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Literature Review: Bioactivity of Alkaloids from Various Plants that Have Potential as Antibacterials

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Abstract
Alkaloid compounds are active secondary metabolite compounds produced by plants. These alkaloid compounds provide extraordinary health benefits for humans because alkaloid compounds are efficacious as antidiarrheal, anti-microbial, anti-diabetic, anti-microbial, and anti-malarial. The purpose of this literature review is to describe plants that produce alkaloid compounds as secondary metabolites and their bioactivity as antimicrobials. This literature-based study was systematically carried out to gather, evaluate, and synthesize research results concerning the antibacterial properties of alkaloids and other natural secondary metabolites from plants. The analysis focused on publications from 2015 to 2025, sourced through a structured search in the Medline database using PubMed and Google Scholar. The results of this literature review explain that there are many plants that produce alkaloid compounds as their secondary metabolites. Alkaloid compounds in each plant have the same bioactivity both as anti-fungal and anti-fungal. Alkaloids in their bioactivity will interfere with and damage cell formation in microbes so that microbial growth will be inhibited.

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INTRODUCTION

Antibiotic resistance has become one of the most urgent global health threats, as pathogenic bacteria increasingly exhibit the ability to survive exposure to previously effective antibiotics (Dadgostar, 2019). This situation not only hinders the success of infection treatment but also contributes to increased morbidity, mortality, and healthcare costs worldwide (Laxminarayan et al., 2020). Recognizing the urgency of this issue, researchers in the fields of organic and natural product chemistry have intensified efforts to explore natural sources for the discovery of novel and effective antibacterial agents (Chassagne et al., 2021). This approach is considered promising because natural compounds-particularly those derived from plants are known to possess a wide range of secondary metabolites with significant biological activities and a relatively lower risk of resistance development compared to synthetic compounds (Pan et al., 2020). Therefore, the search for antibacterial agents based on natural products has become a central focus in the effort to address the antibiotic resistance crisis in a sustainable manner (Hassan et al., 2023).

Plants represent one of nature's most valuable resources and serve as a major source of important bioactive compounds that play a vital role in sustaining life on Earth (Rauf et al., 2017). In addition to fulfilling basic human needs such as food, many plant species have the natural ability to synthesize active compounds known as secondary metabolites. These compounds function not only as a defense mechanism against external threats such as microorganisms, pests, or environmental stress but also offer significant potential for applications in healthcare and industry (Patel et al., 2021). Various plant-derived secondary metabolites have been shown to possess notable biological activities, including antibacterial, anticancer, antidiabetic, antioxidant, and antifungal properties. With their immense biodiversity, plants are regarded as strategic resources for the development of natural bioactive compounds that are both environmentally friendly and sustainable (Chassagne et al., 2021).

Among the secondary metabolites known to inhibit bacterial growth, alkaloids stand out as one of the most prominent groups. Alkaloids are active secondary metabolites widely found in various plant species and are well known for their medicinal properties (Singh et al., 2020). These compounds offer remarkable health benefits, as they have been shown to be effective as antidiarrheal, antimicrobial, antidiabetic, antibacterial, and antimalarial agents. The antimicrobial mechanisms of alkaloids include the destruction of bacteria, viruses, RNA, and DNA, as well as active involvement in DNA intercalation (Umar et al., 2022). In fungi, alkaloids bind strongly to ergosterol, an essential component of the fungal cell membrane, leading to membrane disruption and cell death. Plants that predominantly produce alkaloids as secondary metabolites are angiosperms, with more than 20% of them reported to contain alkaloid compounds (Ningrum et al., 2016). Alkaloids can be found in various plant parts such as flowers, leaves, seeds, twigs, bark, and roots. However, isolating alkaloids from plant tissue often involves complex separation processes due to their typically low concentrations.

In addition to alkaloids, other classes of secondary metabolites also serve as potent antibacterial agents, such as flavonoids, terpenoids, and tannins. Flavonoids exhibit strong antibacterial activity by inhibiting key bacterial enzymes and disrupting cell membrane function (Al-Zain et al., 2021). Terpenoids act by compromising bacterial membrane integrity, interfering with ion transport pathways, and inducing the leakage of essential intracellular contents. Tannins, on the other hand, exert antimicrobial effects by precipitating bacterial proteins and inhibiting crucial bacterial enzymes. The structural diversity and varied mechanisms of these secondary metabolites underscore the vast potential of plants as a source of natural bioactive agents for the development of safer and more sustainable antibacterial therapies (Chassagne et al., 2021). Nonetheless, some of these compounds may also pose toxicity risks, necessitating further studies to assess their efficacy, safety, and long-term effects, particularly in the context of natural product-based drug development.

Based on this background, the present review aims to examine various plant species that have the potential to overcome antibiotic resistance and suppress bacterial growth. This review article seeks to address the issue by summarizing research from 2015 to 2025 related to the discovery of antibacterial compounds derived from medicinal plants that exhibit inhibitory activity against pathogenic bacteria.

METHOD

This study is a literature review conducted systematically to collect, examine, and analyze research findings related to the antibacterial activity of alkaloids and other natural secondary metabolites derived from plants. The review covers literature published between 2015 and 2025. Articles were retrieved through a systematic search of the Medline database using the PubMed and Google Scholar search engines. The keywords used during the search process included "*alkaloid antibacterial activity*," "*plant secondary metabolites*," "n*atural antibacterial agents*," "*phytochemicals and antimicrobial resistance*," and "*medicinal plants antibacterial compounds.*"

Inclusion criteria comprised articles published within the 2015–2025 timeframe, available in full-text format in English or Indonesian, and classified as original research or review articles published in indexed journals. Selected articles were required to discuss the antibacterial activity of natural secondary metabolites specifically derived from plants and to provide data on plant species, active compounds, and antibacterial assay results against pathogenic bacteria. Exclusion criteria included articles focusing solely on synthetic compounds, lacking empirical data, not relevant to the review's scope, or unavailable in full-text format.

The initial search yielded 101 articles from 10 countries, from which 95 articles met the inclusion criteria and were analyzed in this review. These articles identified 22 plant species producing a total of 26 active phytochemical compounds, either in pure form or as components of plant extracts. Data analysis was conducted using a qualitative-descriptive approach, emphasizing the identification of active compounds, antibacterial mechanisms of action contributing to biological activity, and the synergistic potential of phytochemicals when combined with conventional β-lactam antibiotics.

RESULTS AND DISCUSSION

Alkaloids are active compounds that are toxic to humans, but have the potential as drugs so that they are widely used in the medical world. In addition, alkaloids are also used as plant growth regulators, as well as insect attractants or repellents. These compounds are widely distributed in various types of plants and are usually found in the form of organic salts. The process of obtaining alkaloids is carried out through the extraction of plant material using acidified water, where the alkaloids will dissolve in the form of salt. Alternatively, plant material can be given sodium carbonate or ammonia to form a free base, which is then extracted using organic solvents such as chloroform, ether, and the like (Astutiningsih et al., 2012).

Alkaloids generally have characteristics in the form of solid crystals, although some are liquid at room temperature, such as nicotine. This compound is able to rotate the plane of polarization of light, has a bitter taste, is soluble in water in the form of salt, and can be dissolved in organic solvents in free or basic form. Alkaloids are active compounds in plants that are toxic to humans, but can be used as medicine, so their use is quite extensive in the medical world. In plants, alkaloids are generally found in the form of organic salts, and to obtain them, an extraction process is carried out using acidified water so that the alkaloids dissolve as salts (Maisarah et al., 2023).

Traditional medicinal plants have long been the center of attention in the search for new sources of medicine. The use of plants as traditional medicine has developed widely as part of improving public health. One of the important benefits of medicinal plants for humans is as a source of antibiotic compounds. Antibiotics are substances that can kill or inhibit the growth of microorganisms such as bacteria, fungi, and parasites. Antibiotics used to treat infections caused by pathogenic bacteria are known as antibacterials, while compounds used to treat pathogenic fungal infections are called antifungals (Munte et al., 2016).

Indonesia is a country that has various kinds of medicinal plants that can be used as antibiotics and antimicrobials which can protect against various diseases from bacterial attacks. In several articles that have been reviewed, there are several plants that contain alkaloid compounds and act as antimicrobials. Several related studies show that many plants produce secondary metabolites, such as alkaloids, which have an important role in plant self-defense and the potential as a source of natural medicines that are beneficial to human health.

Waterlily (*Nymphaea lotus L.*)

Various species of the genus *Nymphaea* (family *Nymphaeaceae*), such as *N. mexicana* Zucc., *N. pubescens* Willd., *N. lotus* L., and *N. nouchali*, have been studied due to their rich content of secondary metabolites and potential as natural antibacterial agents. These plants contain numerous bioactive compounds, including flavonoids (e.g., naringenin), polyphenols, saponins, alkaloids, tannins, and terpenoids, which have been reported to exhibit antioxidant, cytotoxic, anti-inflammatory, and antimicrobial properties (Din et al., 2022; Rueangsri et al., 2025; Saddiq et al., 2025; Dulal et al., 2022). For instance, *N. mexicana* produces naringenin, a flavonoid that demonstrated antibacterial activity against *Streptococcus aureus* a Gram-positive bacterium responsible for skin infections, pneumonia, and endocarditis with inhibition zones up to 25.6 µg/mL (Din et al., 2022). Meanwhile, extracts of *N. pubescens* showed efficacy against *S. aureus* (MIC: 62.5 mg GAE/mL) and *Escherichia coli* (MIC: 1000 mg GAE/mL), both of which are important human pathogens associated with respiratory and gastrointestinal infections, respectively, with a minimum bactericidal concentration (MBC) of 2000 mg GAE/mL (Rueangsri et al., 2025).

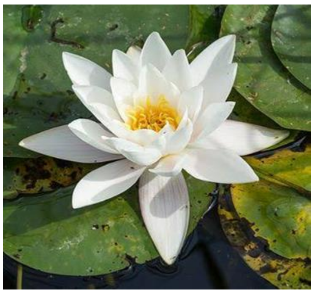

Figure 1. *Nymphaea lotus L.*

In addition, *N. nouchali* has been proven effective in suppressing the growth of *Pseudomonas aeruginosa* (an opportunistic pathogen causing wound and urinary tract infections) and *Enterococcus faecalis* (linked to urinary tract and endodontic infections), with the ethanolic extract exhibiting the highest antimicrobial activity (Dulal et al., 2022). This species has also been used as a natural preservative to maintain the quality of Nile tilapia (*Oreochromis niloticus*) fillets during cold storage by reducing pH, total volatile nitrogen, and spoilage bacteria. Moreover, the leaf fractions of *N. lotus* extracted with ethyl acetate and n-hexane showed antibacterial activity against *S. epidermidis* (known for wound infections and biofilm formation on medical devices), *E. coli*, *Vibrio cholerae* (the causative agent of cholera), and *S. aureus* (Saddiq et al., 2025). The antimicrobial actions of these plants are primarily attributed to the mechanism of secondary metabolites such as flavonoids, which disrupt bacterial cell membranes, inhibit key enzymes, and interfere with protein synthesis. Therefore, the phytochemical exploration of *Nymphaea* species holds great promise in the development of plant-based antibacterial agents as alternatives to conventional antibiotics, particularly in the face of rising antimicrobial resistance.

Chocolate Grape (*Akebia trifoliata*)

Figure 2. *Akebia trifoliata*

Akebia trifoliata (Thunb.) Koidz. is a climbing plant belonging to the family Lardizabalaceae, commonly known as the three-leaf chocolate vine or three-leaf akebia. Morphologically, it is characterized by compound leaves with three ovate, slightly notched leaflets and clusters of purplish-brown flowers. Beyond its use as a food source and ornamental plant, *A. trifoliata* has long been utilized in traditional medicine, particularly in China, Japan, and Korea, where the fruit pericarp has been employed as a diuretic, anti-inflammatory, and antimicrobial agent. Recent phytochemical and pharmacological investigations have confirmed its bioactivity, particularly its significant antibacterial properties. The ethanol extract of the pericarp of *A. trifoliata* (EEPA) has demonstrated inhibitory effects against various Gram-positive bacteria (*Staphylococcus aureus*, *Bacillus subtilis*) and Gram-negative strains (*Escherichia coli, Pseudomonas aeruginosa*) (Chen et al., 2022).

The antibacterial activity of *A. trifoliata* is primarily attributed to its rich content of secondary metabolites, especially triterpenoids. Phytochemical studies by Wang et al. (2015) identified several 30-noroleanane-type triterpenoids from the pericarp, including 3β-akebonoic acid, 2α,3β-dihydroxy-30-noroleana-12,20(29)-dien-28-oic acid, 3α-akebonoic acid, and quinatic acid. These compounds exhibited potent antibacterial activity, particularly against Gram-positive bacteria such as *S. aureus*, methicillin-resistant *S. aureus* (MRSA), *B. cereus*, and *B. subtilis*, with minimum inhibitory concentrations (MICs) ranging from 12.5 to 25 µg/mL. Notably, 3β-akebonoic acid showed stronger antibacterial efficacy against MRSA than kanamycin. In addition, Wang et al. (2015b) reported the presence of oleanane-type triterpenoids, such as oleanolic acid, arjunolic acid, and maslinic acid, which exhibited a broader antibacterial spectrum-including activity against *E. coli*—with MIC values ranging from 0.9 to 15.6 µg/mL. The pharmacological effects of these triterpenoids are closely related to their lipophilic structures, which allow for interactions with bacterial membranes and disruption of membrane integrity, leading to ion leakage and cell death.

Mechanistically, these triterpenoids exert their antibacterial effects through multiple pathways. First, they compromise the bacterial cell membrane via lipophilic interactions, resulting in altered permeability and leakage of intracellular contents. Second, some triterpenoids inhibit key enzymes involved in peptidoglycan biosynthesis, particularly affecting Gram-positive bacteria. Third, they may induce oxidative stress through reactive oxygen species (ROS) generation, damaging membrane lipids, structural proteins, and nucleic acids. The combined action of these mechanisms contributes to the strong bactericidal effects observed, especially against Gram-positive species. Besides the pericarp, the flowers of *A. trifoliata* also display pharmacological potential. A study by Li et al. (2022) revealed that flower extracts obtained via radio frequency-assisted enzymatic extraction (RF-E) are rich in non-anthocyanin polyphenols and flavonoids, including quercetin, kaempferol, and various phenolic acids. These extracts showed moderate antibacterial activity, with inhibition zones of up to 12 mm for *S. aureus* and 6–8 mm for *E. coli*. Phenolic compounds are known to interfere with bacterial protein function and membrane transport, while flavonoids can chelate essential metal ions, interact with bacterial nucleic acids, and inhibit protein synthesis.

In summary, *Akebia trifoliata* represents a promising source of natural secondary metabolites with potent antibacterial activity. Its efficacy is particularly notable against Gram-positive bacteria such as *S. aureus*, MRSA, *B. subtilis*, and *B. cereus*. Although its activity against Gram-negative bacteria like *E. coli* and *P. aeruginosa* is relatively lower, this can potentially be enhanced through synergistic formulations or advanced delivery systems. These findings support the potential of *A. trifoliata* as a candidate for the development of novel antibacterial agents derived from natural products, offering a sustainable and biocompatible alternative for addressing microbial resistance (Wang et al., 2015a; Wang et al., 2015b; Chen et al., 2022; Li et al., 2022; Huang et al., 2022).

Butterfly Pea Flower (*Clitoria ternatea L.*)

Butterfly pea flowers (*Clitoria ternatea* L.) contain various secondary metabolites, including alkaloids, flavonoids, and saponins, which have been identified in kombucha fermentation solutions using Wagner and Dragendorff reagents producing brown and red precipitates as a positive indication of alkaloid presence. These secondary metabolites are known to contribute significantly to the plant's antimicrobial activity. Among them, alkaloids, such as *indole alkaloids* and *quinolizidine derivatives*, exhibit antibacterial effects by interfering with nucleic acid synthesis and disrupting protein formation within bacterial cells. These compounds can intercalate DNA or inhibit key enzymes involved in bacterial replication and transcription processes, leading to cell death.

Figure 3. *Clitoria ternatea*

Additionally, flavonoids, such as *kaempferol* and *quercetin glycosides* found in *Clitoria ternatea*, exert antibacterial action by disrupting the integrity of bacterial cell membranes, chelating metal ions needed for microbial metabolism, and inhibiting efflux pumps that allow bacteria to resist antimicrobial agents. Saponins, another class of bioactive compounds present in the plant, contribute through their surfactant-like properties, which increase membrane permeability and cause leakage of intracellular contents in bacteria.

The combined activity of these secondary metabolites shows a more dominant inhibitory effect against gram-positive bacteria such as *Staphylococcus aureus* and *Bacillus subtilis*. This is primarily due to the relatively simple structure of gram-positive bacterial cell walls, which consist mostly of peptidoglycan and lack the outer membrane found in gram-negative bacteria. The absence of this outer lipid membrane allows easier penetration and interaction of bioactive compounds with intracellular targets. While gram-negative bacteria such as *Escherichia coli* and *Salmonella typhi* are also affected, their outer membrane rich in lipopolysaccharides often provides a stronger barrier against many plant-derived antimicrobials. Nevertheless, some flavonoid and saponin compounds from *Clitoria ternatea* have shown moderate efficacy against these gram-negative strains, particularly when used in fermented forms such as kombucha, which may enhance bioavailability and potency of the active constituents (Abdilah et al., 2022).

Angel's Trumpet (*Datura metel Linn leaves*)

Datura metel Linn., commonly known as Angel's Trumpet, is a medicinal plant from the Solanaceae family that thrives in tropical regions such as Indonesia. This plant is known to contain various secondary metabolites, particularly tropane alkaloids (such as scopolamine, atropine, and hyoscyamine), as well as flavonoids, tannins, and saponins (Sari et al., 2020). These compounds have been demonstrated to exhibit significant antibacterial potential through multiple biological mechanisms against both Gram-positive and Gram-negative bacteria. The antibacterial activity of *Datura metel* leaf extract has been evaluated using disc diffusion assays and measurements of inhibition zones, followed by Minimum Inhibitory Concentration (MIC) tests. A study by Lestari and Nugroho (2018) reported that ethanol extracts of *Datura metel* leaves at a 40% concentration produced an inhibition zone of 13.7 mm against *Staphylococcus aureus* (Gram-positive) and 11.5 mm against *Escherichia coli* (Gram-negative). These results indicate that *Datura metel* possesses broad-spectrum antibacterial properties, although it tends to be more effective against Gram-positive bacteria, which have a thick peptidoglycan layer and are more susceptible to the membrane-disrupting action of lipophilic compounds such as alkaloids.

Figure 4. *Datura metel Linn leaves*

Tropane alkaloids like scopolamine are believed to act by interfering with bacterial cytoplasmic membrane integrity, leading to ion leakage, enzyme inhibition, and impaired protein synthesis (Handayani et al., 2019). Flavonoids may inhibit bacterial DNA gyrase enzymes, disrupting DNA replication, while tannins bind to cell wall proteins, resulting in protein coagulation and altered membrane permeability (Nurrahmi et al., 2021). Saponins enhance antibacterial effects by interacting with membrane cholesterol, leading to pore formation and uncontrolled cell lysis. In addition, *Datura metel* ethanol extracts have shown antibacterial effects against other pathogenic species such as *Salmonella typhi* and *Pseudomonas aeruginosa*. Sari et al. (2020) reported an inhibition zone of 14.1 mm against *S. typhi* at a 50% extract concentration, suggesting the potential of this plant as a natural antimicrobial agent for gastrointestinal infections. The varying efficacy across bacterial strains is influenced by structural differences in cell walls, polarity of active compounds, and extract concentration.

Overall, the results suggest that *Datura metel* leaf extract exhibits moderate to strong antibacterial activity, depending on the bacterial target and concentration used. These effects result from the synergistic actions of various secondary metabolites that simultaneously disrupt essential bacterial structures and metabolic functions. Therefore, *Datura metel* holds herbal antibacterial candidate, although further studies involving fractionation, compound isolation, and mechanistic assays are required to refine its pharmacological potential and specificity.

Common broom (Genista vurali)

Genista vuralii, also known as common broom, is a member of the Fabaceae family and is endemic to Turkey and the Mediterranean region. This plant has gained scientific interest due to its content of secondary metabolites, particularly quinolizidine alkaloids, which are known to possess a broad spectrum of biological activities, including antibacterial effects. The leaves of G. vuralii contain various types of alkaloids, with anagyrine being the most abundant (approximately 93% of the total alkaloid content), along with cytisine, N-methylcytisine, and lupanine (Yilmaz et al., 2009; Aktumsek et al., 2016). These alkaloids are believed to act synergistically in inhibiting the growth of pathogenic bacteria.

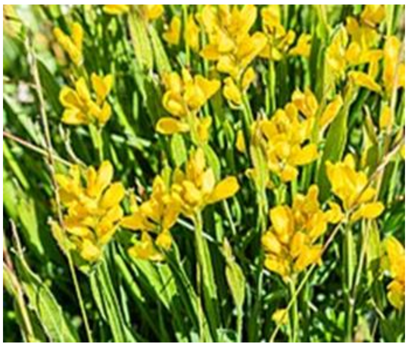

Figure 5. *Genista vurali*

Antibacterial assays of alkaloid-rich extracts from the leaves of G. vuralii have demonstrated strong activity against Gram-positive bacteria such as Staphylococcus aureus and Bacillus subtilis, with a minimum inhibitory concentration (MIC) value of 62.5 µg/mL, indicating promising potential as a natural antimicrobial agent. While some inhibitory activity was also observed against Gram-negative bacteria such as Escherichia coli and Pseudomonas aeruginosa, the effect was relatively lower (MIC ranging from 125 to 500 µg/mL). This lower efficacy is likely due to the more complex outer membrane structure of Gram-negative bacteria, which limits the penetration of active compounds (Tüfekçi et al., 2018).

The antibacterial mechanism of these alkaloids is thought to involve disruption of bacterial cell membrane integrity, leading to leakage of essential ions and intracellular metabolites, ultimately resulting in cell death. Some alkaloids have also been reported to inhibit protein synthesis and interfere with DNA replication, both of which are essential for bacterial survival and proliferation. In addition, there is evidence suggesting that these compounds may disturb bacterial metabolic signaling pathways that are critical for maintaining viability and virulence (Özdemir et al., 2021).

The considerable antibacterial potential of G. vuralii supports its further exploration as a source of phytopharmaceuticals or herbal-based antimicrobials, particularly for treating infections caused by Gram-positive bacteria. However, further research is required to assess its clinical applicability, including toxicological evaluations, pharmacokinetic profiling, and in vivo testing using appropriate animal or human models to confirm its safety and efficacy. Optimization of extraction methods and formulation strategies will also be necessary to ensure the stability and bioavailability of its active constituents.

Lupin (*Lupinus*)

Lupinus spp., a genus belonging to the Fabaceae family, is widely recognized for its ability to produce a variety of secondary metabolites, particularly quinolizidine alkaloids. Three primary species often studied—*Lupinus albus*, *Lupinus luteus*, and *Lupinus angustifolius*—are known to synthesize bioactive compounds such as lupanine, sparteine, angustifoline, and lupinine. These alkaloids serve as natural defense mechanisms against herbivores and pathogens. However, from a pharmacological perspective, these compounds also exhibit promising biological activities, notably antibacterial effects (Romeo et al., 2018; Wink, 1984).

Figure 6. *Lupinus*

Alkaloid extracts from Lupin seeds can inhibit the growth of various pathogenic bacteria, both Gram-positive and Gram-negative. For instance, Romeo et al. (2018) demonstrated that seed extracts from several *Lupinus* genotypes significantly inhibited clinical pathogens such as Klebsiella pneumoniae and Pseudomonas aeruginosa, both of which are commonly resistant to conventional antibiotics. The antibacterial activity was evaluated using disc diffusion and MIC (Minimum Inhibitory Concentration) methods, revealing that genotypes with higher alkaloid content tended to exhibit stronger inhibitory zones. In a related review published in *Biology (MDPI)* (2023), it was highlighted that quinolizidine alkaloids in Lupin may act synergistically with naturally occurring peptides in the seeds, resulting in enhanced antibacterial efficacy against Staphylococcus aureus, Bacillus subtilis, Escherichia coli, and *P. aeruginosa*. The mode of action includes disruption of bacterial cell membrane integrity, inhibition of protein synthesis, and chelation of essential metal ions required for microbial metabolism (Biology MDPI, 2023; Wink, 1984). The highest activity was observed against *S. aureus* and *B. subtilis*, with inhibition zones exceeding 15 mm and MIC values ranging from 1.25 to 2.5 mg/mL depending on the genotype.

Additionally, studies by Wink (1984) and Planchuelo-Ravelo et al. (2007) reported that sparteine and angustifoline exhibited bactericidal effects against *E. coli*, *B. subtilis*, and *S. aureus*, although their activity was relatively weaker against Gram-negative *E. coli*. This may be attributed to the complex lipopolysaccharide layer of Gram-negative bacteria, which acts as a protective barrier against hydrophilic compounds. It is also worth noting that the composition and concentration of alkaloids in *Lupinus spp.* vary significantly depending on genotype, environmental conditions, and seed maturity. This underscores the importance of selective breeding and biotechnological development of Lupin varieties with high alkaloid yields for pharmaceutical, nutraceutical, and food-based applications (Romeo et al., 2018). Plants with high alkaloid content from specific genotypes represent a valuable source of bioactive compounds that can be further developed into natural antibacterial agents, health supplements, and safer therapeutic alternatives to synthetic antibiotics.

In conclusion, the presence of quinolizidine alkaloids in *Lupinus spp.* seeds contributes significantly to the plant's antibacterial activity. Their consistent effectiveness against multidrug-resistant bacteria makes Lupin a promising candidate for the development of natural antimicrobial agents. Further research is still required, particularly in isolating pure compounds, conducting in vivo and systemic toxicity tests, and progressing toward clinical evaluation for pharmaceutical use.

Flower Poppy Tulip (*Tulipa spp*)

The flower poppy tulip (*Tulipa* spp.) is known to contain a wide range of secondary metabolites with potential as natural antibacterial agents. One of the most extensively studied compounds is 6-tuliposide B, a lactone glycoside that can be enzymatically converted into the active compound tulipalin B. This compound has been shown to inhibit the enzyme MurA (UDP-N-acetylglucosamine enolpyruvyl transferase), which plays a critical role in the biosynthesis of peptidoglycan in bacterial cell walls. Research by Nomura et al. (2015) demonstrated that tulipalin B isolated from tulip biomass exhibits antibacterial activity against Gram-negative bacteria such as *Escherichia coli*, even at low concentrations (0.1–0.3 mM), through a MurA inhibition mechanism. Further investigation by Nomura and Kato (2020) identified a novel compound called tuliposide G, an ester glycoside found across various tulip tissues including bulbs and petals, which is also presumed to exhibit antimicrobial properties, although its mechanism of action remains to be elucidated.

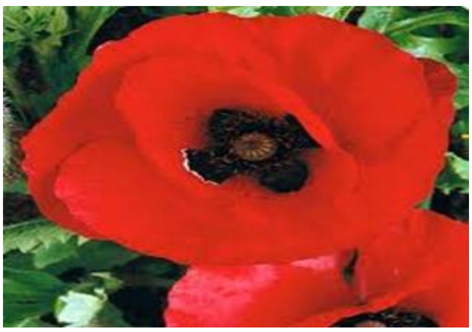

Figure 7. *Tulipa spp*

In parallel, extracts from the vegetative parts of *Tulipa sintenisii*-such as roots, stems, and flowers obtained using ethanol, methanol, and acetone solvents, have shown antibacterial activity against pathogenic bacteria including *Enterobacter aerogenes*, *Staphylococcus aureus*, and *E. coli*. Notably, acetone extracts derived from root tissues displayed inhibition zones comparable to those of the antibiotic streptomycin (Erbil et al., 2021). Moreover, naturally occurring antimicrobial peptides such as Tu-AMP-1 and Tu-AMP-2, isolated from tulip bulbs, were reported to inhibit the growth of various bacterial strains including *Salmonella enteritidis*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, and *S. aureus* (Mashtami et al., 2020). Phenolic and flavonoid compounds present in tulip petals have also been shown to suppress microbial growth, possibly through mechanisms involving disruption of bacterial cell membranes and inhibition of key enzymatic systems. Overall, the flower poppy tulip represents a promising source of antibacterial secondary metabolites, including active lactones such as tulipalin, novel glycosides like tuliposide G, antimicrobial peptides, and phenolic constituents.

Madagascar Periwinkle (*Chatarantus roseus L.*)

Catharanthus roseus (L.) G. Don, widely known as Madagascar periwinkle, is a small shrub native to Madagascar, now widely distributed across tropical and subtropical regions, including Indonesia. This plant belongs to the Apocynaceae family and is recognizable by its striking pink, purple, or white flowers. Beyond its ornamental value, *C. roseus* has long been used in traditional medicine to treat a range of diseases, including diabetes, hypertension, cancer, and microbial infections. Its pharmacological potential is primarily attributed to the presence of diverse and biologically active secondary metabolites. The key secondary metabolites identified in *C. roseus* include over 130 indole alkaloids and terpenoid indole alkaloids, such as vindoline, catharanthine, vinblastine, and vincristine, which are known for their cytotoxic and anticancer properties. Additionally, flavonoids, tannins, saponins, terpenoids, and phenolic compounds are also present in various parts of the plant, especially in the leaves and roots. Several recent studies indicate that these compounds also exhibit significant potential as natural antibacterial agents.

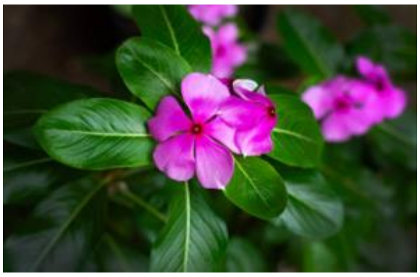

Figure 8. *Chatarantus roseus (L.)*

The antibacterial activity of *C. roseus* has been evaluated through various methods, including disc diffusion, dilution, and minimum inhibitory concentration (MIC) assays. Alhijrah et al (2024) reported that ethyl acetate leaf extract of *C. roseus* effectively inhibited the growth of Staphylococcus aureus (both ATCC 25923 and clinical isolates), with inhibition zones ranging from 5.8 to 8 mm and MIC values of 3-7% (w/v). The observed antibacterial effect is attributed mainly to flavonoids and tannins, which disrupt bacterial membrane permeability and inhibit essential metabolic enzymes. In a study by Alhijrah et al. (2024), ethanolic extracts of *C. roseus* leaves demonstrated significant antibacterial activity against Pseudomonas aeruginosa, Propionibacterium acnes, and Staphylococcus epidermidis, with the highest inhibition zones observed at 75% extract concentration, reaching 8.14 mm (*P. aeruginosa*) and 7.4 mm (*S. epidermidis*). The antibacterial mechanism is presumed to involve interactions between polyphenols, alkaloids, and bacterial cell structures, resulting in ion leakage, membrane disruption, and respiratory inhibition.

Further confirmation was provided by Dwijayanti (2016), whose microdilution assay revealed MIC values in the range of 30-45%, indicating moderate to strong antibacterial efficacy. Active compounds such as vindoline, triterpenoid alkaloids, and phenolic acids (e.g., p-coumaric acid) were suggested to work synergistically in inhibiting bacterial protein biosynthesis and interfering with vital metabolic pathways. This aligns with the findings of Sudharshana et al. (2019), who isolated the endophytic fungus *Alternaria alternata* from *C. roseus* leaves. From the ethyl acetate extract of this fungus, the bioactive compound p-coumaric acid (PC) was identified, which demonstrated broad-spectrum antibacterial activity against Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, and Salmonella typhimurium. The compound disrupts bacterial cell walls and membranes, inhibits nucleic acid and protein synthesis, and ultimately suppresses the proliferation of these pathogenic bacteria.

Collectively, these findings suggest that *Catharanthus roseus* possesses a broad antibacterial spectrum against both Gram-positive bacteria (e.g., *S. aureus*, *S. epidermidis*, *P. acnes*) and Gram-negative bacteria (e.g., *P. aeruginosa*, *E. coli*, *K. pneumoniae*). This activity is supported by a wide range of secondary metabolites acting through multiple mechanisms, including protein synthesis inhibition, membrane disruption, and metabolic enzyme interference. These properties highlight *C. roseus* as a promising candidate for developing natural antibacterial agents, especially in light of the rising global challenge of antibiotic resistance.

Table 1. Antibacterial activity of several flower extracts against target bacteria.

Plant Name	**Secondary Metabolites**	**Target Bacteria**	**Antibacterial Activity**	**citation**
Waterlily (*Nymphaea lotus L.*)	Flavonoids such as naringenin, polyphenols, saponins, alkaloids, terpenoids, tannins, and steroids.	Gram positive (Staphylococcus aureus, Bacillus cereus, Staphylococcus epidermidis, Enterococcus faecalis) and gram negative (Escherichia coli, Pseudomonas aeruginosa, Vibrio cholerae)	Natural topical antibacterial agent for mild to moderate skin infections; natural antiseptic for mild gastrointestinal or respiratory infections; control of microbes that cause food poisoning and spoilage.	Din, et al., 2022; Dulai, et al., 2022; Newman & Cragg., 2020; Rueangsri, et al., 2025; Saddiq, et al., 2025.
Chocolate Grape (*Akebia trifoliata*)	3β-akebonoic acid; 2α,3β-dihydroxy-30-noroleana-12,20(29)-dien-28-oic acid; 3α-akebonoic acid; Quinatic acid; Oleanolic acid; arjunolic acid; maslinic acid; Non-anthocyanin polyphenols flavonoid seperti quercetin dan kaempferol, and phenolic acids.	Gram-positive (Staphylococcus aureus; Methicillin-resistant S. aureus (MRSA); Bacillus subtilis; Bacillus cereus) and gram-negative (Escherichia coli and Pseudomonas aeruginosa)	Inhibits and kills Gram-positive bacteria, Effective against MRSA, Bactericidal against B. cereus and B. subtilis, Active against Gram-negative bacteria, Damages bacterial cell membranes.	Chen, et al., 2022; Huang, et al., 2022; Li, et al., 2022; Wang, et al., 2015.
Butterfly Pea Flower	Alkaloids, Flavonoids,	Escherichia coli, Pseudomonas	Its effectiveness against various	Rani et al., 2019

Plant Name	Secondary Metabolites	Target Bacteria	Antibacterial Activity	citation
(*Clitoria ternatea L.*)	Saponins, Tannins, Sterols and triterpenoids, Phenolic acids, Cyclic proteins.	aeruginosa, Staphylococcus aureus, Bacillus subtilis, Klebsiella pneumoniae	pathogenic bacteria	
Angel's Trumpet (*Datura metel Linn leaves*)	Alkaloids Flavonoids Saponins Tannins Glycosides Amino acids	Bacillus subtilis Bacillus cereus Salmonella typhi Escherichia coli (*E. coli*)	Ethanol extract from D. metel leaves showed great potential as a natural antibacterial agent against both Gram-positive and Gram-negative bacteria.	Krishnan et al., 2017.
Bush broom (*Genista vurali*)	Quinolizidine alkaloids (main: anagyrine 93%)	Staphylococcus aureus & Bacillus subtilis	This plant extract showed significant antibacterial and antifungal activity against Staphylococcus aureus, Bacillus subtilis, and Candida krusei, with an effective MIC value of 62.5µg/mL; while against other bacteria such as Escherichia coli and Pseudomonas aeruginosa, the MIC value was in the range of 125–500µg/mL.	Duran & Dural, 2019.
Lupin (*Lupinus*)	11S Globulin (α-conglutin), Basic Subunit (BS) is the active part of 11S globulin, and Polyphenols	Listeria monocytogenes, Klebsiella oxytoca, Listeria ivanovii, Staphylococcus aureus, Proteus mirabilis, Pseudomonas aeruginosa, Salmonella typhimurium	Disrupts bacterial cell membranes through electrostatic and hydrophobic interactions causing deformation and cell death.	Shafi et al., 2023
Tulip with Ruffled Petals (*Papaver glaucum* dan *Papaver decaisnea*)	Antibacterial Analgesic Antispasmodic Psychotropic Antimalarial	Gram-positive: Staphylococcus aureus (PTCC 1189) and Listeria monocytogenes (PTCC 1297) Gram-negative: Klebsiella pneumoniae (PTCC 1290) and Pseudomonas aeruginosa (PTCC	All alkaloid extracts showed antimicrobial activity, but were stronger against fungi (C. *albicans*) than bacteria.	Ismaili et al., 2017.

Plant Name	Secondary Metabolites	Target Bacteria	Antibacterial Activity	citation
		1310) Fungi: Candida albicans (PTCC 5027)		
Madagascar Periwinkle (*Chatarantus roseus L.*)	Vincristine (VCR) Vinblastine (VBL) Vinorelbine (VRL) Vindesine (VDS) Vinflunine	Anticancer activity and microtubules in cells	inhibits microtubule formation by binding to tubulin	Moudi et al., 2013.

Andaliman (*Zanthoxylum acanthopodium DC.*)

Andaliman (*Zanthoxylum acanthopodium DC*.) is a plant native to North Sumatra, Indonesia, which has traditionally been used to treat various health problems such as toothache, cough, rheumatism, stomach cramps, and fever. This study shows that andaliman has significant antibacterial activity against various types of bacteria, both gram-positive and gram-negative. The leaves and fruits of this plant were extracted using solvents such as methanol, water, and ethyl acetate. The leaf extract was shown to be effective against Escherichia coli, while the fruit extract also showed effectiveness against these bacteria as well as against Staphylococcus aureus and Salmonella typhimurium. The higher the concentration of the extract used, the wider the inhibition zone formed.

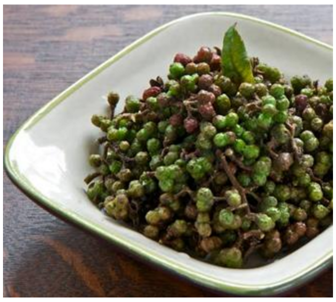

Figure 9. *Zanthoxylum acanthopodium DC.*

The secondary metabolite content in andaliman such as flavonoids, alkaloids, saponins, and tannins play an important role in its antibacterial activity. Flavonoids are known to damage the structure of bacterial cell walls, alkaloids interfere with the formation of cell layers, and saponins cause damage to bacterial cell membranes. Overall, andaliman shows great potential as an antibacterial agent that can be further developed in the field of medicine (Hutapea et al., 2024).

Various studies have identified the presence of phenolic compounds, flavonoids, alkaloids, and particularly essential oils in andaliman fruit. The main essential oil components identified through steam distillation include α-pinene, limonene, linalool, β-myrcene, and 1,8-cineole, all of which are known for their antimicrobial properties. These compounds act by penetrating bacterial cell walls, disrupting membrane integrity, and interfering with cellular metabolism (Sirait et al., 2021).

In addition to essential oils, ethanolic extracts of andaliman fruit contain quercetin, kaempferol, gallic acid, and chlorogenic acid which is the compounds that belong to the phenolic and flavonoid groups. These compounds contribute to antibacterial activity by inhibiting key bacterial enzymes and compromising membrane structure (Wienaldi & Wang, 2024). Interestingly, the antibacterial potential of andaliman fruit is derived not only from its phytochemicals, but also from endophytic bacteria that inhabit the fruit's tissues. A recent study successfully isolated endophytic bacteria from andaliman fruit that produced secondary metabolites with significant antibacterial activity against *S. aureus* and *E. coli* (Rizqoh et al., 2024). This dual source of bioactivity highlights the fruit's potential as a natural antimicrobial reservoir from both the plant itself and its symbiotic microbes.

Cempedak (*Artocarpus integer (Thunb.) Merr*)

Artocarpus integer (Cempedak Fruit) is one of the plants that is part of Indonesia's biological wealth. Cempedak (Artocarpus integer) is a tropical fruit plant that belongs to the Moraceae family and has high economic value. This plant originates from Southeast Asia and is widely distributed, starting from Tenasserim in Burma, the Malay Peninsula (including Thailand), to several parts of the Indonesian Archipelago such as Sumatra, Kalimantan, Sulawesi, Maluku, and Papua. Cempedak is recognized as the second most typical fruit in Southeast Asia after durian (Fitmawati et al., 2018).

Figure 10. *Artocarpus integer (Thunb.) Merr*

In the test of alkaloid content in the outer skin of cempedak fruit using ethanol showed positive results because it produced an orange color when sprayed with dragendorff color reagent and there was a white precipitate when Mayer's reagent was added. Testing the bioactivity of alkaloids from ethanol extract of the outer skin of cempedak fruit as an antimicrobial was carried out on Escherichia coli and Staphylococcus aureus bacteria (Saputri et al., 2019).

Alkaloids inhibit bacterial growth by disrupting the structure of bacterial cell walls. In addition, this compound also acts as a DNA intercalator and inhibits the activity of topoisomerase enzymes in bacterial cells. Based on the results of the study, the outer skin of cempedak fruit shows potential as an effective antimicrobial agent to inhibit the growth of microorganisms such as Escherichia coli and Staphylococcus aureus. Ethanol extract from the outer skin of cempedak shows broad antimicrobial activity, because it is able to fight various types of microorganisms, including gram-positive, gram-negative bacteria, and even several types of fungi, protozoa, and viruses (Saputri et al., 2019).

Lime (*Citrus aurantifolia*)

Figure 11. *Citrus aurantifolia*

Phytochemical screening of Citrus aurantifolia (lime) leaf extracts revealed the presence of various secondary metabolites, including flavonoids, phenolics, tannins, saponins, alkaloids, and terpenoids. These compounds are well-known for their antimicrobial properties. Flavonoids and phenolics can damage bacterial cell walls and inhibit nucleic acid synthesis, while tannins precipitate proteins, leading to cell lysis. Terpenoids and saponins disrupt cell membranes by altering permeability and causing leakage of intracellular contents. These bioactive compounds contribute synergistically to the antibacterial activity observed in lime leaf extracts (Indriani et al., 2023).

Lontar (*Borassus flabellifer L.*)

Figure 12. *Borassus flabellifer L.*

Lontar or also known as siwalan is a type of palm that grows in South Asia and Southeast Asia. In lontar plants, alkaloid compounds are detected in sopi and moke, with sopi showing positive alkaloid content and moke having weak positive alkaloid content. Sopi and moke have antimicrobial activity, which is thought to be caused by the presence of alkaloid compounds, phenol hydroquinone, and saponin. Alkaloids have antibacterial properties, while phenol hydroquinone and saponin function as antimicrobial compounds that can be used as alternative disinfectants. Phenol hydroquinone and saponin compounds in moke can be indicators that support the antimicrobial properties of both materials that can be used as natural alternative disinfectants (Detha & Datta, 2016).

Papaya Plant (*Carica papaya L.*)

Figure 13. *Carica papaya L*

Papaya (*Carica papaya L.*) is a herbal plant that is widely known and used by the public. This plant can grow in various regions in Indonesia and has a relatively short growth period. Papaya leaves contain the enzyme papain and the alkaloid compound carpaine. Papain is known to have proteolytic abilities and antimicrobial properties, while carpaine acts as an antibacterial agent. In addition, papaya leaves also contain various active compounds that can increase the total antioxidant capacity in the blood and reduce levels of fat peroxidation. Some of them are papain, chymopapain, cystatin, α-tocopherol, ascorbic acid, flavonoids, cyanogenic glycosides, and glucosinolates. Ethanol extract of papaya leaves also shows pharmacological activities such as anthelmintic, antimalarial, antibacterial, and anti-inflammatory. The content of chemical compounds in this ethanol extract is thought to be the main factor in these various pharmacological activities (Jati et al., 2019).

Black Plum (*Vitex doniana*)

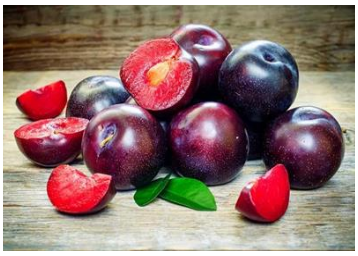

Figure 14. *Vitex doniana*

Vitex Doniana commonly known as black plum, is a species of savanna plant in wooded grasslands and can be found along the forest edges. V. doniana is used in the treatment of conjunctivitis, skin rashes due to measles, chicken pox, respiratory tract infections and stomach disorders and diarrhea. The results obtained from the proximate analysis of V. doniana determined that these seeds can be classified as oil-rich seeds. The low water content of these seeds will inhibit the growth of microorganisms and their shelf life will be long. At varying concentrations, this plant was able to inhibit the growth of B. subtilis, S. aureus, E. faecalis, P. aeruginosa and S. typhi bacteria. The seed extract of this plant has been shown to be effective against several gram-positive and gram-negative microorganisms and Bacteria albicans. The susceptibility pattern of the tested microorganisms also indicated the presence of a broad-spectrum antimicrobial agent (Udeani et al., 2021).

Rambai (*Baccaurea Motleyana*)

Rambai plants are a type of plant that belongs to the genus Baccaurea. This plant can be found in Kalimantan, Java, Sumatra, and the Bangka Belitung Islands. Rambai leaves are medicinal plants originating from the Bangka Belitung Province which are used as antibacterials to obtain alternative antibacterials derived from plants. Based on related research, rambai plants have been identified as containing secondary metabolite compounds, namely alkaloids, tannins, flavonoids, saponins, steroids, and terpenoids.

Figure 15. *B. Motleyana*

Antibacterial testing was carried out to determine the antibacterial strength of rambai leaf extract against Staphylococcus aureus and Escherichia coli bacteria. In the antibacterial test of rambai leaf acetone extract, the inhibition zone against S.aureus bacteria was much larger than the inhibition zone for E.coli bacteria. This is due to the difference in the types of test bacteria, namely S. aureus bacteria which are gram-positive bacteria, while E. coli bacteria are gram-negative bacteria. Gram-positive bacteria have a simpler structure than gram-negative bacteria, so gram-positive bacteria are more easily damaged than gram-negative bacteria. In addition to the differences in the types of bacteria, the antibacterial inhibition strength is influenced by the presence of bioactive compounds in the extract. As evidenced by qualitative phytochemical tests, this plant extract contains alkaloids, tannins, flavonoids, saponins, steroids, and terpenoids. These bioactive compounds have the potential to be antibacterial. Alkaloids damage bacterial cell membranes by inhibiting the formation of peptidoglycan, flavonoids can cause bacterial cell death by disrupting the components of peptidoglycan in the cell, and tannins cause bacterial cells to become less perfect because they can damage cell wall polypeptides, as well as saponins which have a detergent-like surface so that they can damage the permeability of cell membranes (Fransiska et al., 2024).

Tomato (*Skopolamin lycopersicum L.*)

Antimicrobial compounds from medicinal plants can inhibit the growth of bacteria, fungi, viruses, and protozoa through mechanisms different from currently used antimicrobials and may have significant clinical value in the treatment of resistant microbial strains.

Figure 16. *Skopolamin lycopersicum L.*

Tomato plant, S. lycopersicum L., produces cholesterol-derived steroidal alkaloids tomatine and tomatidine. Tomatidine selectively and potently inhibits small colony variants of S. aureus bacteria that cause opportunistic infections in patients with cystic fibrosis and also has strong fungistatic activity against Candida spp. with low toxicity to human cells. Its biosynthesis starts from the precursor dehydrotomatidine through enzymatic dehydrogenation, isomerization, and sequential reduction. Scopolamine is a type of TA found in many plants of the Solanaceae family and is classified as an essential medicine by WHO. Scopolamine exhibits considerable antifungal activity (Huang et al., 2022).

Table 2. Antibacterial activity of several fruit extracts against target bacteria.

Plant Name	Secondary Metabolites	Target Bacteria	Antibacterial Activity	citation
Andaliman (*Zanthoxylum acanthopodium DC.*)	α-pinene, limonene, linalool, β-myrcene, 1,8-cineole, quercetin, kaempferol, gallic acid, chlorogenic acid, flavonoids, alkaloids, saponins, & tannins.	*Staphylococcus aureus, Escherichia coli, Salmonella typhimurium*	Inhibits the growth, Interferes with bacterial enzyme and protein synthesis (phenolics, flavonoids, alkaloids), Endophytic bacteria within the fruit.	Hutapea et al., 2024; Rizqoh et al., 2024; Sirait et al., 2021; Wienaldi & Wang, 2024.
Cempedak (*Artocarpus integer (Thunb.) Merr*)	Saponin Tanin Flavonoid Alkaloid	Escherichia coli dan Staphylococcus aureus	inhibits and kills Gram-positive and Gram-negative bacteria	Saputri et al., 2019; Subagio et al., 2018;
Lime (Citrus aurantifoli)	flavonoid, terpenoid, fenolik, limonoid, alkaloid, dan	Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae,	The main working mechanism is that phenolic compounds cause denaturation of	Indrianiet al., 2023

Plant Name	Secondary Metabolites	Target Bacteria	Antibacterial Activity	citation
	essential oil	Pseudomonas spp., Salmonella spp.	bacterial cell proteins and disruption of cell membranes.	
Lontar (*Borassus flabellifer L.*)	saponin, flavonoid, glikosida, triterpenoid, dan fenol.	Staphylococcus aureus dan Bacillus subtilis	Palmyra fruit extract (Borassus flabellifer) has quite strong antibacterial activity against Gram-positive bacteria such as Staphylococcus aureus and Bacillus subtilis, but is not effective against Gram-negative bacteria such as Escherichia coli and Pseudomonas aeruginosa.	Mahayasih & Mahayasa. 2022
Papaya Plant (*Carica papaya L.*)	Alkaloid Flavonoid Glikosida Saponin Tanin Steroid Triterpenoid	Staphylococcus aureus and Pseudomonas aeruginosa; Propionibacterium acnes (P. acnes); Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus, Bacillus cereus; Gram-positive : Bacillus subtilis, Staphylococcus aureus, Gram-negative : Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Shigella boydii; Staphylococcus epidermidis	Can inhibit skin infections and nosocomial infections; 60% concentration provides the most optimal effectiveness in inhibiting P. acnes; gastrointestinal tract infections, wounds, and skin infections; resistant bacterial infections; Inhibits Gram-positive causes of acne, skin infections, urinary tract infections, and abscesses; acne, skin infections, urinary tract infections, and abscesses.	Karo-Karo dkk. 2022; Purwandhini dkk. 2024; Lohidas dkk. 2015; Dagne dkk. 2021; Marpaung dkk. 2022.
Black Plum (*Vitex doniana*)	Alkaloids, flavonoids, tannins, phenolics, saponins, terpenoids	S. aureus, B. subtilis, E. coli, S. typhi	Dominant inhibition zone in methanolic seed extract; low MIC/MBC against S. epidermidis and S. aureus	Aziz, A & Banerjee s, 2018
Rambai (*Baccaurea Motleyana*)	fenolik, flavonoid, tanin, saponin, dan alkaloid	Staphylococcus aureus (MSSA & MRSA),	One fruit extract was found to have moderate to weak antibacterial activity	Begum et al., 2015

Plant Name	Secondary Metabolites	Target Bacteria	Antibacterial Activity	citation
		Pseudomonas aeruginosa	against several Gram-positive and Gram-negative bacteria. For example, activity against Staphylococcus aureus was generally higher than against Escherichia coli or Pseudomonas aeruginosa.	
Tomato (*Skopolamin lycopersicum L.*)	succinic acid, citric acid, tartaric acid) as well as glycoalkaloids such as tomatine and esculeoside A	Escherichia coli, Staphylococcus aureus, Enterobacter, Salmonella spp., and Pseudomonas spp.	The antibacterial activity of tomatoes is related to organic acids that disrupt microbial metabolism. Furthermore, fermentation of tomato waste produces an extract that exhibits a minimum bactericidal concentration (MBC) of around 12.5–25 mg/mL against pathogenic bacteria such as E. coli, S. aureus, B. cereus, Salmonella spp., and Pseudomonas spp.	Ricci et al., 2021

Goatweed (***Ageratum conyzoides L***.)

Ageratum conyzoides L., known as bandotan, is a wild plant rich in secondary metabolites such as alkaloids, flavonoids, tannins, and saponins. These compounds have been shown to possess important biological activities, particularly as antibacterials. Alkaloids in A. conyzoides leaves can disrupt bacterial enzyme metabolism and damage the integrity of microbial cell membranes (Hajar et al., 2025). Flavonoids and tannins work by forming complexes with cell wall proteins and bacterial enzymes, thereby inhibiting bacterial growth and causing cell lysis (Maulidya et al., 2020; Cowan, 1999 in Maulidya et al., 2020). This content has been confirmed through phytochemical tests that showed the presence of alkaloids, flavonoids, tannins, and triterpenoids in bandotan leaf extract (Naibaho & Arjadi, 2025; Hayati et al., 2020).

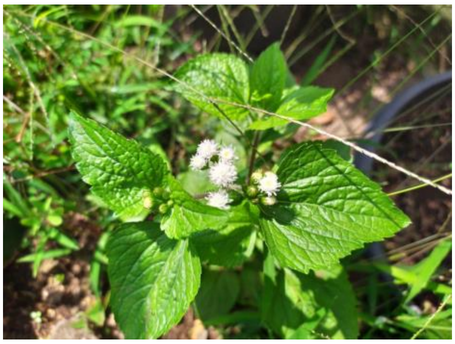

Figure 17. *Ageratum conyzoides L*

Empirically, A. conyzoides leaf extract has been shown to be effective in inhibiting the growth of pathogenic bacteria, particularly Gram-positive bacteria such as Staphylococcus aureus, including resistant strains such as MRSA. In a study using the disc diffusion method, ethanol extract of A. conyzoides at a concentration of 12.5% was able to produce an inhibition zone of up to 25.1 mm against MRSA, which is comparable to the antibiotic gentamicin (Maulidya et al., 2020). In addition, the bioactive compounds in this plant are also effective against Streptococcus pyogenes and Propionibacterium acnes, which shows broad potential in therapeutic applications, including in the treatment of skin infections (Naibaho & Arjadi, 2025). These findings suggest that A. conyzoides can be used as a natural antibacterial alternative to support efforts to reduce resistance to conventional antibiotics (Hayati et al., 2020).

Sea Grapes (*Caulerpa racemosa*)

The Caulerpa racemosa plant, known as sea grapes, is a type of green macroalgae that is commonly found in tropical waters. This plant has various bioactive compounds, one of which is alkaloids. Alkaloids are organic compounds that generally contain nitrogen and have basic properties. In C. racemosa, the alkaloid content is relatively low, but remains significant in the context of antibacterial potential. Although specific studies on alkaloids in this plant may be limited, the presence of alkaloids in various algae species has been known to contribute to various biological activities.

Figure 18. *Caulerpa racemosa*

Alkaloids have an effective mechanism of action against bacteria. Here are some ways that alkaloids work as antibacterials: Alkaloids can interfere with cellular metabolism processes in bacteria, thereby inhibiting their growth. Some alkaloids can affect the components of bacterial cell walls, such as peptidoglycan, which is important for the stability of cell structure. By damaging the cell wall, alkaloids can cause bacterial cell death. Alkaloids can also inhibit protein synthesis in bacterial cells by disrupting ribosome function, which plays an important role in protein production. Some alkaloids can interact with bacterial DNA or RNA, disrupting the replication and transcription processes, thereby inhibiting bacterial growth and reproduction. Overall, alkaloids in Caulerpa racemosa show potential as antibacterial agents with various mechanisms that can inhibit the growth of pathogenic bacteria. Further research is needed to better understand the types and concentrations of alkaloids found in this plant and their effectiveness in medical applications (Marfuah et al., 2018).

Kirinyuh (*Chromolaena odorata*)

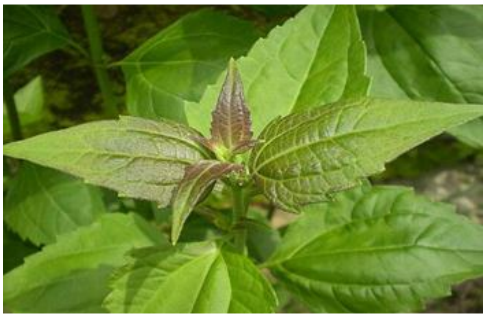

Figure 19. *Chromolaena odorata*

The kirinyuh plant is a plant that is used as a traditional medicine. Kirinyuh can also be used as a therapy for infections caused by bacteria. The main focus of this utilization lies in the leaves. The leaves of the kirinyuh plant have been applied in various countries as a therapy or medicine for several diseases such as malaria, antiseptic, anti-inflammatory, antidiarrheal, antimicrobial, and wound healing. Although it is famous for its properties, in Indonesia this plant is not yet very popular in its use as an antibacterial therapy treatment because of the kirinyuh plant (Gultom, 2022).

The content of secondary metabolite compounds found in kirinyuh leaves are alkaloids, flavonoids, steroids and saponins. However, the most dominant active compound is alkaloids. This is the reason why kirinyuh leaves are more likely to be used as antimicrobials to inhibit the growth of bacteria such as Staphylococcus aureus, Escherichia coli, and Bacillus subtilis. The bioactivity of kirinyuh leaves in overcoming and inhibiting the growth of these bacteria can be done by antimicrobial testing. These bacteria are spotted on kirinyuh leaves which are in organic solvent fractions or extracts such as methanol. The inhibition zone which is getting bigger and is directly proportional to the increase in the concentration of kirinyuh leaf extract shows positive results. The ability of kirinyuh leaves to inhibit the growth of these bacteria is none other than the presence of dominant alkaloid active compounds (Munte et al., 2016).

Pomel (*Hammada scoparia*)

The plant studied in this study is Hammada scoparia or rimth plant which is known in traditional medicine and has various health benefits, including antibacterial and antioxidant activities. The process of its bioactivity as an antibacterial begins with the collection of plant leaves, which are then extracted using solvents such as ethanol and methanol. This extraction method aims to remove bioactive compounds, including alkaloids, which are believed to contribute to its therapeutic properties (Bouaziz et al., 2016).

Figure 20. *Hammada scoparia*

After extraction, various fractions of the extract were tested against a number of pathogenic microorganisms, including Gram-positive bacteria such as “Staphylococcus aureus” and Gram-negative bacteria such as “Escherichia coli”. The test results showed that all extracts, except the hexane extract, had significant antibacterial activity, with the diameter of the inhibition zone varying between 8 and 30 mm. This activity indicates the potential of H. scoparia in controlling bacterial infections. Two major alkaloids isolated from the extract, namely “carnegine” and “N-methylisosalsoline”, were also tested for their antibacterial activity. Carnegine was shown to have a stronger antibacterial effect, with a low minimum inhibitory concentration (MIC), indicating that this compound may be effective in alleviating infections. On the other hand, N-methylisosalsoline showed better antioxidant activity, indicating that this compound may function as a cell protector from oxidative damage (Bouaziz et al., 2016).

Overall, this study highlights the potential of “Hammada scoparia” as a natural source for the development of antibacterial and antioxidant agents. With increasing resistance to synthetic antibiotics, the utilization of this plant as a therapeutic alternative may pave the way for further research and clinical application in the treatment of bacterial infections. Further research is expected to deepen the understanding of the mechanism of action of the active compounds in this plant and its potential use in the formulation of new drugs (Bouaziz et al., 2016).

Bay leaf (*Syzygium polyanthum*)

Bay leaf (Syzygium polyanthum) is one of the plants that grows well in Indonesia. This plant is often used as a spice to give aroma to cooking and is also known by the community as a plant that has medicinal properties. Bay leaves are commonly used by the community to help overcome gout, high cholesterol, high blood pressure, diabetes mellitus (diabetes), stomach ulcers (gastritis), and diarrhea.

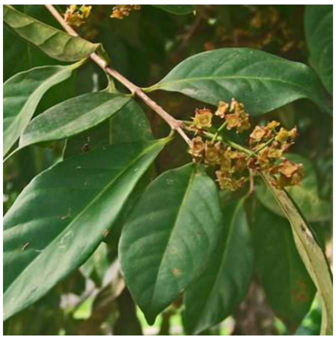

Figure 21. *Syzygium polyanthum*

This bioactivity is due to the presence of secondary metabolite compounds in Salam. Phytochemical tests of ethanol extracts of fruit from the Salam plant (Syzygium polyanthum) showed the presence of secondary metabolite compounds of the saponin, tannin, alkaloid, triterpenoid and flavonoid groups. Salam leaf extract (Syzygium polyanthum) contains secondary metabolite compounds in the form of alkaloids, saponins, steroids, phenolics, and flavonoids. A total of 10 triterpenoid compounds have been successfully identified from Syzygium guineense (Myrtaceae) plant extracts, including 4 compounds, namely arjunolic acid, asiatic acid, terminolic acid, and 6-hydroxyic acid, showing antibacterial activity against Escherichia coli, Bacillus subtilis, and Shigella sonnei bacteria. (Habibi et al., 2018).

Sekilang (*Embeliaborneensis scheff*)

The sekilang plant with the Latin name (Embelia Borneensis Scheff) is a plant whose bark is commonly used by the community, especially the Dayak tribe, as a material for catching fish. Based on previous research, sekilang bark extract is believed to be able to be an antibacterial agent because the bark of this plant contains several active compounds with alkaloids dominating.

Figure 22. *Embeliaborneensis scheff*

In its bioactivity test, alkaloids in the skin of the sekilang plant can inhibit the growth and spread of infections from Propionibacterium acnes bacteria found in skin follicles and Staphylococcus epidermidis bacteria which will cause acne if the bacteria have spread to the skin. The way alkaloids work to inhibit the growth of these bacteria is by disrupting the peptidoglycan components in bacterial cells, so that the cell wall layer is not formed completely and causes the death of the entire cell (Saptowo et al., 2022).

Table 3. Antibacterial activity of several leaf extracts against target bacteria.

Plant Name	Secondary Metabolites	Target Bacteria	Antibacterial Activity	citation
Goatweed (*Ageratum conyzoides L.*)	flavonoid (kaempferol, quercetin and glikosida-nya), alkaloid, tannin, coumarin, chromene, terpenoid	Staphylococcus aureus and also some Gram-negative bacteria.	Goatweed leaf and flower extracts show good antibacterial activity, and several laboratory studies have noted that phenolic and flavonoid compounds may play a role in inhibiting bacterial growth through synergistic effects with antibiotics.	Patil et al., 2019
Sea Grapes (*Caulerpa racemosa*)	Alkaloid Flavonoid Saponin Steroid Triterpenoid Taniny	Escherichia coli and Staphylococcus aureus	bacterial enzyme inhibition	Nurdiani et al., 2019.
Kirinyuh (*Chromolaena odorata*)	flavonoid, fenol, alkaloid, saponin, tanin, steroid, and terpenoid	Staphylococcus epidermidis, Streptococcus viridans, Pseudomonas aeruginosa, Bacillus subtilis, Bacillus cereus, and Shigella dysenteriae	Weak–moderate activity: MIC 30–40mg/mL, inhibition zone ≤7–10mm (most effective against B. subtilis and S. epidermidis)	Gultom et al., 2020
Pomel (*Hammada scoparia*)	Carnegine and N-methylisosalsoline; Alkaloids, Saponins, Triterpenes and sterols, Flavonoids ,Gallic tannins, Mucilage	Gram positir *(Staphylococcus aureus* ATCC 25923, *Staphylococcus epidermidis* ATCC 12228, *Bacillus cereus* ATCC 14579, *Enterococcus faecalis* ATCC 29212) dan gram negatif (*Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Klebsiella pneumoniae* CIP 32147, *Proteus vulgaris* (isolat klinis))	Carnegine is more active as an antibacterial and N-methylisosalsoline is more active as an antioxidant; carvacrol has the potential to damage microbial cell membranes.	Bouaziz dkk. 2016; Drioiche et al., 2019.
Bay leaf (*Syzygium polyanthu*)	flavonoid, alkaloid, tanin, saponin, and terpenoid/sterol,	Staphylococcus aureus, S. pyogenes, MRSA, K. pneumoniae	Antibacterial tests showed that the methanol extract of	Wahab & Ja'afar, 2021

Plant Name	Secondary Metabolites	Target Bacteria	Antibacterial Activity	citation
			bay leaves was effective in inhibiting Gram-positive bacteria such as Staphylococcus aureus, S. pyogenes, and MRSA (MIC 6.25–12.5mg/mL; inhibition zone between 8.6–14.0mm).	
Sekilang (*Embeliaborneensis scheff*)	alkaloid, flavonoid, tanin, and saponin	Staphylococcus epidermidis and Propionibacterium acnes	Antibacterial activity test using the disk diffusion method showed that the extract had moderate activity against Staphylococcus epidermidis and Propionibacterium acnes, with an inhibition zone of approximately 6–8 mm at a concentration of 2.5–20%.s	Hayon dat al., 2023

CONCLUSION

Alkaloid compounds are active secondary metabolites naturally synthesized by various plants, including tomato, *Chromolaena odorata* (Kirinyuh) leaves, lontar, lime, cempedak, *Clitoria ternatea* (Telang) flowers, andaliman *Zanthoxylum acanthopodium*, papaya, black plum, rambai, bay leaves, *Catharanthus roseus* (tapak dara), and *Datura species*. These alkaloids exhibit broad-spectrum bioactivity, especially as antimicrobials capable of disrupting microbial cellular functions, leading to inhibited growth or cell death. Their proven roles as antidiarrheal, antimalarial, antibacterial, and antiviral agents have made them valuable in traditional medicine and increasingly relevant in modern pharmacology, especially in the fight against antimicrobial resistance (AMR). The impact of this review underscores the therapeutic potential of alkaloid-rich plants as sustainable sources for novel drug development. However, considering that some alkaloids may possess toxic properties, especially in plants like Datura or Catharanthus roseus, further research is needed to evaluate their safety profiles, mechanisms of action, and clinical efficacy. Future studies should focus on comprehensive phytochemical analyses, toxicological assessments, and in vivo validations, while also comparing synthetic versus plant-based alkaloid derivatives to optimize their biomedical applications.

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