Chempublish Journal
Journal Homepage: online-journal.unja.ac.id/chp
Department of Chemistry
Faculty of Science and Technology
Universitas Jambi
ISSN (Online): ISSN 2503-4588
No. 23/E/KPT/2019

Review

Melastoma malabathricum Natural Compounds as Inhibitors of Resistant Bacterial Development

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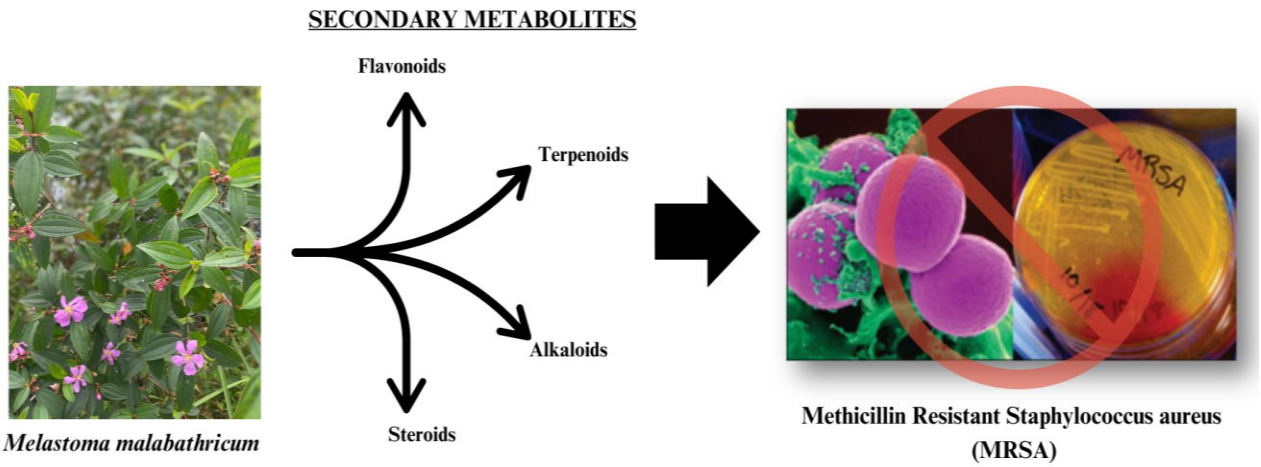
Abstract

Melastoma malabathricum, also known as senduduk, is a plant of the Melastomataceae family widely found in tropical Asia. It has a long history of use as an herbal remedy in traditional Chinese medicine. Modern research has identified various pharmacological properties of *M. malabathricum*, including significant antibacterial activity, even against antibiotic-resistant bacteria. Studies have shown that extracts from *M. malabathricum* contain bioactive compounds such as flavonoids, terpenoids, alkaloids, and steroids. These studies have demonstrated that these compounds inhibit the growth of various bacteria, including resistant strains. This antibacterial potential makes *M. malabathricum* very promising for further development and application in the treatment of infections caused by resistant bacteria.

Keywords: *Antibacterial activity; Melastoma malabathricum; natural compounds; pharmacology; traditional medicine*

Graphical Abstract



Introduction

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DOI: https://doi.org/10.22437/chp.v9i1.41114
Received January 16th 2025; **Accepted** April 20th 2025; **Available online** June 01st 2025

Microorganisms, including bacteria, fungi, algae, and protists, thrive in diverse environments, forming complex communities [1]. Bacteria are one of the microorganisms that can become pathogenic if abnormal growth occurs and can cause infection in the target host [2]. The ongoing challenge of bacterial infections has spurred the continuous search for new treatments, particularly from natural sources. Herbal plants exhibit strong potential as alternative antibacterial agents [3]. Over 70,000 herbal plant species contain bioactive compounds that can be utilized for natural-based medicine. This approach offers the promise of effective treatment with potentially fewer side effects compared to some pharmaceutical products [4]. The use of plants as natural therapeutic agents has demonstrated a broad pharmacological spectrum, encompassing the prevention and treatment of various human diseases, including cancer, respiratory disorders, diabetes, and cardiovascular diseases [5]. The diverse mechanisms of action of active plant compounds explain the continued growth and reliance on traditional medicine by a significant portion of the global population [6]. In fact, traditional medicine, with its wide-ranging pharmacological effects—such as anti-inflammatory, hemostatic, anticoagulant, antioxidant, and hepatoprotective properties—is relied upon by over 80% of the world's population for combating various diseases [7].

Antibacterial resistance is a serious global health problem. Methicillin-resistant *Staphylococcus aureus* (MRSA) is one example of human pathogenic bacteria that has developed resistance to various types of antibiotics [12]. To determine the effectiveness of an antibacterial in inhibiting bacterial growth, Minimum Inhibitory Concentration (MIC) testing is used [13]. MIC is the lowest concentration of an antibacterial that can inhibit bacterial growth [14]. An antibacterial is considered susceptible to bacteria if it inhibits their growth at MIC concentrations that remain safe for the human body. Conversely, resistant bacteria show high MIC values, indicating the need for higher doses or even treatment failure. An increase in MIC value over time in a bacterial population indicates the development of antibacterial resistance [15]. According to the World Health Organization (WHO), antibacterial resistance has caused approximately 700,000 deaths annually and is expected to continue to increase if there are no effective preventive measures One of the strategies to overcome this problem is to explore the potential of the *Melastoma malabathricum* plant, as seen in Figure 1, as an alternative source of antibacterial compounds.

Figure 1. *Melastoma malabathricum* plant. Stem (a), root (b), flower (c), dan fruit (d). Source: personal documentation

Melastoma malabathricum is a commonly occurring plant species in Southeast Asia. The genus Melastoma, which includes this species, is highly diverse with a total of 22 species, 2 subspecies, and 3 varieties [8]. Various parts of this plant, ranging from leaves and stems to roots, have long been utilized in traditional medicine and continue to be researched for their therapeutic potential, including as antibacterial agents. The content of bioactive compounds in various parts of the plant is responsible for its antibacterial activity [9,10]. This article aims to collect published research on *Melastoma malabathricum* natural compounds as inhibitors of resistant bacteria development.

Methods

This study employs a qualitative descriptie approoach that aims to prove the antibacterial activity and antibacterial resistance of the senduduk plant (*Melastoma malabathricum*). This review compiles references from national and international databases published in the last 10 years (2014-2024) which include secondary metabolite compounds from *Melastoma malabathricum*, using search words such as antibacterial effectiveness test and antibacterial resistance. The journals obtained will be evaluated according to the criteria of antibacterial studies and antibacterial resistance of the senduduk plant (*Melastoma malabathricum*) and will be presented in tabular format as shown in Table 1.

Table 1. Parts of the *M. malabathricum* plant that showed antibacterial activity

Plant Parts	Solvent	Content	Bacteria Type	MIC Category	References
Leaves	Water	-	- *Bacillus subtilis* - *Staphylococcus aureus*	Resistent	[11]
	Ethanol	Flavonoids Tannins Terpenoids	- *Staphylococcus aureus* - *Propionibacterium acnes*	Susceptible	[12]
	Ethanol	Flavonoids Phenols Terpenoids	- *Staphylococcus epidermidis* - *Bacillus subtilis* - *Escherichia coli* - *Bacillus cereus* - *Staphylococcus aureus* - *Proteus mirabilis*	Resistent	[17]
	Ethanol	-	- *Staphylococcus aureus* - *Escherichia coli* - *Bacillus cereus*	Resistent	[18]
	Ethanol	Flavonoids Saponins Tannins Alkaloids	- *Salmonella typhi* - *Escherichia coli* - *Staphylococcus aureus*	Susceptible	[19]
	Methanol	Terpenoids Lipids	- *Bacillus subtilis* - *Escherichia coli* - *Pseudomonas aeruginosa* - *Staphylococcus aureus*	Resistent	[20]
	Ethyl acetate	Triterpenoid Saponins Flavonoids Steroids Tannins	- *Escherichia coli* - *Staphylococcus aureus*	Resistent	[21]
	Ethanol	Flavonoids Phenolics	- *Streptococcus pyogenes* - *Klebsiella pneumoniae*	Susceptible	[22]

Plant Parts	Solvent	Content	Bacteria Type	MIC Category	References
		Tannins Terpenoids			
Stems	Ethanol	Alkaloids Flavonoids Tannins Steroids Triterpenoid Carbohydrate Saponins	- *Propionibacterium acnes*	Resistent	[23]
	Acetone	Triterpenoid Lipids	- *Streptococcus mutans*	Susceptible	[24]
Roots	Ethanol	Saponins Flavonoids Triterpenoid Tannins	- *Escherichia coli*	Resistent	[25]
Flowers	Ethanol	-	- *Shigella dysenteriae*	Susceptible	[26]
	Methanol: water	Flavonoid Steroids Terpenoids Phenolics Lipids	- *Staphylococcus aureus* - *Bacillus cereus*	Resisten	[27]
	Ethanol	Flavonoids	- *Staphylococcus aureus*	Resistent	[28]
	Methanol	Flavonoids	- *Listeria monocytogenes* - *Staphylococcus aureus* - *Escherichia coli* - *Salmonella typhimurium*	Resistent	[29]
	Methanol	Tannins Steroids Phenols Flavonoids	- *Listeria* monocytogenes - *Staphylococcus aureus*	Resistent Intermediate	[30]

Results and Discussion

Senduduk's bioactive compounds and antibacterial potential.

Melastoma malabathricum, well-known as senduduk, is widely distributed in various parts of Southeast Asia. Apart from being an ornamental plant, senduduk also has potential as a source of natural antibacterial compounds due to its bioactive compounds. Various plant parts, including leaves, stems, flowers, and roots, contain bioactive compounds [31]. Phytochemical screening of *Melastoma malabathricum* plants showed that the presence of secondary metabolites such as alkaloids, flavonoids, carbohydrates, saponins, and tannins could show an excellent potential to develop as an alternative treatment agent, including treatment against resistant bacteria [12]. The content of bioactive compounds in senduduk plants, namely saponins, tannins, flavonoids, triterpenoids, and steroids, can potentially control the development and growth of bacteria [31]. Saponins can increase the permeability of bacterial cell membranes and cause the release of intracellular compounds [32]. In addition,

flavonoids in senduduk can form complexes with extracellular proteins, potentially damaging bacterial cell membranes [33].

According to research by Faradiba et al. (2016) [34], senduduk contains flavonoids rich in phenol compounds that can cause protein denaturation, damage cell membranes, and damage protein structures. These flavonoids have the potential to act as antibacterial substances with the mechanism of disrupting bacterial metabolism, damaging cell walls, disrupting protein synthesis, and inhibiting the performance of bacterial enzymes [35]. Therefore, flavonoids contained in senduduk can reduce bacterial proliferation and support the reduction of the number of disease-causing bacteria [36]. Another content contained in this plant is steroids, which are permeable and can interact with phospholipids in bacterial cell membranes. The resulting interaction can cause morphological disturbances in bacterial cells and ultimately can cause damage to the bacterial cell wall gradually [37]. Compounds found in senduduk may show significant potential in treating various diseases, including antitumor, anti-inflammatory, antiviral, and antibacterial. These findings support the use of senduduk in traditional medicine practices [38].

Secondary metabolites are produced through complex biosynthetic pathways, starting from primary metabolites (fundamental organic matter) such as carbohydrates, amino acids, and isoprenoid units. Plants rich in these primary metabolites have the potential to produce a variety of unique secondary metabolites [45].

Table 2. Senduduk compounds that show pharmacological activity

Secondary Metabolites	Activities	References
Alkaloids	Antimicrobial, anti-inflammatory	[39]
Saponin	Anti-carcinogenic, antimicrobial, immunomodulatory properties, anti-inflammatory, influence on blood pressure	[40]
Tanin	Antimicrobial, anti-inflammatory, antioxidant,	[41]
Terpenoids	Anti-carcinogenic, antimicrobial, anti-inflammatory, cholesterol lowering effect	[42]
Steroids	Anticancer, anti-inflammatory, antibacterial, antifungal, antiviral	[43]
Flavonoids	Antioxidant, anti-alzheimer, antimicrobial, anticancer, anti-inflammatory, antidiabetic	[44]

Secondary metabolites have extensive potential in pharmacology. As shown in Table 2, these compounds can function as antioxidants, antimicrobials, anticancers, anticoagulants, and inhibit carcinogenic effects, among others. In addition, secondary metabolites can also utilize as environmentally friendly pest control antiagents [45].

Figure 2 shows the interaction of natural compounds such as flavonoids, terpenoids, alkaloids, and steroids with bacterial cell membranes [46]. These compounds can interact with various membrane components, including proteins, lipids, and peptidoglycans. These interactions can alter membrane permeability, disrupt protein function, or even damage membrane structure. Flavonoids, for example, are known to have antibacterial activity [47]. An in-depth understanding of these interaction mechanisms may pave the way for developing more effective and selective drugs and reduce the problem of antibacterial resistance [48].

How Natural Compounds in Senduduk Can Inhibit the Growth or Kill Bacteria

Bacteria can resist antibacterials through various mechanisms, one of which is by modifying their cellular structure. For example, bacteria can alter their ribosomes through the action of methyltransferase enzymes that are affected by the antibacterial itself [45]. Prolonged antibiotic use contributes to resistance, necessitating the

search for alternative treatments such as natural compound. Natural medicines like those produced by senduduk generally have minimal side effects, more affordable costs, and easier distribution [48].

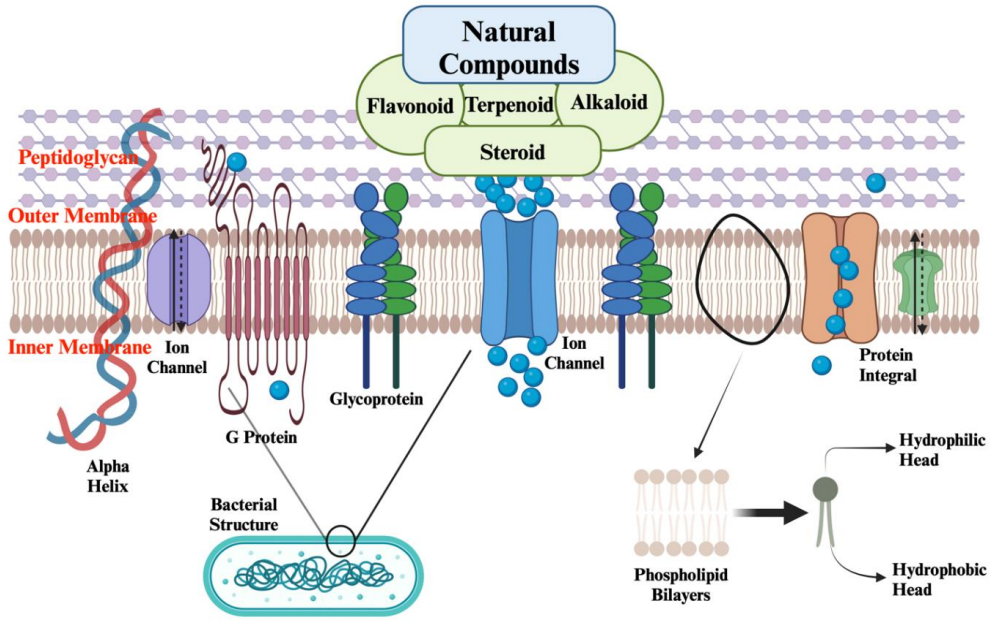

Figure 2. Natural compounds interaction with bacteria cell membrane [46]

Plants produce primary and secondary metabolites for their survival [49]. Secondary metabolites, such as terpenoids, alkaloids, polyketides, and sulfur-containing compounds, have potential as natural antibacterial agents. These compounds can inhibit the growth or kill pathogenic bacteria through various mechanisms, such as inhibiting protein synthesis, damaging cell membranes, or inhibiting essential enzymes for bacteria [49]. The potential of biological compounds with such bioactivity is very promising to be further developed and researched as an alternative treatment against pathogens [50].

Effects of Flavonoids.

Flavonoids are secondary metabolites commonly found in various plants. These compounds not only play a role in providing attractive colors to flowers and fruits to attract insects for pollination [51], but also have important functions as antibacterials. Flavonoids help plants fight pathogen infections by enhancing immunity and through complex biosynthesis processes [52].

Considering the potential of flavonoids in fighting pathogens, various studies have been conducted to test the antibacterial effect in humans. The mechanism of action of flavonoids is different from that of conventional drugs [53]. Several studies have shown that flavonoids can disrupt bacterial cell membrane function, inhibit growth and metabolism, damage cell walls, inhibit protein synthesis, and inactivate enzymes important for bacteria [35,54].

Based on the antibacterial mechanism shown in Figure 3, flavonoids have great potential as new antibacterial agents. These compounds can inhibit bacterial growth by damaging cell membranes, inhibiting nucleic acid synthesis, and disrupting biofilm formation. This potential makes flavonoids a promising candidate. However, further research is needed to address the growing problem of antibacterial resistance to optimize their biological activity and evaluate the safety of their use [55].

Figure 3 shows the various mechanisms by which flavonoid compounds can inhibit bacterial growth. Some of the main mechanisms include disruption of the cell membrane (1), inhibition of nucleic acid synthesis through dihydrofolate reductase, helicase, and gyrase enzymes (2a-c), inhibition of biofilm formation (3&4), disruption

of macromolecular synthesis (6, 7a-b), and inhibition of the electron transport chain through NADH-cytochrome c reductase and ATP synthase complexes [8,9,56].

The structure of flavonoid compounds plays an important role in determining antibacterial activity. Flavonoids generally consist of two benzene rings connected by three carbon atoms (Figure 3). The position and type of functional groups on this basic skeleton significantly affect flavonoids' physicochemical properties and biological activity, including their ability to interact with various biomolecular targets [57].

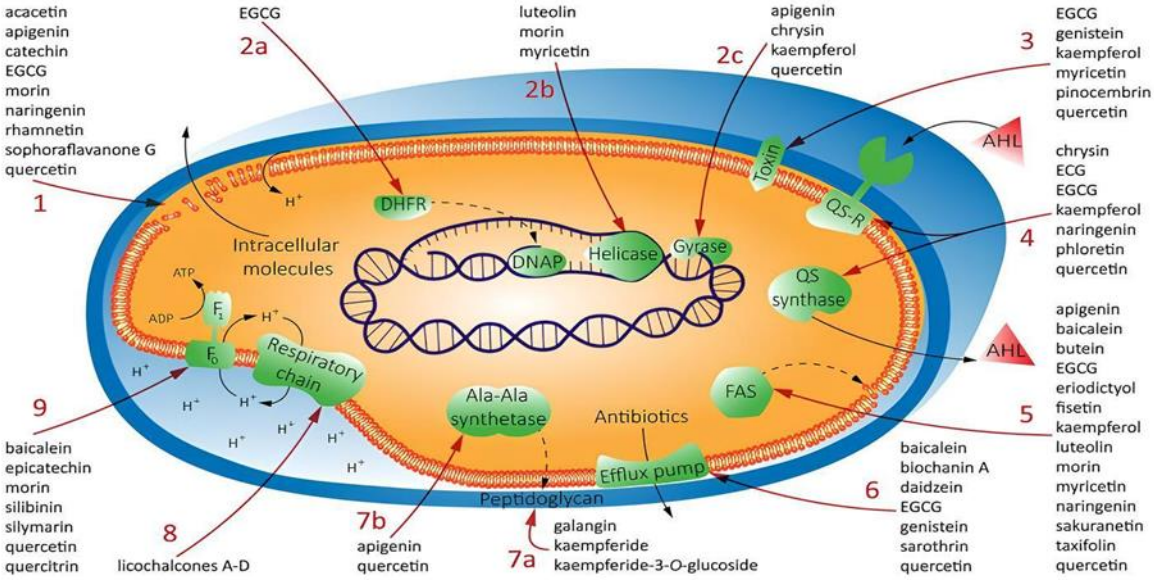

Figure 3. Antibacterial mechanism of flavonoids compounds [56]

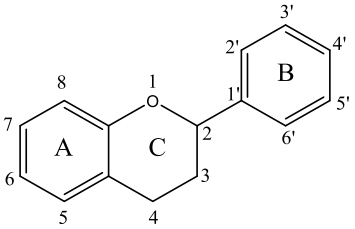

Figure 4. Basic structure of flavonoids compound

Structural modification of flavonoids can affect their antibacterial activity (Figure 4). Adding hydroxyl groups (-OH) at positions C-5, C-7, C-3', and C-4' increases the antibacterial potential. The increase is due to stronger interactions with bacterial proteins and more effective disruption of cell membrane integrity [58]. In contrast, substituting hydroxyl groups with methoxy groups (-OCH_3) at positions C-3' and C-5 decreases antibacterial activity. The decrease suggests that the presence and position of functional groups strongly influence the interaction between flavonoids and bacterial target molecules. The presence of methoxy groups can inhibit the formation of hydrogen bonds, which play an important role in the binding of flavonoids to bacterial targets. This reduction in hydrogen bond potential can decrease binding affinity, resulting in a decrease in antibacterial activity [59,60]. Besides hydroxylation and methoxylation, prenylation is an important structural modification that can enhance the antibacterial activity of flavonoid compounds. The addition of isoprenyl groups to flavonoid structures, especially the C-5, C-7, and C-4' positions, often results in compounds with strong antibacterial activity, including against resistant pathogenic bacteria such as *Staphylococcus aureus* (MRSA). Combining prenylation and hydroxylation at specific positions can produce synergistic effects, increasing the potential of flavonoids as effective antimicrobial agents [61].

Some pure compounds successfully isolated from senduduk plants are kaempferol, quercetin [62], and rutin [63]. Kaempferol, a flavonoid with a distinctive structure characterized by hydroxyl

groups at positions 5, 7, 3, and 4', has shown significant antibacterial activity by inhibiting FabG and enoyl-acyl carrier protein reductase enzymes. This mechanism interferes with the biosynthesis of fatty acids essential for bacterial cell membrane integrity and biofilm formation [64]. In vitro studies reported IC_{50} values of kaempferol against Staphylococcus aureus and Escherichia coli of 3.125 mg/mL and 6.25 mg/mL, respectively, indicating potential as a potent antibacterial agent [65]. The IC_{50} value is the lowest compound concentration required to inhibit 50% bacterial growth [66]. This parameter is crucial in evaluating antibacterial activity for new drug development. The lower the IC_{50} value, the stronger the compound's ability to inhibit bacterial growth, allowing for more optimal dosing and minimizing the risk of side effects [67].

Quercetin, another flavonoid similar in structure to kaempferol, also has broad antibacterial activity. Its main mechanism of action is inhibiting the enzyme D-alanine: D-alanine ligase, which inhibits the synthesis of peptidoglycan, an essential component of bacterial cell walls [68]. In a study by Zhang et al. (2022) [69], quercetin showed potential as a potent inhibitor of the OXA-48 beta-lactamase enzyme with IC_{50} values between 0.042 mg/mL to 0.413 mg/mL. OXA-48 enzyme plays an important role in antibacterial resistance. These results indicate that quercetin can restore the effectiveness of antibacterials such as piperacillin and imipenem against resistant Escherichia coli strains. In addition to its antibacterial effects, quercetin has anti-inflammatory and antioxidant properties that can potentially accelerate the wound healing process [70]. Furthermore, rutin is a flavonol glycoside derived from quercetin with an added sugar group. Rutin has potent antioxidant activity and shows potential as an antibacterial and antibiofilm agent [71]. Its mechanism of action includes inhibition of biofilm formation, which is a collection of bacterial cells encased in an extracellular polymer matrix. Biofilms provide protection for bacteria against antibiotics. By inhibiting biofilm formation, rutin can increase the effectiveness of antibiotics [72]. Rutin showed an IC_{50} of 97.8 µg/mL for inhibiting the Helicobacter pylori urease enzyme. The value increased significantly when rutin was formulated into nanocrystals, reducing the IC_{50} to 6.85 µg/mL. This indicated that the nanoformulation of rutin increased its effectiveness in inhibiting the urease enzyme, which is a key factor in the survival and pathogenicity of *Helicobacter pylori* [73].

Effects of Terpenoids.

Terpenoids are natural compounds that play important roles in various biological processes in plants. The lipophilic nature of terpenoids allows these compounds to penetrate bacterial cell membranes mostly composed of lipids [74]. Besides functioning as photosynthetic pigments and growth hormones, terpenoids are also known as effective antibacterial agents [75]. The lipophilic nature of terpenoids allows these compounds to penetrate bacterial cell membranes mostly composed of lipids [76][77].

After penetrating the membrane, terpenoids can interfere with various bacterial cell functions. One of the main mechanisms is damage to the integrity of the cell membrane. By forming pores in the membrane, terpenoids cause leakage of important ions and molecules and disrupt the concentration gradient necessary for cell survival. In addition, terpenoids can also inhibit the production of ATP, the main energy source of cells, thereby disrupting various cellular metabolic processes [11,78].

One of the significant problems in treating infections is the emergence of resistant bacteria. Resistant bacteria often have defense mechanisms that allow them to evade the effects of antibacterials, such as changes in the structure of the cell membrane or drug-target enzymes. Uniquely, terpenoids can overcome these resistance mechanisms differently [79]. Terpenoids have multiple target molecules inside bacterial cells, making it difficult for bacteria to develop resistance to all targets at once [80-82]. Further antibacterial mechanisms of terpenoid compounds can be seen in Figure 4.

Figure 5 visually presents a comprehensive picture of the diversity of terpenoid molecular targets in bacterial cells. These compounds are shown to be able to intervene in various essential

processes in bacterial cells, thus inhibiting their growth and survival. The main mechanisms depicted include: (1) cell membrane disruption; terpenoids can damage the integrity of bacterial cell membranes, causing leakage of vital cellular components and disruption of cell homeostasis [83]. (2) modulation of efflux pumps; these compounds can inhibit bacterial efflux pumps that play a role in removing antibacterials from the cell, thereby increasing the effectiveness of concomitantly administered antibacterials [84]. (3) inhibition of oxygen uptake; by interfering with the process of cellular respiration, terpenoids limit the production of energy that bacteria need to survive [85]. (4) disruption of oxidative phosphorylation; terpenoids can interfere with the electron transport chain, thereby inhibiting the production of ATP as the cell's primary energy source [86]. (5) inhibition of virulence factors; some terpenoids are able to inhibit the production of bacterial virulence factors, which play an important role in the infection process [87]. (6) reduction of cell adhesion ability; by inhibiting the ability of bacteria to adhere to surfaces, terpenoids can prevent biofilm formation and the spread of infection [88]. Finally, (7) suppression of biofilm formation; terpenoids can inhibit the formation of bacterial biofilms, which are communities of bacterial cells embedded in the extracellular matrix and challenging to eradicate [89].

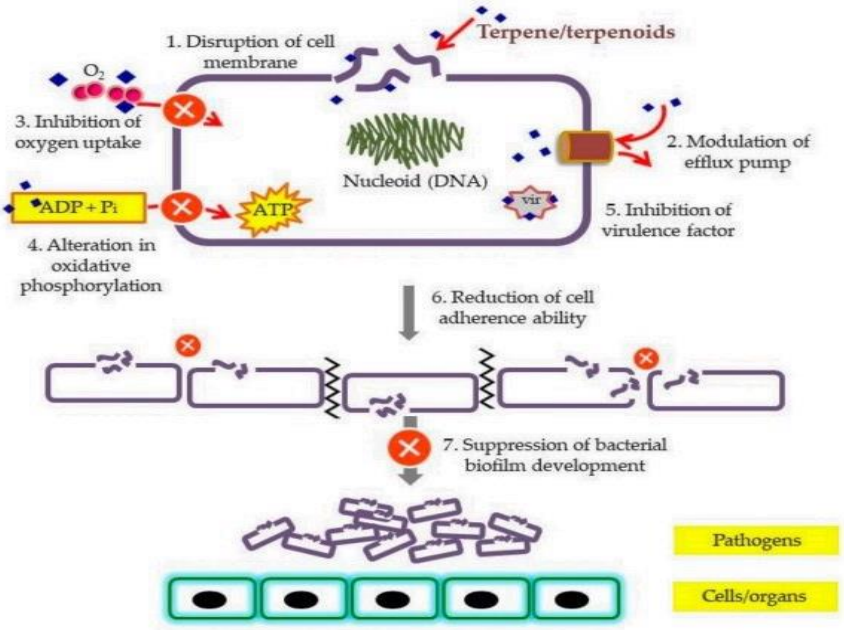

Figure 5. Antibacterial mechanism of terpenoids compound [75]

The structure of terpenoid compounds is very diverse due to the various bonding possibilities (single, double), ring formation (cyclization), and the addition of different functional groups. It is this structural variation that gives terpenoids their unique physical and chemical properties, as well as a wide range of biological activities [90]. The basic building unit of all terpenoids is isoprene, a molecule with five carbon atoms (Figure 6).

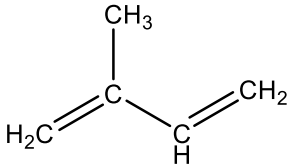

Figure 6. Structure of the isoprene unit

The presence of a hydroxyl group (-OH) on the terpenoid structure often enhances its antibacterial activity compared to hydrocarbon compounds. This can be seen in the example of eugenol and terpineol compounds. These two compounds have the ability to kill bacteria quickly because they can damage the bacterial cell membrane [91].

α-Amyrin, a purified terpenoid successfully isolated from the senduduk plant [92], shows broad pharmacological potential, including anti-inflammatory and antioxidant properties. In the rat ear edema test, α-amyrin was shown to be very effective in inhibiting inflammation with an

IC_{50} value of 0.0469 mg/mL [93]. α-Amyrin is a major precursor in forming ursolic acid, a compound with high commercial value thanks to its various health benefits. The enzyme α-amyrin synthase catalyzes the conversion of (3S)-2,3-oxidosqualene to α-amyrin in its biosynthesis process [94, 95].

***Effects of Alkaloids*.**

Alkaloids, as secondary metabolites rich in nitrogen and alkaline in nature, are commonly extracted from plants but can also be found in animals and microorganisms. The structural diversity of alkaloids confers their broad biological activities, encompassing favorable pharmacological effects such as analgesic, antipyretic, and anticancer, as well as significant potential toxicity [96][97].

Alkaloids have diverse antibacterial activities. These compounds can inhibit bacterial growth and replication by disrupting the synthesis of nucleic acids and proteins that are essential for bacterial cells. Furthermore, alkaloids can also damage the integrity of bacterial cell membranes, causing leakage of vital cellular components and ultimately cell death (Figure 7) [98].

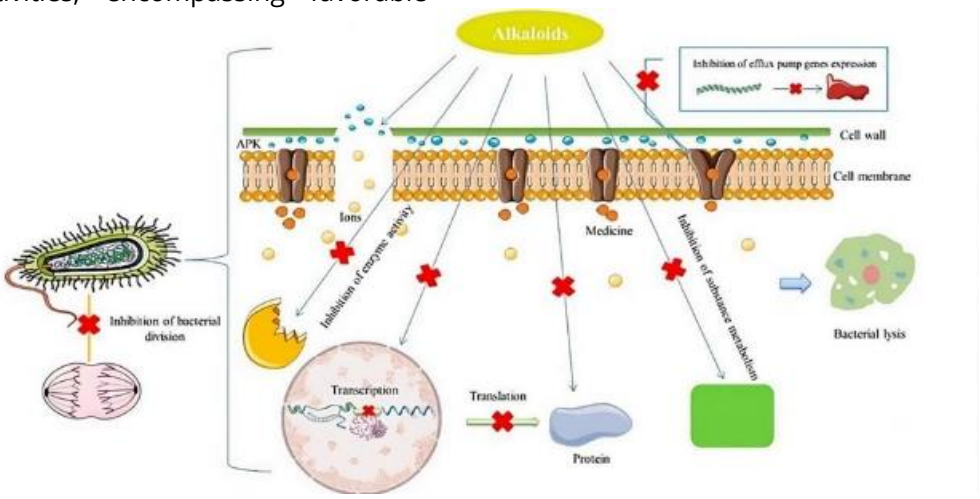

Figure 7. Antibacterial mechanism of alkaloids compound [98]

Figure 6 shows some of the ways alkaloids work to inhibit growth and kill bacteria. Alkaloids can interfere with various important processes in bacterial cells. First, alkaloids can inhibit bacterial cell division so the bacteria cannot multiply [99]. Secondly, alkaloids can also interfere with bacterial protein synthesis by inhibiting the transcription and translation processes [98]. This process is essential for bacteria to produce the proteins needed to survive. Besides, alkaloids can also damage bacterial cell membranes [100]. By damaging the cell membrane, alkaloids cause leakage of cell contents and eventual bacterial cell death. Another possible mechanism is the inhibition of important enzymes in bacteria, such as enzymes involved in energy metabolism [101]. Lastly, alkaloids can also affect efflux pumps in bacteria [102]. Efflux pumps are proteins that pump out foreign substances from inside bacterial cells. By inhibiting efflux pumps, alkaloids allow harmful substances, including themselves, to remain inside the bacterial cell and cause damage [103]. The ability of alkaloids to interfere with various cellular processes in bacteria makes them attractive compounds to be developed as alternative antibacterials.

The mechanism of action of alkaloids is very diverse and is influenced by their complex chemical structure. Differences in functional groups, such as methylenedioxy (-O-CH_2-O-) and methoxyl (-OCH_3), on the benzene ring structure can significantly affect their biological activity. A study in 2009 showed that methylenedioxy groups generally enhanced antibacterial activity more than methoxyl groups [104].

Auranamide and patriscabratine are new alkaloids successfully isolated from senduduk

plants [92]. Both have unique structures that correlate with their antibacterial activity. The amide groups in both compounds are thought to play a role in forming hydrogen bonds with bacterial protein targets, thus inhibiting essential protein functions. The aromatic ring provides structural rigidity and interacts hydrophobically with the cell membrane, disrupting its integrity. The hydroxyl group increases solubility, while the methoxy group on patriscabratine likely affects membrane permeability. Auranamide showed no toxicity to cells up to a concentration of 5.066 mg/mL and dose-dependently inhibited the production of nitric oxide and proinflammatory cytokines in mouse macrophages. In addition, this compound activated the NRF2 pathway, which plays a role in cellular defense mechanisms against oxidative stress [105]. Patriscabratine also exhibits anti-inflammatory activity and activates the NRF2 pathway. The similarity in structure to aurantiamide acetate, a cathepsin L inhibitor, suggests that patriscabratine might also inhibit the enzyme. The IC_{50} value of patriscabratine is thought to be similar to that of aurantiamide acetate, although the exact value is yet to be determined [106].

***Effects of Steroids*.**

Steroids, secondary metabolites of plant and animal origin, have been widely used in medicine. These compounds have broad pharmacological potential and are often used as the basis for developing drugs for various diseases [107]. Recent research has shown that bacteria such as actinobacteria and proteobacteria can degrade steroids [108]. This potential opens up opportunities for developing new steroid compounds that are more effective in fighting infections. Several in vitro studies have also demonstrated the effectiveness of steroid compounds in inhibiting the growth of microorganisms and reducing infections.[109].

The basic structure of steroids consists of a perhydrophenanthrene core (Figure 8). This core can be modified with various functional groups, including nitrogen, to increase its effectiveness against bacteria. Nitrogen-containing steroids, such as azasteroids, often show strong antibacterial activity, especially against gram-positive bacteria [110]. Their mechanism of action may involve interference with bacterial cellular processes, such as pigmentation. Even at low concentrations, these compounds are already quite effective. Moreover, to antibacterial activity, steroids also have important roles in various biological processes, such as hormones that regulate growth, development, and metabolism. Cholesterol, a type of steroid, is an important component of cell membranes. Some other steroids, such as vitamin D, play a role in calcium absorption [111].

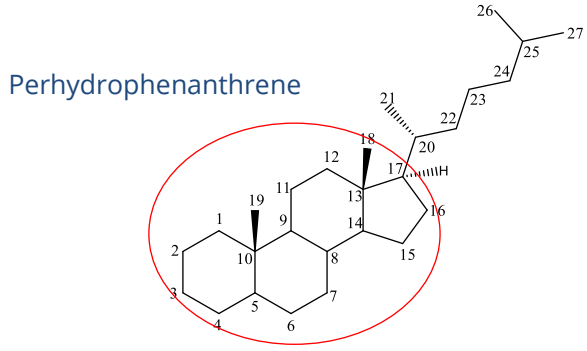

Figure 8. Basic structure of steroid compound

Steroid compounds can fight bacteria in various ways, such as damaging the bacterial cell membrane, disrupting activities within the bacterial cell, and stimulating the immune system [112]. For example, the linoleic acid ester 17α-hydroxyprogesterone damages bacterial membranes [113]. Besides damaging bacterial cell membranes through mechanisms such as membrane destabilization and cell lysis, steroid compounds can also inhibit protein synthesis, damage DNA, or modulate bacterial cellular regulatory systems [112][114][115]. Some steroid compounds can even stimulate the host immune system to fight infection through increased activity of defense enzymes such as superoxide dismutase and catalase and increased synthesis of endogenous antibacterial compounds [116]. Recent studies have shown that specific steroid compounds, such as the linoleic acid ester 17α-hydroxyprogesterone, interact with bacterial membrane components such as phosphatidylethanolamine, leading to membrane destabilization and bacterial cell lysis. In addition, steroid derivatives such as androst-4-ene compounds have been shown to enhance

host defenses by increasing defense enzyme activity and salicylate synthase content [117]. The unique mechanism of action of antibacterial steroids, which often involves disrupting the bacterial cell membrane, provides hope in overcoming the growing problem of antibacterial resistance. However, further research is needed to comprehensively understand these compounds' mechanism of action, safety, and clinical efficacy.

Senduduk plants contain various types of steroids, such as sitosterols, which have strong antibacterial activity. Although the amount is relatively small, these steroids contribute significantly to the antibacterial properties of senduduk plants. Research shows that sterols comprise about 5.77% of the total compounds in its leaf extract [118]. Antibacterial tests showed that specific sterols, especially fucosterol and epicoprostanol, have potent antibacterial activity against gram-negative bacteria with IC_{50} values ranging from 0,2663 to 0,4258 mg/mL [119]. Furthermore, the study showed that sitosterol, isolated from the hydroid *Aglaophenia cupressina* Lamouroux, exhibited significant antibacterial properties, especially against *Staphylococcus aureus* and *Shigella* sp., with the most effective concentration of 30 ppm producing the largest zone of inhibition for both bacteria. This study shows that sitosterol has a bacteriostatic effect, i.e., it inhibits the growth of *Staphylococcus aureus* and *Shigella* sp. without killing the bacteria, indicating its potential use as a natural antibacterial agent in various applications [120].

Conclusion

Melastoma malabathricum, also known as senduduk, is a common herbal plant in Indonesia. Research in the past decade (2014-2024) has consistently demonstrated the strong antibacterial potential of all parts of this plant against both gram-positive and gram-negative bacteria. This antibacterial activity is attributed to its diverse content of bioactive compounds, such as flavonoids, terpenoids, alkaloids, and steroids. These bioactive compounds in senduduk possess complex mechanisms of action, including inhibiting bacterial cell growth, damaging cell walls, and inducing apoptosis. With this promising potential, the senduduk plant is not only valuable in preserving traditional medicine, but also opens up new opportunities in the development of natural pharmaceuticals, particularly in combating drug-resistant bacteria. Further research should focus on isolating and characterizing the specific bioactive compounds responsible for its antibacterial effects, as well as exploring its efficacy in clinical trials. This will help to fully realize the therapeutic potential of M. malabathricum and contribute to the development of novel antibacterial agents.

Acknowledgement

This research supported by the Directorate of Talent Management of the National Research and Innovation Agency (BRIN) for the Degree by Research (DBR) program.

Author Contributions

Conceptualization, Methodology, dan Validation, M.E., F.E.S., S., A.W.S.; Writing – Original Draft Preparation, F.E.S.; Writing – Review & Editing, M.E., F.E.S., S., A.W.S.

Conflict of Interest

The authors declare no conflict of interest

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