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Antimicrobial and antioxidant test of several mistletoe extracts (*Scurrula ferruginea* (Roxb. Ex.Jack) Danser) from avocado plants

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Abstract

Scurrula ferruginea (Roxb. Ex. Jack) Danser is a mistletoe plant which is used by the community as a medicine for lowering blood pressure, cough medicine, diabetes, diarrhea, wounds, smallpox, skin infections, ulcers, diuretics and hypertension. This study aims to determine the antimicrobial potential, determine the Minimum Inhibitory Concentration (MIC) and Minimum Lethal Concentration (MLC) as well as determine the antioxidant activity and total polyphenols from fresh, boiled and steeped extracts of mistletoe (*S. ferruginea*) from avocado plants. The microbial tests used in this study were *S. aureus, E. coli*, and *C. albicans.* This study carried out in experimented methods and designed in nested pattern. The results showed that the inhibition zone of the avocado parasite extract had a significantly different effect on *S. aureus* and *E. coli,* but did not have a significantly different effect on the *C. albicans* test microbe. The MIC of fresh extract is true against *S. aureus* and *E.coli* which is 6.125% with 50% MLC. The optimal antioxidant value was obtained from fresh mistletoe extract with an IC50 value of 117.8 µg/ml in the medium activity category and the highest total polyphenols obtained from fresh extract was 67.80 mg. GAE/ml.

Keywords: Antimicrobial; Antioxidant; MIC; MLC; *Scurrula ferruginea*

1. Introduction

Indonesia has high biodiversity that can be used as traditional medicines. Indonesian people generally believe that traditional plants can help cure various diseases [1].

One type of plant used as medicine is the mistletoe from the avocado plant (*Scurrula ferruginea* Roxb. Ex. Jack, Danser) which belongs to the Loranthaceae family. Traditionally, mistletoe is used as blood pressure lowering drugs, cough medicines, diabetes, diarrhea, wounds, smallpox, skin infections, ulcers, diuretics and hypertension [3,4]

Infectious disease is a disease that is still a major health problem in both developing and developed countries [6]. Antibiotic drugs and the like have reduced the symptoms caused by infectious diseases. Public use of antimicrobials that are widely used, obtained without a health prescription, inappropriate use, and lack of knowledge has resulted in the emergence of antimicrobial resistance [29].

S. ferruginea has secondary metabolites that can act as antimicrobials. The secondary metabolites present in *S. ferruginea* are phenolic compounds, flavonoids, tannins, alkaloids and terpenoids [17]. The content of chemical compounds in the mistletoe is influenced by the type of host plant. mistletoe of the same species will contain different chemical compounds if the host plants they host are different [22].

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In addition, the body also needs antioxidant substances that can neutralize free radicals [5]. Free radicals are produced by normal metabolic processes, which are considered to be the cause of damage to the function of body cells, thus triggering the onset of degenerative diseases [15]. The potential of antioxidant compounds contained in plants can be seen from the size of the IC50 value using the DPPH free radical antidote method [30]

This study aims to determine the antimicrobial activity of fresh extract, decoction and steeping of *S. ferruginea* leaves of the avocado plant against the tested microbes, to determine the best extraction for the antimicrobial test and the antioxidant content of the mistletoe (*S. ferruginea*) from the avocado plant, and to determine the Minimum Inhibitory Concentration (MIC) and Minimum Lethal Concentration (MLC) of avocado mistletoe.

2. Material and methods

2.1. Research methods

This research was conducted using a nested pattern design with 2 factors and 3 repetitions. Factor A: Microbial Test (A1: *S. aureus* ATCC 25923, A2: *E. coli* ATCC 25922, A3: *C. albicans*) and Factor B: Treatment of mistletoe extract (B1: fresh extract of mistletoe leaf, B2: boiled extract of dried mistletoe leaf, B3: brewed extract of dried mistletoe leaf.

2.2. Material

The materials used were fresh samples and dried samples of mistletoe leave obtained from Lambuang Bukik, Pauh District, Padang City, pure cultures of *S. aureus* ATCC 25923, *E. coli* ATCC 25922, and *C. albicans*, medium Nutrient Agar (NA), Potato Dextrose Agar (PDA), Mueller Hinton Agar (MHA), Sabouraud Dextrose Agar (SDA), aquadest, alcohol, spirit, Folin-Ciocalteu, Sodium Carbonate, DPPH solution, and methanol.

2.3. Work procedures

2.3.1. Fresh Mistletoe Leaf Extract

The part of the avocado mistletoe taken is the fresh leaves as much as 5 grams. Then the mistletoe is cleaned and washed with sterile distillate water Furthermore, the avocado mistletoe is crushed using a mortar that has been cleaned with alcohol, filtered using filter paper and put into a measuring cup [14]. The filter results were put into Eppendorf and centrifuged for 5 minutes at 10,000 rpm.

2.3.2. Dried Mistletoe Leaf Boiled Extract

The cleaned mistletoe leaves were chopped into small pieces and air dried, then weighed as much as 2 grams (equivalent to 5.7 grams fresh). Then the sample was put into a tea bag and boiled in Erlenmeyer with a volume of 100 ml of water on a hot plate. After that, close the container tightly and leave it to cool.

2.3.3. Dried Mistletoe Leaf Brewed Extract

The cleaned mistletoe leaves were chopped into small pieces and air dried, then weighed as much as 2 grams (equivalent to 5.7 grams fresh). Then heat 100 ml of water on a hot plate until it boils. Samples that have been put into tea bags are brewed with hot water in a sterile Erlenmeyer. After that, close tightly and leave it to cool.

2.4. Preparation of Test Microbial Suspension

Total of 2 oses of rejuvenation test bacteria were suspended in 2 mL of physiological NaCl in a sterile test tube and homogenized with a vortex for 15 seconds, then the turbidity was seen by comparing the standard turbidity of 0.5 Mc. Farland (equivalent to $1.5x10^8$ CFU mL^{-1})

2.5. Determination of Microbial Free Areas Using the Disc Method (Diffusion)

The MHA/SDA medium was poured aseptically into a petri dish and allowed to stand until it solidified. Then 1 ml of bacterial suspension was taken and inoculated on the surface of the medium evenly using a sterile cotton swab, then left for a while at room temperature. After that, dip the 6 mm paper disc aseptically into the sample and place the paper disc on the surface of the medium with sterile tweezers. Incubate for 24 hours and measure the diameter of the clear zone formed (Madigan *et al.,* 2012). The positive control used was chloramphenicol (1 mg/mL) for antibacterial, fluconazole (1 mg/mL) for antifungal and the negative control was the solvent used in the extraction, namely aquadest.

2.6. Testing of Samples on Test Microbes with the Dilution Method

Provide 12 tubes, then tubes 1-10 are inserted with 2 ml of SDB/MHB medium aseptically. Added 2 ml of avocado mistletoe extract (*S. ferruginea*) in tube one, diluted to tube 10 and 1 ml of test microbe into each tube. All tubes were incubated at 37ºC for 1 x24 hours, the diameter of the clear zone formed around the disc paper is measured

2.7. Determination of Antioxidant Activity by DPPH Method

The antioxidant activity test was carried out using the free radical scavenging effect of DPPH (1,1-Diphenyl-2- Picryl-Hydrazine). The DPPH method refers to Molyneux [21]. Dissolved 1.9 mg of DPPH with 100 ml of methanol to obtain a DPPH solution with a concentration of 0.05 m. M. This solution is known as the DPPH solution. Next, 4 ml of 0.05 mM DPPH solution was dissolved with 1 ml of the test solution. Antioxidant activity was analyzed using a spectrophotometer with a wavelength of 517 nm. In the antioxidant activity test, Vit C/ascorbic acid was used as a comparison.

2.8. Gallic Acid Standard Curve

Gallic acid powder was measured at 0.025 g and put into a 100 ml glass beaker and filled up to 100 ml with aquadest, then homogenized. Standard solutions of gallic acid were prepared at various concentrations of 0, 50, 100, 150 and 200 ppm. Pipette 1 ml of standard gallic acid solution and put into a test tube then add 1 ml of Folin-Ciocalteu reagent and homogenize. After 5 minutes, 1 ml of sodium carbonate solution (Na2CO3) was added, then distilled water was added until the volume reached 10 ml, then homogenized and incubated for 90 minutes, and the absorbance value was measured.

2.9. Calculation of Total Polyphenol Content

S. ferruginea extract was carried out using the Folin-Ciocalteu Assay method with several modifications based on the procedure described by Satiova [2]. Dilute 1g of the extract with 4 ml of distilled water. Take 1 ml of sample *S. ferruginea*, then mixed with 1 ml of Folin-Ciocalteu reagent (a phenol reagent was made in the ratio (0.25 ml) Folin- Ciocalteu reagent: (2.25 ml) sterile distilled water = 1: 9). % was added to the mixture and made with distilled water until the volume reached 10 ml. Each tube of the solution was filled with 10 ml of distilled water. The tube was kept in a dark place for 90 minutes and the absorbance value was measured using a spectrophotometer at a wave of 765 nm. In the total activity, test polyphenols used gallic acid as a comparison.

3. Results and discussion

3.1. Antimicrobial activity

Based on the antimicrobial test results of fresh, boiled and steeped mistletoe leaf extract using the disc diffusion method, it was found that fresh, boiled and steeped mistletoe leaf extracts could inhibit the growth of *S. aureus* and *E. coli* but could not inhibit the growth of *C. albicans*. This can be seen from the formation of an inhibition zone due to the antimicrobial activity produced from avocado mistletoe leaf extract. Fresh mistletoe extracts produced the largest inhibition zones for the tested microbes *S. aureus* and *E. coli,* while the brewed mistletoe extract produced the lowest inhibition zones (Table 1) and (Figures 1,2,3).

Table 1 The average diameter of the inhibition zone of avocado mistletoe leaf extract against the tested microbes (*S. aureus, E. coli,* and *C. albicans*)

No	Extract	The average diameter of the inhibition zone (mm)					
		S. aureus		*E. coli*		*C. albicans*	
1	Fresh mistletoe	14.68	**a**	13.61	**a**	6.00	**a**
2	Boiled	9.60	**b**	8.23	**b**	6.00	**a**
3	Brewed	8.61	**c**	6.62	**c**	6.00	**a**

Note: The numbers followed by lowercase letters that are not the same in the same column are significantly different in DMRT 5%

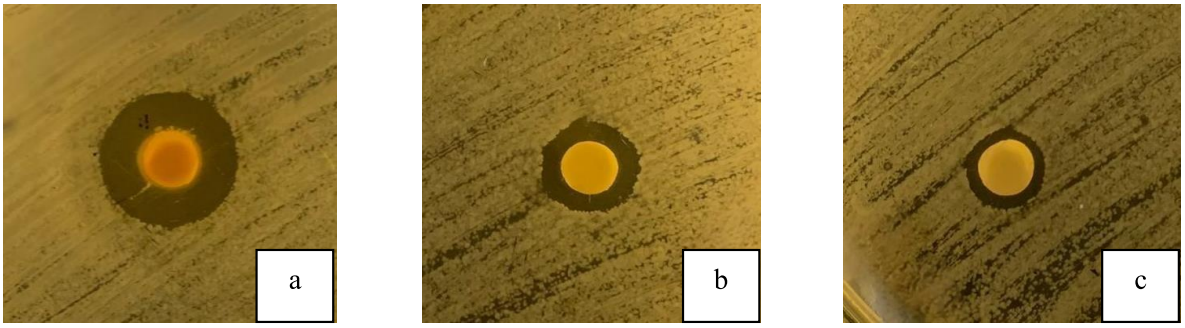

Figure 1 Diameter of the inhibition zone produced by avocado mistletoe leaf extract on the growth of *S. aureus.*

Description: (a) Fresh mistletoe extract, (b) Boiled, (c) Brewed

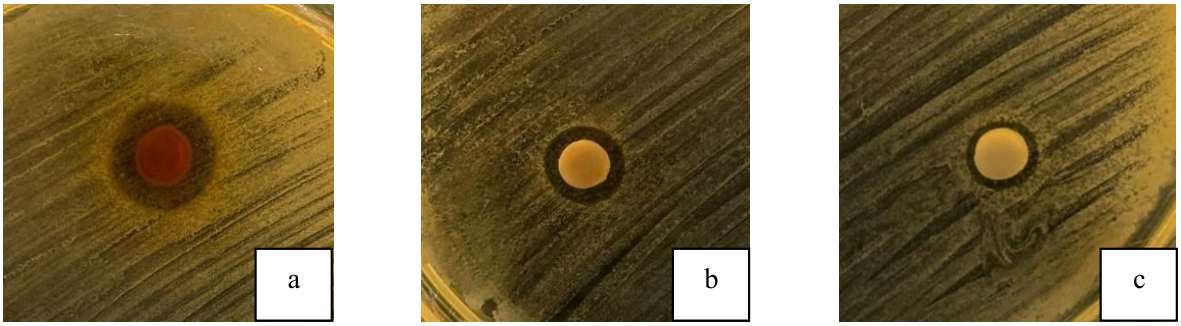

Figure 2 Diameter of the inhibition zone produced by avocado leaf extract on the growth of *E. coli*

Description: (a) Fresh mistletoe extract, (b) Boiled, (c) Brewed

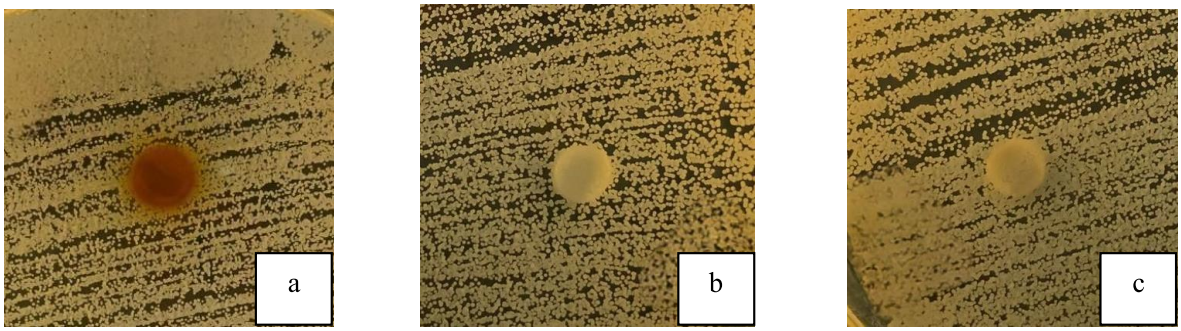

Figure 3 Diameter of the inhibition zone produced by avocado mistletoe leaf extract on the growth of *C. albicans.*

Description: (a) Fresh mistletoe extract, (b) Boiled, (c) Brewed

The formation of the diameter of the inhibition zone is due to the presence of active compounds in avocado mistletoe leaf extract which act as antimicrobials [17]. According to Dzotam *et al.* [11] stated that *S. ferruginea* contains secondary metabolites of polyphenols, flavonoids, tannins, saponins, alkaloids, and sterols which are active against pathogenic microorganisms. The mechanism of action of flavonoids as antimicrobials is to form complex compounds with extracellular proteins, inhibit nucleic acid synthesis and energy metabolism which will cause cell wall damage [12]. Saponins work by lowering surface tension, causing leakage of cell contents such as nucleic acids and proteins [10]. The mechanism of action of tannins is to bind bacterial proteins with hydrogen so that bacterial proteins are unable to attach to cells and metabolism will be disrupted [9,16].

In addition to secondary metabolites, differences in inhibition zones are also strongly influenced by the extraction method from the avocado mistletoe. Based on the results of the tests that have been carried out, it can be seen that the fresh extract produces a larger inhibition zone. This is because the fresh extract does not use solvents so that the resulting extract is more concentrated.

The next biggest inhibitory zone producer is true decoction extract. Heating during the extraction process is very influential in attracting plant secondary metabolites. The decoction extract produces a larger inhibition zone than

the steeping extract because the steeping extract does not go through a heating process. Where the heating process can increase the solubility of compounds in avocado mistletoe leaves. Fatimah [13], stated that the higher the heating temperature causes the vacuoles to open making it easier for the active compounds to come out of the cells, especially polyphenols.

From the results of this research, the allergic mistletoe gave a significantly different effect on the tested microbes of *S. aureus* and *E. coli.* The fresh extract produced the largest inhibition zones on *S. aureus* (14.68 mm) and *E. coli* (13.61 mm). The inhibition zone on *E. coli* is not as big as the inhibition zone on *S. aureus*. According to Poeloengan [24], this occurs due to differences in the sensitivity of Gram-positive and Gram-negative bacteria to antimicrobial substances.

In the *C. albicans* microbial test, the avocado mistletoe leaf extract was not able to inhibit the growth of the fungus so that an inhibition zone was not formed (Figure 4). This is because the structure of the cell wall in *C. albicans* is more complex, making it difficult for foreign compounds to penetrate. Rijayanti [28] stated that the structure of the *C. albicans* cell wall is glucan, chitin, monoprotein fat and organic salts. In accordance with the opinion of Resignol *et al.* [30]; Ramage et al. [27], which stated that *C. albicans* has high resistance to antimicrobials.

3.2. Value of Minimum Inhibitory Concentration (MIC) and Minimum Lethal Concentration (MLC)

Table 2 MIC and MLC Values of Avocado mistletoe Fresh Extract Against Test Microbes

No		Microbes Test	MIC (%)	MLC (%)
1	*S. aureus*		6.125%	50%
2	*E. coli*		6.125%	50%

Based on Table 2, the results showed that fresh parasite extract was able to inhibit the growth of *S. aureus* and *E. coli* at a MIC value of 6.125%, capable of killing *S. aureus* and *E. coli* bacteria at a MIC value of 50%. The MIC value can be seen from the lowest concentration which shows the solution remains clear after 24 hours of incubation at 37°C. Whereas KBM was seen from the lowest concentration seen from the results of the culture which remained clear after being cultured in a petri dish and there was no microbial growth.

In the diffusion method, the avocado mistletoe leaf extract did not produce an inhibition zone on *C. albicans,* so a dilution test was not carried out. Furthermore, the active compounds produced by fresh mistletoe extract at a concentration of 6.125% can already inhibit the growth of *S. aureus* and *E. coli* and at a concentration of 50% can kill the growth of *S. aureus* and *E. coli.* This shows that at a concentration of 6.125% fresh parasite extract against *S. aureus* and *E.ecoli* is bacteriostatic. According to Volk and Wheeler [36], plant extracts that produce low concentrations are bacteriostatic and at high concentrations are bactericidal. Purwanto (2016), states that the higher the concentration of antimicrobial substances, the higher the content of the active compounds so that the killing power of microbes will also be higher.

3.3. Antioxidant Activity and Total Polyphenols

Table 3 Antioxidant Activity (IC50 Value) and Total Polyphenols of Avocado Mistletoe Leaf Extract.

No	Extract	Polyphenols	Antioxidant
1.	Fresh mistletoe	67.80 mgGAE/ml	117.8 µg/ml
2.	Boiled	57.28 mgGAE/ml	124.3 µg/ml
3.	Brewed	53.02 mgGAE/ml	124.4 µg/ml

Based on Table 3, it was found that the highest levels of polyphenols were obtained in fresh misteltoe extract with a value of 67.80 mg GAE/ml, boiled extract with a value of 57.28 mg GAE/ml, and brewed with a value of 53.02 mg GAE/ml. Phenol compounds are the main class of antioxidants that are most widely distributed in plants [20]. Flavonoid compounds are included in the group of complex polyphenols. From the phytochemical tests conducted by Devehat *et al*. [7], stated that the components of the flavonoid compounds contained in *S. ferruginea* include; quercetin, quercithrin and 4-O-acetylquercithrin, and showed that the quercetin contained in *S. ferruginea* is an active antioxidant.
The antioxidant activity of phenolic compounds is formed due to the ability of phenolic compounds to form phenoxide ions which can give an electron to free radicals so that they can react again and form non-radical compounds [8,35].

The reduction in the concentration of DPPH free radicals occurs because it is reduced which is marked by a reduction in the intensity of the purple color which can be measured with a spectrophotometer. From the measurement results of the DPPH method, fresh extract of avocado mistletoe has an IC50 value of 117.8 µg/ml, boiled extract with IC50 = 124.3 µg/ml, and brewed with IC50 = 124.4 µg/ml. Fresh extracts, decoctions and infusions fall into the moderate activity category [21]. IC50 value affects free radical scavenging activity, the smaller the value, the stronger the antioxidant activity.

The lowest IC50 value was obtained from the fresh extract with a value of 117.8 µg/g, this indicated that the fresh extract produced the highest antioxidant activity. This is supported by Rohman *et al.* [33] and Perwiratami and Suzery [23],, which stated that the strength of antioxidant activity was affected by the total phenolic and flavonoid content so that the total flavonoids were directly proportional to the antioxidant activity.

4. Conclusion

From the research that has been done, it can be concluded that fresh mistletoe extract has the best antimicrobial activity against *S. aureus* and *E. coli* test microbes. In addition, the optimal antioxidant value is also found in fresh mistletoe extracts with moderate activity category. From this study it is suggested that for infectious diseases caused by the test *microbes S. aureus* and *E. coli*, alternative external treatment can use fresh mistletoe extracts while for internal treatment use boiled extracts.

Compliance with ethical standard

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Disclosure of conflict of interest

There is no conflict of interest between the authors of this research work. The authors agreed and assigned in hand to all matters arising to this piece of research work.

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