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Antimicrobial Potential of Coleus Atropurpureus and its Metabolites Content: A Literature Review

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Abstract: *The increasing prevalence of multidrug-resistant bacterial infections underscores the urgent need for new antimicrobial agents, especially those derived from plant-based sources. Coleus atropurpureus, a medicinal plant used extensively in Asia and Oceania, contains various bioactive compounds, including flavonoids, terpenoids, and phenolic acids, which have demonstrated antimicrobial properties. This review examines studies published between 2015 and 2025, highlighting the antibacterial activity of ethanolic and methanolic extracts of C. atropurpureus, particularly against methicillin-resistant Staphylococcus aureus (MRSA). Phytochemical analysis reveals that these extracts exert their antimicrobial effects through multiple mechanisms, including the disruption of microbial membranes, enzyme inhibition, the induction of reactive oxygen species, and immunomodulatory actions. Furthermore, the extracts have shown synergistic effects when combined with antibiotics, suggesting their potential as adjunct therapies. The evidence gathered supports the therapeutic potential of C. atropurpureus as a natural antimicrobial agent, offering a promising alternative to conventional antibiotics in combating drug-resistant infections.*

1. INTRODUCTION

Opportunistic bacterial infection caused by multidrug-resistant pathogens have become a growing public health concern worldwide. The advent of antimicrobial resistance has added significant impact of infectious diseases, in number of infectins, as well as added healthcare costs. These concerns prompted the World Health Organization (WHO) to launch a Global Action Plan on antimicrobial resistance in 2015 (Organization 2015).

The rising incidence of drug-resistant pathogens highlights an urgent need to discover and isolate new medicinal compounds from plants. Acoording to WHO, an estimated 80% of the developing countries still rely on the use of traditional medicines derived from plants (Organization 1978). WHO has also recommended the names of over 20.000 medicinal plant species as one of the potential sources for developing new drugs. The use of and search for drugs derived from plants have accelerated in recent years. Medicinal plant components could

provide novel approaches as one of the potential sources of new antimicrobe. While 25 to 50% of current pharmaceuticals are derived from plants, none are used as antibiotics (Vaou et al. 2021).

Coleus atropurpureus is a member of the Lamiaceae family, known as a decorational plant and traditional medicinal applications found in Southeast Asia, East Asia, and the Australasia and Oceania regions.(Büttner 2001) It is used for treating conditions such as skin infections, ear and eye infections, digestive disturbances, to inflammation.(Quisumbing 1978; Roosita et al. 2008; Quattrocchi 2012; Plants of the World Online 2023).

The genus Coleus is known with notable biological properties, such as antioxidant, antifungal, antiparasitic, anti-inflammatory, anti-diabetic, anti-cancer, and antibacterial effects (Ridwan and Ayunita 2007; Zakaria et al. 2008; Namsa et al. 2009; Arumugam et al. 2016; Barbosa et al. 2023). Specifically, parts and content of C. atropurpureus is abundant in a wide variety of metabolites content, such as flavonoids, phenolic acids, alkaloids, saponins, tannins, and terpenes (Lamprecht et al. 1975; Devriese et al. 1988; Mu et al. 1996; Ragasa et al. 2001; Lukhoba et al. 2006; Ito et al. 2018) which have been reported to have antimicrobial properties.

To date, no narrative review has comprehensively summarized the bioactive mechanisms and potential clinical application of Coleus atropurpureus as an antimicrobial agent. This review aims to summarize the antimicrobial efficacy of Coleus atropurpureus and highlights the role of its metabolite content based on existing in vivo studies. The most relevant studies regarding the antimicrobial activity of C. atropurpureus plant extract, underlying mechanisms of action, and the challenges and future perspectives of the medicinal plant derived antibiotics are analyzed in this review.

2. METHOD

A comprehensive literature search was carried out across the databases PubMed, Scopus, Science Direct, and Google Scholar search engine. The terms used in the searches included, “phytochemicals”, and “antimicrobial” of “Coleus, Plectranthus, Solenostemon atropurpureus or scutellarioides or blumei”, among others related to the subject of the review. “AND” or “OR” Boolean operators were used depending on the combination of terms. In vivo studies, in vitro studies, and research articles were included. Inclusion criteria for this review were (1) studies published within the last 10 years (2015-2025), (2) articles in English or Bahasa Indonesia, and (3) accessible full text. Only studies that gave details on the mechanism of action, reliable data on antimicrobial activity, and the origin of the agents were selected for this review.

3. RESULT AND DISCUSSION

Result

Coleus atropurpureus

Coleus atropurpureus (or Coleus scutellarioides, Solenostemon scutellarioides, Plectranthus scutellarioides, Coleus blumei, Plectranthus blumei)(Paton et al. 2004) is a decorational plant with medicinal benefits belonging to the Lamiaceae family, Equisetopsida class, of the Streptophyta phylum. Plectranthus scutellarioides is distributed across tropical and subtropical regions, including the Bismarck Archipelago, New Guinea, the Solomon Islands, and Vanuatu in Oceania; the Philippines, Indonesia (Java, Sumatra, Sulawesi, Maluku, and the Lesser Sunda Islands), Malaysia, Thailand, Vietnam, Cambodia, Laos, Myanmar, and Singapore in Southeast Asia; southern China and Taiwan in East Asia; as well as parts of northern and western Australia, including the Northern Territory, Queensland, and Western Australia.(Plants of the World Online 2023) It is a subshrub and grows primarily in the wet tropical biome. The leaves of this plant can be up to 7 to 11 cm in length and 4 to 6 cm in width, heart shaped.(Wiart 2006) The yellow color of C. blumei leaves is mainly due to flavonoids like luteolin and quercetin,(Moektiwardoyo et al. 2011) while anthocyanins are responsible for the red or purple hues;(Nguyen and Cin 2009) other key compounds include organic acids,(Bauer et al. 2002) abietane-type diterpenoids,(Mu et al. 1996; Ito et al. 2018; Kubinová et al. 2019) and triterpenes such as β-amyrin and daucosterol.(Thomas 2006) In vitro studies have shown that these compounds can be extracted from both the aerial parts (e.g. stem, leaves) and roots of the plant.(Levita et al. 2016; Ito et al. 2018; Astuti et al. 2019; Bismelah et al. 2022; Kowalczyk et al. 2024)

Antibacterial Activity

The majority of reviewed studies in Table 1 used methanolic or ethanolic leaf extracts, which consistently showed activity against both Gram-positive and Gram-negative bacteria. Its antimicrobial potential was found to be active against S. aureus,(Bismelah et al. 2019; Bismelah et al. 2022; Bismelah et al. 2025; Hanum et al. [no date]) E. coli, P. aeruginosa,(Kaunang et al. 2016) B. subtilis, and C. albicans,(Karo et al. 2018) achieving moderate antimicrobial activity of 20–40% effectiveness compared to standard antibiotics (chloramphenicol, tetracycline, and chlotrimazole).(Ragasa et al. 2001) The antimicrobial efficacy was generally stronger against Gram-positive bacteria (e.g. S. aureus than E. coli), possibly due to differences in cell wall permeability.

Table 1. Phytochemicals Isolated from C. Atropurpureus with Antimicrobial Activity.

Phytochemical	Tested microorganism	Extract	Activity	Author (Year)
Mixed metabolites (flavonoids, tannins, terpenoids, saponins)	*S. aureus*	Ethanol extract	ZOI: 13-14.56 mm (100 mg/mL) MIC: 1.56 mg/mL MBC: 3.1 mg/mL	Bismelah et al. (2019)
Flavonoid	*A. actinomycetemcomitans, P. gingivalis, P. intermedia, S. mitis, S. oralis, S. salivarius, S. sanguinis, T. forsythia, T. denticola*	Ethanol extract (quercetin-3-glucoside, quercitrin, quercetin 3-(6″-acetylglucoside), quercetin 3-*O*-acetylrhamnoside)	ZOI: 13-19 mm (100 mg/mL) ZOI: 10-22 mm (200 mg/mL) MIC: 1.56 mg/mL (aerobes) MIC: 3.12 mg/mL (anaerobes) MBC: 3.13 mg/mL (aerobes) MBC: 6.25 mg/mL (anaerobes)	Bismelah et al. (2022)
Mixed metabolites (flavonoids, tannins, terpenoids, saponins)	*A. viscosus*	Ethanol extract	ZOI: 17 mm (100 mg/mL) ZOI: 21 mm (200 mg/mL) MIC: 3.6 mg/mL MBC: 12.5 mg/mL	Bismelah et al. (2025)
N/A	*S. aureus, E. coli*	Ethanol extract	ZOI: 7.32-9.83 mm (400 mg/mL)	Hanum et al. (2022)
Abietane diterpene	*S. aureus* CCM 4750 (MRSA)	Methanol extract (Sincoetsin C, Scutellarioidone A, Spirocoleon 7-O-b-D-glucoside, 3-Hydroxyspirocoleon 7-O-b-D-glucoside)	MIC: 128 µg/mL (Sincoetsin C) MIC: 512 µg/mL (others)	Jurkaninová et al. (2019)
Mixed metabolites (alkaloid, polyphenol, flavonoid, monoterpenoid and sesquoterpenoid, steroid and triterpenoid, quinone)	*S. aureus* ATTC 25923, MRSA	Ethanol extract	ZOI: 10.3-11.5 mm (62.5 mg/mL) ZOI: 11.5-13.6 mm (125 mg/mL) ZOI: 13.3-15.1 mm (250 mg/mL) ZOI: 16.2-21.1 mm (500 mg/mL)	Mustarichie et al. (2022)

ZOI, zone of inhibition; MIC, minimum inhibitory concentration; MBC, minimum bactericidal concentration; MRSA, *methicilin-resistant Staphylococcus aureus*; N/A, not available.

Several studies have systematically evaluated the antimicrobial potential of Coleus atropurpureus, using different extracts, phytochemicals, and microbial targets. In vitro studies consistently shows that extracts from C. atropurpureus, particularly those prepared with methanol or ethanol, possess significant antimicrobial activity against a range of pathogens. Based on the results of the in vitro antibacterial culture tests, C. atropurpureus extract concentration of 10-40% can be categorized in moderate inhibition ability. The higher extract concentration, the more bacterial destruction is expected. The relatively low MIC/MBC values suggest that C. atropurpureus metabolites are not only bacteriostatic but also shows bactericidal activity. The extract likely interfered with the bacterial cell division process, leading to distorted and irregular damage to the peptidoglycan layer and the cell membrane (Bismelah et al. 2025). Across all studies, S. aureus and MRSA were consistently more susceptible than Gram-negative bacteria such as E. coli, which reflects the typical resistance of Gram-negative strains due to the absence of an outer lipopolysachharide protective outer membrane.

The effectiveness of a plant extract's antimicrobial properties is influenced by the solvent used during the extraction process. Specifically, organic solvents tend to be more effective at extracting the phytochemicals responsible for antimicrobial activity compared to water-based (aqueous) extracts (DAR 2016; Bismelah et al. 2025). It has been established that ethanol and methanol extracts contain more secondary metabolites and less impurities than water.

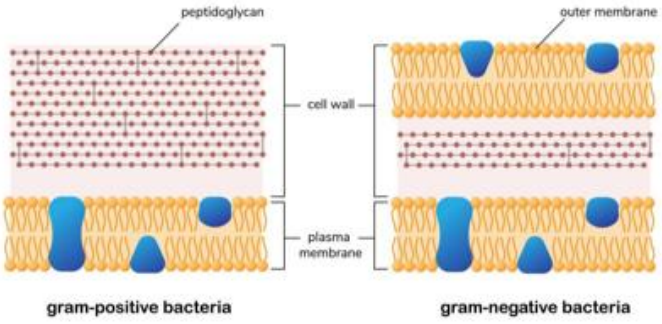

Figure 1. Gram-Positive versus Gram-Negative Bacteria Cell Wall.

The antimicrobial spectrum of C. atropurpureus spans Gram-positive bacteria, Gram-negative bacteria, fungi, and mycobacteria. Gram-positive bacteria have a simpler, single-layered peptidoglycan wall, while Gram-negative bacteria are protected by a complex outer membrane containing lipopolysaccharides, which acts as a formidable barrier against many antimicrobial agents. The density of the lipopolysaccharide in the outer bacterial cell wall layer (Figure 1) is much highter in the Gram-positive strain than Gram-negative strain. They are also found to suppress the growth of M. tuberculosis (Yanto et al. 2020; Marlina et al. 2021;

Pakadang et al. 2022; Rosamarlina et al. 2022). The compound abietane dipertenoids from C. atropurpureus possess anti-MRSA (methicillin-resistant Staphylococcus aureus) activity, showing inhibition zones observed at higher leaf extract concentrations fall within the "moderate to strong" activity range typically used in antimicrobial assays (i.e., >15 mm) (Jurkaninová et al. 2019; Mustarichie et al. 2022). Fungal pathogens such as C. albicans also show moderate susceptibility, broadening the spectrum of activity in opportunistic fungal infections.

When combined with conventional antibiotics such as ciprofloxacin and ampicillin, C. atropurpureus extracts showed synergistic effects. When its extracts are used with conventional antibiotics like ciprofloxacin and ampicillin, they can create a synergistic effect. This not only boosts the overall antimicrobial power but also allows for lower doses of the conventional drug. Findings also suggest that the leaf extract may serve as adjuvant therapy with anti-TB (Tuberculosis) drugs, such as rifampicin (Rosamarlina et al. 2021). This points to a potential role in combination therapy, reducing required doses of antibiotics and potentially delaying drug resistance.

Discussion

Mechanism of Action

Multiple studies confirm the presence of diverse bioactive compounds in C. atropurpureus leaves, including flavonoids (such as quercetin and luteolin), phenolic acids (such as rosmarinic acid), terpenoids (notably abietane-type diterpenoids), tannins, and saponins. These secondary metabolites contribute to the plant's antimicrobial activity through various mechanisms. Although direct mechanisms are not fully studied, suggested theories include disruption of microbial lipid membranes by terpenoids (Mahizan et al. 2019), enzyme inhibition by flavonoid-metal ion chelation (Kejík et al. 2021), reactive oxygen species (ROS) causing oxidative damage (Veiko et al. 2023), and bacteria DNA gyrase inhibition (Górniak et al. 2019). The multi-compound nature of the plant extract allows it to interfere with bacteria through several mechanisms simultaneously. By disrupting these various cellular functions, the active compounds extract can make the bacteria more vulnerable to the effects of a conventional antibiotic, effectively lowering the concentration of the drug needed to achieve a therapeutic effect.

C. atropurpureus may support antimicrobial activity by enhancing the host's immune response. During bacterial infections, inflammation and local tissue hypoxia can increase the expression of HIF-1α a key regulator that boosts immune defense by promoting phagocytosis, nitric oxide synthase (NOS) activity, and the production of antimicrobial peptides

(Ramakrishnan et al. 2014; Yanto et al. 2020). These factors help directly eliminate pathogens. In addition, inflammation stimulates ICAM-1, which facilitates the movement of immune cells to the site of infection, further strengthening the body's defense against microbes (Bhalla et al. 2015).

Terpenoids (isoprenoids) are categorized as monoterpenes, diterpenoids, sesquiterpenes, and others. Terpenes have a lipophilicity tendency to penetrate and destroy bacteria cell wall, resulting in the difference in intra- and extracellular ATP concentration which disrupts the cell membrane, capsules, or biofilms, thus conducting the antibacterial activity (Nazzaro et al. 2013). In general, terpenoids exhibit substantial effects on Gram-positive and Gram-negative strains, with Gram-positive bacteria having greater antimicrobial vulnerability due to differences in membrane structure. They are also found to inhibit the quorum sensing communication system of bacteria coordination. The quorum sensing system is the main reason for the emergence of anitbiotic resistance (Sharma et al. 2020). In addition, terpenoids also work as inhibitors of protein synthesis, and protein denaturing agents, which can achieve an antimicrobial effect.

In vitro study shows that antioxidants, such as flavonoids have been reported to enhance the number of CD4+ T-cells and increase the production of IFN-γ levels, a key cytokine involved in the activation of macrophages and the promotion of cellular immunity (Ullah et al. 2020; Pakadang et al. 2022). IFN-γ is critical in enhancing the antimicrobial functions of immune cells, including the upregulation of phagocytosis and the production of reactive oxygen and nitrogen species (Hosseinzade et al. 2019; Jomova et al. 2025). Flavonoids work by the methylation of the active hydroxyl groups generally eliminated or weakened the bacteria, by inhibiting their metabolism, disrupting the cell wall of bacteria, increasing its cell membrane permeability, and reducing the expression of virulence factors (Tran et al. 2012).

Tannins are a natural and diverse group of phenolic compounds that can bind to and clump together with proteins. (Xu et al. 2017; Farha et al. 2020) They are capable of binding with lipopolysaccharides and destabilize the integrity of the outer membrane and inhibit the biosynthesis of fatty acids.(Delehanty et al. 2007; Wu et al. 2010) Along with saponins, they may precipitate microbial proteins and interfere with membrane integrity or function.(Cui et al. 2018; Abd El-kader et al. 2020; Li and Monje-Galvan 2023) The results of an acute toxicity study indicate that the C. atropurpureus extract exhibits a favorable safety profile in mice, with no observed mortality up to a dose of 5000 mg/kg body weight. This suggests a positive indicator of the extract for further investigation into its safety for human use (Khattak et al. 2011).

Challenges and Future Prospects

Improvements in global health over recent decades are under threat because microorganisms that cause human diseases and medical conditions have become resistant to a wide range of antibiotics. Clinicians need to use last-resort medicines that are more costly, may have more side effects, and are often unavailable of unaffordable in low- and middle-income countries (Organization 2015). The development for new antibiotics has been alarmingly stagnant, with very few novel classes developed, which is a major concern because it allows for the emergence of drug-resistant "superbugs". The misuse and overuse of existing antibiotics are primary drivers, both in healthcare settings and in agriculture. Particularly important gaps in knowledge that need to be filled are understanding how resistance develop in the environment (e.g. the specific pathways and genetic factors that allow bacteria to develop resistance),and exploring new sources of antimicrobial agents for novel drug discovery.

The main challenges of developing C. atropurpureus into a viable antimicrobial agent are the lack of active compounds identification and standardization, proving its safety and effectiveness through clinical trials, and ensuring a sustainable supply. C. atropurpureus extract contains a complex mix of secondary metabolites, but currently the specific compounds responsible for its antimicrobial activity are not fully identified or quantified. The lack of standardized extracts makes it challenging to ensure batch-to-batch consistency in terms of potency and therapeutic efficacy. Further research on isolating and identifying these specific compounds are also needed to understand ther exact mechanisms of action.

While traditional use suggests the plant is safe (Quisumbing 1978; Roosita et al. 2008) research on toxicity studies are still lacking. To be approved as a potential medicine, testing of C. atropurpureus on animal cells to human cells are needed, especially with long term use. The effectiveness of the extracts compound in the human body is also unknown how well they are absorbed, metabolized, and delivered to the site of infection. Most research is at the basic science level. Previous in vitro studies may show strong antibacterial activity, but that does not guarantee the same result in a living organism (in vivo). Large scale controlled clinical studies are then needed to be compared to existing antibiotics. To transition from a fold remedy to a globally recognized medicine, future studies will need to move beyond in vitro lab experiments to large scale clinical human trials.

Despite the aforementioned challenges, future prospects on C. atropurpureus as anovel therapeuticagents are considerable through pharmacological approaches. The complex phytochemcal profile of C. atropurpureus is its greatest strength, as it could provide a source for new drugs that use multi target mechanisms (unlike single compound antibiotics), which

would be harder for microorganisms to develop resistance to. This could then be used to combine purified plant compound with existing antibiotic. This approach provides a cost-effective and potentially less toxic alternative to developing entirely new synthetic drugs, which is a slow and expensive process.

4. KESIMPULAN

C. atropurpureus demonstrates promising antimicrobial activity against a broad spectrum of bacterial pathogens, largely attributed to its rich phytochemical content. Its extracts exhibit both standalone antimicrobial effects and synergistic potential when combined with standard antibiotics.

There is potential for C. atropurpureus to act as an adjuvant therapy alongside conventional antibiotics, however limitations are substantial. First, the limited number of in vivo studies and variability in methodologies across research (e.g. clinical trials) make it difficult to draw definitive conclusions regarding its clinical efficacy. Second, differences in methodologies, such as extraction method and microbial strains create variability that limits cross-study comparability. Third, data on pharmacokinetics, toxicity, and safe dosage are still lacking.

Further research is necessary to evaluate the safety, pharmacokinetics, and efficacy of standardized C. atropurpureus extracts in animal models and clinical trials. Future research should address these gaps by prioritizing standardization of extracts, such as identification of marker compuds for quality control. More in vivo studies are needed, followed by randomized clinical trials and toxicity studies. As resistance continues to rise, plant-based therapeutics should come to consideration.

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