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A LITERATURE REVIEW: THE POTENTIAL OF KARAMUNTING PLANT (Rhodomyrtus tomentosa) AS ANTIBACTERIAL AGENT

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ABSTRACT

Infectious disease is a major health problem with a relatively high mortality rate. Indonesia is rich in natural ingredients that have potential as antibacterials, one of which is the Karamunting plant (Rhodomyrtus tomentosa). Several studies on this plant have been conducted to observe its activity as an antibacterial. This study aims to determine the antibacterial activity of Karamunting plants using the literature review method. The literature search method uses journals from the Google Scholar, Pub Med and Elsevier databases. Each journal is determined based on inclusion and exclusion criteria. Journals that meet the inclusion criteria are descriptive and explained in detail. From the journals obtained, there were 11 journals that met the criteria. Karamunting plants (Rhodomyrtus tomentosa) contain secondary metabolites namely flavonoids, glycosides, saponins, tannins, triterpenoids, steroids, acylphloroglucinol (rhodomyrtone, tomentosone, rhodomyrtosone) and meroterpenoids (rhotomentodiones). Antibacterial activity test using the diffusion method showed an optimum inhibition zone diameter of 21.5 mm against Staphylococcus aureus bacteria in the ethyl acetate fraction of Karamunting leaves with a concentration of 600 mg/ml, while using the microdilution method of ethanol extract of Karamunting leaves the minimum inhibition level was 0.5 µg/ml on Staphylococcus aureus bacteria. The leaves' part presents the best antibacterial activity.

Keywords: Karamunting; Rhodomyrtus tomentosa; Antibacterial; Literature review

1. INTRODUCTION

Infectious disease still as a matter of serious concern of health problems in the world. Most of the infectious diseases that occur in humans are caused by bacterial infections. One of the most common bacteria found in cases of infection is Staphylococcus genus of bacteria. Staphylococcus bacteria are also one of the most resistant bacteria to antibiotics. Antibiotic resistance can cause serious problems because it can complicate the healing process for diseases caused by bacterial infections (Joegijiantoro, 2019).

Based on data from the 2018 Global Burden of Diseases, infectious diseases are one of the biggest causes of death in the world (Institute for Health Metrics and Evaluation (IHME), 2018). In 2019, around 2.6 million people died from lower respiratory tract infections, with around 7000 deaths every day. From these data, infectious diseases are included in the top 4 diseases that cause the most deaths (World Health Organization, 2019).

Indonesia is a country with thousands of plant species. Among the various types of plants in Indonesia, there are many plants that can be used as natural medicines. Of the 40,000 types of medicinal plants known to the world, around 30,000 of them are found in Indonesia. Of that amount, 25 percent or about 7,500 plant species have potential medicinal properties. However, only about 1,200 species of plants have been used as raw materials for natural or herbal medicines. Thus, the discovery of new potential natural sources is fundamental (Salim & Munadi, 2017).

Karamunting plant (*Rhodomyrtus tomentosa*) is a plant that grows a lot and thrives in Indonesia. Based on research by (Shou et al., 2014), plants from the same genus, *Rhodomyrtus psidioides*, showed potential antibacterial activity from compounds isolated from the leaves of the *Rhodomyrtus psidioides* plant. Karamunting plants are widely used as antibacterial, anti-inflammatory, anticancer and rich in antioxidants (Salampe et al., 2020; Yuliana et al., 2021). Flavonoid and anthocyanin compounds are phenolic compounds found in these plants. In addition, Karamunting has high nutritional value, namely high in fiber, vitamins and minerals, low in fat and low in sugar (Sinaga et al., 2019). Literature study on the activity of this plant as an antibacterial potential is urgently needed to provide a scientific basis and a summary of the data which is expected to provide additional alternative tests for allowing antibacterial alternatives from natural sources in the future.

2. METHODS

This research is a qualitative research with a non-experimental design that is descriptive in nature to determine the potency of the Karamunting plant (*Rhodomyrtus tomentosa*) as an antibacterial. The information collected in this study comes from the results of research conducted by previous researchers related to this research. Secondary data sources in this study were primary or original scientific reports contained in journals or articles indexed by Google Scholar, Pubmed, Scopus and Elsevier regarding the potency of Karamunting (*Rhodomyrtus tomentosa*) as an antibacterial. The journals reviewed are adjusted to the following inclusion criteria: a. Inclusion criteria:

- Type of journal: Scientific articles or original research article that have a publication range of the last 10 years (2011-2021)
- Source: Pub Med, Google Scholar, Elsevier
- Keywords: Karamunting, Rhodomyrtus tomentosa, Antibakteri (Indonesian), Antibacterial
- Journal in Indonesian or English
- Fully accessible journal
- b. Exclusion criteria: review journal

3. RESULTS AND DISCUSSION

The search results for research journals on the potential of the Karamunting plant (*Rhodomyrtus tomentosa*) from the Google Scholar database yielded 58 articles, of which 33 articles were from Google Scholar, 18 were from Pub Med and 7 were from Elsevier. Examined as many as 58 sheets and obtained 25 duplicate sheets then eliminated. After screening, 33 journals were checked for eligibility based on inclusion and exclusion criteria, 22 journals were excluded. A total of 11 journals that were examined from the results obtained, the leaves and branches of the Karamunting plant contained several compounds listed in **Table 1. Table 2** shows the results of testing the antibacterial activity of extracts of various parts of the Karamunting plant against various bacteria. Several tests were carried out on ethanol extract (EE), methanol extract (EM), ethyl acetate fraction (FEA), n-hexane fraction (FH), methanol fraction (FM) at various concentrations.

No	Part	Compound class	Compound	Reference	
1	Leaves	Flavonoid, glikosida, saponin,	-	(Sinulingga et al.,	
		tannin, triterpenoid, dan steroid		2018)	
2	Leaves	Acylphloroglucinol	Rhodomyrtone	(Lan et al., 2021)	
3	Leaves	Acylphloroglucinol	Tomentosone C	(HX. Liu et al., 2016)	
4	Leaves	Acylphloroglucinol	Rhodomyrtosone B	(Zhao et al., 2019)	
5	Leaves	Meroterpenoids	Rhotomentodiones C,	(H. Liu et al., 2020)	
	and		Rhotomentodiones D,		
	Branch		Rhotomentodiones E		

Table 1. Compound Identification	n Results in Karamunting P	Plants (Rhodomyrtus tomentosa)
Table 1. Compound Identification	i itesuits in itaramaning i	iants (ianouomynus tomentosu)

Table 2. Results of Antibacterial Activity Test of Karamunting Plants (Rhodomyrtus tomentosa)

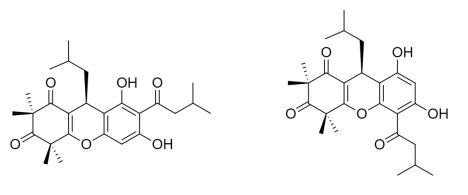
No	Part	Method	Bacteria	Concentration	Minimum inhibitory concentration (µg/mL)	Diameter Zone of Inhibition (mm)	Author
1	Leaves	Agar diffusion method	Staphylococcus aureus	EE: 200 mg/ml 400 mg/ml 600 mg/ml FH: 200 mg/ml 400 mg/ml 600 mg/ml FEA: 200 mg/ml 400 mg/ml 600 mg/ml Kalmicetine (chloramphenicol)	-	12.56±0.75 13.46±0.18 14.5±0.14 17.8±0.14 19.23±0.27 20.13±0.25 17.75±0.27 20.76±0.75 21.5±0.75 32.96±0.27	(Sinulingga et al., 2018)
2	Leaves	Micro dilution and Agar diffusion method	Staphylococcus aureus	EE: 20 μl	0.5	13.1±0.8	(Lan et al., 2021)
3	Leaves	Micro dilution	Staphylococcus aureus	-	3.66	-	(HX. Liu et al., 2016)
4	Leaves	Agar diffusion method	Staphylococcus aureus	-	-	EM: 11 FH: 6 FEA: 7 FM: 10 EM:9 FH: 13 FEA: 10 FM: 16	(Rosli et al., 2017)
	Stem					EM: 11 FH: 7 FEA: 6 FM: 10	
5	Leaves	Micro dilution	Staphylococcus aureus	-	FH: 2.5 Rhodomyrtosone B: 0.62	-	(Zhao et al., 2019)
6	Leaves	Agar diffusion method	Staphylococcus aureus	-	-	5.5	(Zulita et al., 2018)
7	Leaves and Branch	Micro dilution	Staphylococcus epidermidis	-	Rhotomentodione C: >100 Rhotomentodione D: >100 Rhotomentodione E: >100 -	-	(H. Liu et al., 2020)

No	Part	Method	Bacteria	Concentration	Minimum inhibitory concentration (µg/mL)	Diameter Zone of Inhibition (mm)	Author
8	Leaves	Micro	Streptococcus	-	EE: 62.5-31.2	-	(Na-
0	Leaves	dilution	agalactiae		Oksitetrasiklin: 1		Phatthalung et al., 2017)
9	Leaves	Micro dilution	Streptococcus iniae	-	EE: 7.8 Oksitetrasiklin:	-	(Na- Phatthalung
10	Leaves	Micro dilution	Escherichia coli	-	>32 500	-	et al., 2017) (Shankar et al., 2017)
11	Leaves	Agar diffusion method	Escherichia coli	-	-	EM: 10 FH: 8 FEA: 8 FM: 10	(Rosli et al., 2017) (2017)
	Fruits					EM: 9 FH: 11 FEA: 9 FM:12	
10	Stem					EM: 12 FH: 9 FEA: 7 FM: 13	
12	Leaves	Agar diffusion method	Pseudomonas aeruginosa	EE: 200 mg/ml 400 mg/ml 600 mg/ml		14.56±0.14 15.4±0.3 16.13±0.48	(Sinulingga et al., 2018)
				FH: 200 mg/ml 400 mg/ml 600 mg/ml FEA:		18.3±0.25 15.8±0.38 14.8±0.07	
				200 mg/ml 400 mg/ml 600 mg/ml Kalmicetine (chloramphenicol)		15.73±0.25 19.23±0.25 21.43±0.24 32.8±0.67	
13	Branch	Micro dilution	Propionibacterium Acnes	-	25.0 12.5 50.0	-	(H. Liu et al., 2020)
	Leaves				50.0 25.0 100.0		
14	Leaves	Micro dilution	Methicillin- resistant Staphylococcus aureus	-	Rhodomyrtosone B: 1.25	-	(Zhao et al., 2019)
15	Leaves	Micro dilution	Vancomycin- resistant Enterococcus faecium	-	Rhodomyrtosone B: 2.5		(Zhao et al., 2019)
16	Leaves	Agar diffusion method	Shigella Sp	-	-	12.5	(Zulita et al., 2018)
17	Leaves	Agar diffusion method	Vibrio cholerae	EE: 6.25% 12.5% 25% 50% 100% Ciprofloxacin:	-	6.97 7.57 8.98 11.07 13.61	(Dwicahmi, 2015)
				5 µg/disc		24.77	

No	Part	Method	Bacteria	Concentration	Minimum inhibitory concentration (µg/mL)	Diameter Zone of Inhibition (mm)	Author
18	Leaves	Agar	Salmonella	EE:	-		(Saputra et
		diffusion	Typhimurium	0.3%		7.42	al., 2016)
		method		0.4%		8.99	
				0.5%		12.25	
				0.6%		14.39	
				0.7%		16.36	
				0.8%		18.87	

Based on the results of a literature search on the compounds found in the Karamunting plant (*Rhodomyrtus tomentosa*) shown in Table 1, the part of the Karamunting leaf that has been studied the most contains the bioactive compounds. Karamunting leaves contain compounds belonging to the class of flavonoids, glycosides, saponins, tannins, triterpenoids and steroids based on the results of a 2018 phytochemical screening (Sinulingga et al., 2018). The compound was obtained through the extraction and fractionation process of Karamunting leaves with ethanol, n-hexane, and ethyl acetate as solvents. Identification of these compounds was carried out using the phytochemical screening method.

Karamunting leaves contain various compounds of the acylphloroglucinol group, namely tomentosone, rhodomyrtone, and rhodomyrtosone B. (Lan et al., 2021; H.-X. Liu et al., 2016; Zhao et al., 2019). Compounds of the acylphloroglucinol class have been identified using Nuclear Magnetic Resonance (NMR) equipment. NMR instruments are analytical tools capable of identifying chemical compounds, as well as structures of chemical compounds from natural materials that have not been identified, the conformations of peptide hormones and dynamic polymers.



RhodomyrtoneRhodomyrtosone BFigure 1. Chemical Structure of Compound Rhodomyrtone and Rhodomyrtosone B (Zhao et al., 2019)

Karamunting leaves containing a Rhodomyrtone compound that obtained from the extraction process with ethanol solvent. Rhodomyrtone was identified using thin layer chromatography (TLC) (Lan et al., 2021). Based on the antibacterial activity test of *Staphylococcus aureus* and *Salmonella typhimurium* using the microdilution method, it was found that the ethanol extract of Karamunting leaves had antibacterial activity with a MIC value of 0.5 μ g/ml indicating the presence of antibacterial activity from the ethanol. Karamunting extract leaves behind *Staphylococcus aureus* bacteria. Meanwhile, *Salmonella typhimurium* bacteria did not show antibacterial activity. Apart from Rhodomyrtone and Tomentosone, Rhodomyrtosone B also has an antibacterial effect and belongs to the acylphloroglucinol compound class. The **Figure 2** showed the chemical structure of the compounds. Tests were also carried out to see antibacterial activity on methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant

Enterococcus faecium (VRE) (Zhao et al., 2019). The results of the MIC values were 0.62-1.25 μ g/ml and 2.5 μ g/ml respectively.

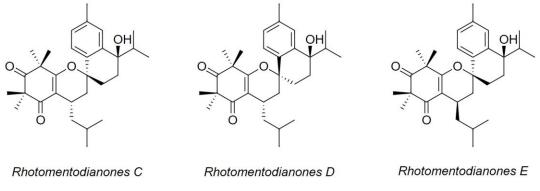


Figure 3. The Chemical Structure of Rhotomentodianones C-E (H. Liu et al., 2020)

In 2020, Liu et al. identified a new subcompound of rhotomentodianone obtained by fractionating the leaves and branches of Karamunting with chloroform and named the compound rhotomentodianone C-E as described in **Figure 4**. Antibacterial activity tests were carried out on the three compounds using the *Propionibacterium acnes* microdilution method. The results of the antibacterial test of this compound were compared with the tetracycline drug. Rhotomentodianone C-E showed a MIC of 25.0; 12.5; 50.0 μ g/ml; and 25 μ g/ml tetracycline. The results of rhotomentodianone C and D showed better antibacterial activity than rhotomentodianone E.

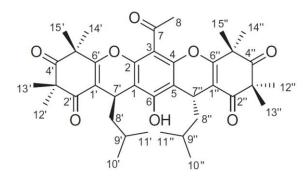


Figure 5. The Chemical Structure of Tomentosone C (H.-X. Liu et al., 2016)

Liu et al (2016) in the antibacterial activity test on Karamunting leaves found the tomentosone C compound which could significantly inhibit *Staphylococcus aureus* bacteria with an MIC value of $3.66 \,\mu$ g/ml. The tomentosone C compound was obtained by extracting 20 kg of Karamunting leaf powder with 95% ethanol, then a separation process was carried out by gradual fractionation using n-hexane, ethyl acetate and distilled water to obtain tomentosone C. The structure of the compound is shown in **Figure 6**.

Based on the results of the descriptions of several scientific journals on the compounds contained in *Rhodomyrtus tomentosa*, it was concluded that the Karamunting plant contains secondary metabolites with antibacterial activity, such as flavonoids, glycosides, saponins, tannins, triterpenoids, and steroids (Sinulingga et al., 2018). In the research that has been done, Karamunting leaves contain compounds belonging to the acylphloroglucinol group, namely rhodomyrtone, tomentosone, rhodomyrtosone and compounds belonging to the meroterpenoids group, namely rhotomentodiones (Lan et al., 2021; H. Liu et al., 2020; H.-X. Liu et al., 2016; Zhao et al., 2019). Rhodomyrtosone B and rhodomyrtone compounds have good antibacterial activity with minimum inhibition values of 0.62 μ g/mL and 0.5 μ g/mL. Rhodomyrtosone B and rhodomyrtone compounds have good antibacterial activity with minimum inhibition values of the acylphloroglucinol group which are derivatives of phenolic compounds where these compounds can damage bacterial membranes and inhibit the

formation of biofilms in bacteria. The mechanism of rhodomyrtone compounds causes cell enlargement in bacteria, abnormalities occur in the bacterial cell wall and membrane, and binds competitively with proteins that play a role in cell division so that bacterial cell division can be inhibited (Zhao et al., 2019). In addition, rhodomyrtone exerts an effect on pneumococcal carbohydrate metabolism leading to reduced biosynthesis and capsule formation. The effect of rhodomyrtone on MRSA causes aberrations in cell morphology based on visualization with an electron microscope. In addition, rhodomyrtone can increase MRSA membrane permeabilization, cell wall changes, and cell membrane integrity. This causes disruption of the cytoplasmic components and damages the bacterial cell. Rhodomyrtone also causes the release of ATP and cytoplasmic proteins which can interfere with the metabolic processes of bacterial cells. However, it is not known for sure how the direct effect of rhodomyrtone in the process of structural and physical cell changes that occur in bacteria (Traithan et al., 2020).

The results of a study in the scientific journal of the Karamunting plant (*Rhodomyrtus tomentosa*), found that the leaves, stems, twigs and fruits of Karamunting have antibacterial activity. The best test results with the agar diffusion method obtained the diameter of the bacterial inhibition zone of 21.5 mm against *Staphylococcus aureus* in the ethyl acetate fraction of Karamunting leaves at a concentration of 600 mg/ml. Whereas the microdilution method obtained the best minimum inhibitory content from the ethanol extract of Karamunting leaves at a level of 0.5 μ g/mL against *Staphylococcus aureus* bacteria. Karamunting plant has good potential to be developed as an antibacterial agent. This study was limited to antibacterial activity, so further studies are needed for various potential other bioactivities from each part of the Karamunting plant so that it can become a scientific basis for the development of herbal medicines from plants in Indonesia.

4. CONCLUSION

Based on a literature review of the results of testing antibacterial activity using the agar diffusion and microdilution methods against several bacteria, the Karamunting plant (*Rhodomyrtus tomentosa*) has been scientifically proven to inhibit bacterial growth. Glycosides, saponins, tannins, and flavonoids and the active compounds acylphloroglucinol (rhodomyrtone, tomentosone, rhodomyrtosone), and meroterpenoids (rhotomentodiones) are thought to contribute to bioactivity as antibacterials. The leaf part of the plant is the part that has the most potential to provide antibacterial activity.

5. ACKNOWLEDGEMENTS

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6. CONFLICT OF INTEREST

The author states that there is no conflict of interest in conducting this research.

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