolar, and nonpolar (Azizah, Elvis, & Zulharmita, 2020).

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The yield of avocado leaf ethanol extract obtained was 15.07%. The amount of extract yield obtained depends on the type of solvent used. The polarity level of a solvent indicates the high or low dielectric constant of the solvent and will affect the value of the extract yield. The higher the polarity, the higher the dielectric constant value and the more interesting compounds there will be, so the yield will also be greater (Putra, Putra, & Wrasiati, 2020). Ethanol has high polarity and has two sides consisting of an –OH group which is polar and a CH2CH3 group which is nonpolar so that it can extract active compounds both polar and nonpolar which will influence the amount of yield produced (Julianti, Ikrawan, & Iwansyah, 2019).

The yield of avocado leaf ethanol extract obtained was smaller than the yield value stated in the Herbal Pharmacopoeia Edition II, namely 26% (Endarini, 2016). This low value can be caused by factors, one of which is the maceration method used. In this research, the method used was maceration so that the results obtained were smaller. The maceration method uses room temperature during the soaking process so that the yield obtained will be less compared to the reflux or soxhletation method which uses heating. Heating is one method used to improve the dissolution process of active substances so that the method used will obtain a greater and optimal yield compared to maceration which does not use heating (Wijaya, Novitasari, & Jubaidah, 2018).

Preparation of n-Hexane Fraction of Avocado Leaves

Tabel 2. Results of Making N-hexane Fraction of Avocado Leaves

Ethanol Extract Weight	Weight of n-Hexane Fraction	Yield Value
50 gram	3,25 gram	6,50%

Fractionation is a process of separating compounds based on their polarity. Polar compounds will dissolve in polar solvents and nonpolar compounds will dissolve in nonpolar solvents (Yuliani, Sambara, & Mau , 2016). N-hexane is a nonpolar solvent that will be able to attract nonpolar secondary metabolites. The yield of the n-hexane fraction of avocado leaves obtained was 6.50% and this result was higher when compared to the fraction results carried out which was 4.7% and Jerz et al (Ramos-Jerz, Villanueva, Jerz,, Winterhalter, & Deters, 2013) which was 2.8%. The large number of yields produced shows the large number of nonpolar compounds which are of interest in the fractionation process.

Evaluation of Avocado Leaf Fransi n-Hexane Gel Preparations
Organoleptic Test

Tabel 3. Organoleptic Test Results of Blank Preparations and Gel Fractions of n-Hexane Avocado Leaves

Formula	Observation result		
	Shape	Color	Smell
Blanko Gel	Semi Solid	Clear	Odorless
F1	Semi Solid	Deep green	Typical
F2	Semi Solid	Deep green	Typical
F3	Semi Solid	Deep green	Typical

Information : F1 = Concentrated n-hexane fraction gel preparation 5%
F2 = Concentrated n-hexane fraction gel preparation 10%
F3 = Concentrated n-hexane fraction gel preparation 15%

Organoleptic testing was carried out visually and directly using the five senses to observe the shape, color, and aroma of the avocado leaf n-hexane fraction gel preparation made. The gel from the n-hexane fraction of avocado leaves showed a semi-solid consistency at each dosage concentration with a characteristic odor of avocado leaves and a dark green color. The color obtained in the gel preparation is due to the dye from the thick n-hexane fraction of avocado leaves mixed with the gel base.

The color intensity of the preparation will increase along with the increase in the concentration of the n-hexane fraction of avocado leaves used. Not only the color, the aroma produced in the gel preparation will become sharper in line with the amount of extract used. The results of organoleptic observations of the gel preparation showed a semisolid consistency because the gel preparation consisted of a suspension made from small inorganic particles or large organic molecules that were penetrated by a liquid (Megawati, Roosevelt, & La Ode, 2019).

Homogeneity Test

Tabel 4. Homogeneity Test Results of Blank Preparations and Gel Fractions of n-Hexane Avocado Leaves

Formula	Observation result
Blanko	Homogen
F1	Homogen
F2	Homogen
F3	Homogen

Homogeneity Test Results for Blank Preparations and n-Hexane Avocado Leaf Gel Fractions. Homogeneity tests carried out on gel preparations showed homogeneous results for both blank preparations and gel preparations with variations in concentration as indicated by the absence of coarse grains in the preparations and good color distribution in the preparations. This test aims to see the homogeneous composition of the resulting gel preparation without visible coarse grains of the preparation and even the color of the preparation.

pH Test

Tabel 5. pH Test Results of Blank Preparations and Gel Fractions of n-Hexane Avocado Leaves

Formula	P1	P2	P3	pH
Blanko	6,5	6,0	5,9	6,13
F1	5,0	5,1	5,3	5,13
F2	5,2	5,3	5,4	5,3
F3	5,2	5,4	5,5	5,36

The pH value of a good gel preparation must be close to the skin's pH value, which is in the range of 4.5-6.5 (Mappa, Edy, & Kojong, 2013). Compliance between the pH value and the skin is very necessary because it will have an impact on the skin using the preparation. It is feared that gel preparations that are too alkaline will cause reactions on the skin such as making the skin drier, while gel preparations that are too acidic are feared to cause irritation to the skin after use (Tranggono & Latifah, 2007). The decrease in the pH value is in line with the increase in the concentration of the fraction used in the gel preparation, indicating that the pH of the preparation is influenced by the fractions in the preparation, that is, the higher the concentration, the lower the pH of the resulting preparation.

Spreadability Test

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Tabel 6. Spreadability Test Results of Blank Preparations and Gel of Avocado Leaf n-Hexane Fraction

Formula	Spread Power (cm)		
	No burden	50 gram	100 gram
Blanko	5	5,4	5,7
F1	4	5	5,3
F2	5	5,5	5,7
F3	6,1	6,6	7

The good spreadability of del preparations according to SNI standards is between 5-7 cm. This test aims to determine the level of distribution of the preparation on the skin which is related to the ability to spread the active substance and the amount of contact between the preparation and the skin. The greater the spreadability will increase the spread of the active substance and expand the contact between the preparation and the skin (Niazi, 2009).

The best spreadability value is obtained in the F3 preparation and the magnitude of the spreadability occurs with increasing concentration of the preparation causing the greater the concentration of the fraction used, the thicker the preparation will be so the greater the spreadability.

Antibacterial Activity Test of Avocado Leaf n-Hexane Fraction Gel Preparation

Tabel 7. Results of Inhibitory Power Test of Avocado Leaf n-Hexane Fraction Gel Preparation Against Staphylococcus Aureus Bacteria

Avocado Leaf Fraction Concentration (*Staphylococcus aureus*)	Repetition			Average	Sig.
	I	II	III		
5%	8,4	9	10,95	9,45 ± 1,33^{ab}	0,000
10%	8,7	9,6	10,6	9,63 ± 0,95^{ac}	
15%	9,4	10,1	11,4	10,3 ± 1,02 ^{ac}	
(+)	8,8	8,1	8,8	8,56 ± 0,40 ^{ac}	
(-)	0,0	0,0	0,0	0,00 ± 0,00 ^{ac}	

The results of testing the inhibitory power of the avocado leaf n-hexane fraction gel preparation on S. aureus bacteria showed an increase in the inhibitory power value of the preparation along with increasing fraction concentration used so that the 15% concentration had the highest inhibitory power value compared to the 5% and 10% concentrations. and higher than positive. Likewise, testing of the inhibitory power of the n-hexane gel fraction of avocado leaves carried out on E.coli bacteria showed that a concentration of 15% also had the highest inhibitory power value compared to concentrations of 5% and 10% and was higher than positive.

The results of the antibacterial test of the gel preparation on E. coli bacteria were observed by looking at the magnitude of the inhibitory power against the bacteria, showing an increase in the inhibitory power value along with increasing fraction concentration. The inhibitory power values analyzed statistically showed that there was a significant difference between gel preparations with concentrations of 5% and 10% with negative ($p<0.05$) but there was no difference with positive ($p>0.05$) and gel preparations with The largest concentration, namely 15%, shows a significant difference between positive and negative.

The ability of the avocado leaf n-hexane fraction gel preparation as an antibacterial is shown by the inhibitory power value being higher than positive and this ability is directly proportional to the concentration of the fraction used in the gel preparation. In testing the antibacterial properties of gel preparations using the diffusion method with the principle of diffusing the antibacterial

compound into a solid medium containing test microbes that have been inoculated by observing whether or not a clear area forms around the paper disc which displays an inhibitory zone for bacterial growth (Nurhayati, Yahdiyani, & Hidayatulloh, 2020).

The use of discs in testing antibacterial gel preparations is carried out by saturating the disc paper which acts as a medium for absorbing antimicrobial materials with the n-hexane fraction gel preparation of avocado leaves, then placing it on the surface of agar media which has been inoculated with the test microbes and incubating. The antibacterial activity of the gel preparation was seen by the formation of a clear zone around the paper disc which indicated the absence of growth of S. aureus and E. coli bacteria. A concentration of 15% shows an inhibition zone for S. aureus bacteria of 10.97 cm and an inhibition zone for E. coli bacteria of 10.30 cm. The greater inhibition zone for S. aureus bacteria as gram-positive bacteria compared to the inhibition zone for E.coli bacteria, namely gram-negative bacteria, is because gram-negative bacteria generally have better resistance to antibacterial compounds because they have a complex cell wall structure (Nurhayati, Yahdiyani, & Hidayatulloh, 2020)

The size of the inhibition zone of the n-hexane fraction preparation is in line with the research results of Sari, et al (10) which showed that the inhibition zone of the n-hexane fraction of avocado leaves on S. aureus bacteria and E.coli bacteria at a concentration of 10% was 9.47 cm and 10 .09 cm and this zone is larger when compared with the zone obtained from the ethyl acetate and n-butanol fractions with the same concentration. The formation of an inhibitory zone from the gel preparation shows the bacterial inhibitory ability of the preparation on gram-positive and negative bacteria.

4. Conclusion

The n-hexane fraction of avocado leaves can be formulated in the form of a hand sanitizer in the form of a gel, showing a homogeneous semisolid preparation, a pH that corresponds to the pH of the skin and a spreadability that meets the requirements for the spreadability of a gel preparation ranging from 5-7; The n-hexane fraction gel preparation of avocado leaves which had the highest antibacterial activity was obtained at a concentration of 15%.

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