



## Review

Antibacterial Activity of *Avicennia* MangroveYeni Mulyani<sup>a\*</sup>, Yuniar Mulyani<sup>b</sup>, Aisyah Aisyah<sup>b</sup><sup>a</sup>Department of Marine Science, Universitas Padjadjaran<sup>b</sup>Department of Fisheries, Universitas Padjadjaran

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Received 22 March 2025, Revised 14 April 2025, Accepted 17 June 2025, Published 30 September 2025

**Keywords:**antibiotics;  
bioactive;  
drug-resistant;  
environmental;  
secondary  
metabolites.

**ABSTRACT.** The rise of antibiotic resistance presents a major challenge, reducing the efficacy of conventional antibacterial treatments and necessitating the discovery of novel antimicrobial agents. The use of natural products has played a pivotal role in the development of antibiotics. Specifically, marine organisms, with a notable emphasis on mangroves of the genus *Avicennia*, have played a crucial role in this process. *Avicennia marina*, *Avicennia officinalis*, *Avicennia alba*, and *Avicennia germinans* have been found to contain secondary metabolites, including flavonoids, tannins, alkaloids, and terpenoids, which exhibit antibacterial properties against drug-resistant pathogens. The review was conducted based on literature published between 2005 and 2025. These compounds act through diverse mechanisms such as disrupting bacterial cell walls, inhibiting protein synthesis, and interfering with quorum sensing and biofilm formation. Evaluations through disk diffusion, microdilution assay, and biofilm inhibition assays have demonstrated the significant antibacterial activity of *Avicennia* extracts, suggesting their potential as alternative therapeutics in combating resistant bacteria. Future research should focus on enhancing these bioactive compounds' bioavailability, stability, and large-scale production while addressing potential toxicity and navigating the complex regulatory requirements for drug approval. The continued exploration of *Avicennia*-derived compounds may contribute to developing novel antibiotics, offering sustainable solutions to antibiotic resistance.

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## INTRODUCTION

Mangrove forests are vital components of coastal ecosystems that play a crucial role in supporting fisheries and providing various ecological services. These intertidal ecosystems are characterized by unique environmental conditions, including high salinity, fluctuating tides, and low oxygen levels, which have led to the evolution of specialized plant communities, such as *Avicennia* (Nizam *et al.*, 2022). Recent research has highlighted the remarkable potential of bioactive compounds derived from *Avicennia* mangroves as promising agents for antibacterial, antioxidant, and anticancer applications (Cerri *et al.*, 2022; Molaei *et al.*, 2017; Assaw *et al.*, 2020).

**Cite this as:** Mulyani, Y., Mulyani, Y., and Aisyah, A. (2025). Antibacterial Activity of *Avicennia* Mangrove. *ALCHEMY Jurnal Penelitian Kimia*, 21(2), 180-197. doi: [http://dx.doi.org/10.20961/alchemy.21.2.100706.180-197](https://doi.org/10.20961/alchemy.21.2.100706.180-197).

*Avicennia*, commonly known as api-api, is a dominant genus in mangrove forests worldwide, particularly in the Indo-Pacific region (Basyuni *et al.*, 2022). These plants have adapted to thrive in harsh coastal environments and have developed a rich repertoire of secondary metabolites with diverse biological activities (Dahibhate *et al.*, 2019). Traditional communities have long utilized the genus *Avicennia* for various medicinal purposes, providing anecdotal evidence for their therapeutic potential. Scientific investigations have begun to validate these traditional uses, revealing the presence of various bioactive compounds, including alkaloids, flavonoids, tannins, terpenoids, and steroids, within the genus *Avicennia*.

The antibacterial properties of *Avicennia* extracts have been demonstrated against a range of bacterial pathogens, including both Gram-positive and Gram-negative species (Ravikumar *et al.*, 2011). These studies suggest that *Avicennia*-derived compounds may offer a valuable source of novel antibacterial agents, particularly in the face of increasing antibiotic resistance. Furthermore, the antioxidant activity of *Avicennia* extracts has been documented, indicating their potential to protect against oxidative stress and related diseases (Thatoi *et al.*, 2016). The antioxidant properties of these plants are attributed to the presence of various phenolic compounds and other bioactive metabolites.

Beyond their antibacterial and antioxidant activities, the genus *Avicennia* has also shown promising anticancer potential. Studies have demonstrated the cytotoxic effects of *Avicennia* extracts against various cancer cell lines, suggesting their potential use in cancer prevention or treatment (Cerri *et al.*, 2022). The diverse bioactive compounds found in *Avicennia* mangroves, their traditional medicinal uses, and their demonstrated biological activities warrant further investigation into their potential therapeutic applications. A comprehensive understanding of the chemical composition, mechanisms of action, and pharmacological properties of *Avicennia*-derived compounds is essential for their development into effective therapeutic agents. This review is expected to provide an exhaustive overview of the bioactive potential of the *Avicennia* genus, especially antibacterial activities, and a reference point for future research in developing natural material-based medicines.

This review was conducted through a comprehensive literature search using scientific databases such as PubMed, ScienceDirect, and Google Scholar. Relevant studies published in the last two decades (2005 – 2025) were prioritized to ensure up-to-date information on the antibacterial potential of *Avicennia* mangroves. Keywords such as “*Avicennia mangrove* antibacterial,” “mangrove-derived bioactive compounds,” and “marine natural products” were used to retrieve relevant articles. The selected literature was critically analyzed to summarize the key bioactive compounds, their antibacterial mechanisms, and their potential applications. The ecological importance of mangrove conservation and its impact on future drug discovery were also discussed. This review aims to provide an interdisciplinary perspective by integrating microbiology, marine ecology, and pharmacology findings.

## OVERVIEW OF MANGROVES AND THEIR ECOLOGICAL SIGNIFICANCE

Mangrove ecosystems are unique coastal forests found in tropical and subtropical regions, thriving at the interface between land and sea (Md Isa and Suratman, 2021). These ecosystems are dominated by mangrove trees and shrubs that have adapted to saline and waterlogged conditions, enabling them to flourish in environments challenging for most plant species. Mangroves serve as biodiversity hotspots, providing essential habitats for many species, including fish, crustaceans, birds, and other wildlife. Their complex root systems offer shelter and breeding grounds, supporting rich biodiversity (Těšitel *et al.*, 2015). Additionally, mangroves play a crucial role in coastal protection by stabilizing shorelines, reducing erosion, and buffering against storm surges and tsunamis, which help safeguard coastal communities. Furthermore, they are highly effective carbon sinks, sequestering significant amounts of carbon dioxide in their biomass and the surrounding soil, contributing to climate change mitigation.

Mangrove species possess remarkable adaptations that allow them to survive in harsh coastal conditions. Many species have specialized root systems that filter out salt, enabling them to take up freshwater in saline environments (Kim *et al.*, 2016). Structures such as pneumatophores, or aerial roots, facilitate gas exchange in waterlogged soils, ensuring the plants receive necessary oxygen. Some mangrove species also exhibit vivipary, where seeds germinate while still attached to the parent tree, allowing seedlings to establish quickly upon dispersal. These specialized traits reflect the unique biology of individual mangrove species and contribute to the formation of complex and dynamic ecosystems. Mangrove forests, composed of diverse plant species adapted to intertidal zones, provide essential habitats for many marine and terrestrial organisms.

Despite their ecological importance, mangrove ecosystems face several threats. Deforestation due to aquaculture, agriculture, and urban development has led to significant habitat loss (Horváth *et al.*, 2019). Climate change further exacerbates the situation, as rising sea levels, increased storm frequency, and altered precipitation

patterns pose risks to mangrove health and distribution. Additionally, mangroves are susceptible to pollution from land-based sources, including agricultural runoff and plastic debris, which can degrade these habitats (Suyadi and Manullang, 2020). Understanding and preserving mangrove ecosystems are crucial for maintaining coastal biodiversity, protecting shorelines, and mitigating climate change impacts.

Mangroves play a critical role in coastal protection and climate regulation. The intricate root systems of mangrove forests act as natural barriers by stabilizing shorelines, dissipating wave energy, and reducing the impact of coastal erosion and storm surges (Spencer *et al.*, 2013). This function is especially vital as climate change and rising sea levels increase the frequency and severity of coastal hazards. In addition to protecting coastlines, mangroves are highly effective carbon sinks, sequestering large amounts of atmospheric carbon within their biomass and sediments (Zhu and Yan, 2022). This ability to store carbon helps combat climate change and supports a diverse array of wildlife, providing habitat for numerous fish species, birds, and other organisms that rely on these unique ecosystems for survival.

Beyond their role in physical and climatic resilience, mangrove ecosystems are essential biodiversity hotspots that support a wide array of species (Carugati *et al.*, 2018). They provide critical habitats and nursery grounds for numerous marine and terrestrial organisms, including juvenile fish, crustaceans, and migratory birds, which are fundamental to sustaining local fisheries and maintaining ecological balance (Whitfield, 2020). The rich biodiversity within these ecosystems enhances ecosystem productivity and resilience and underpins the livelihoods of communities that depend on coastal resources (Steenbergen *et al.*, 2017). Such ecosystems are increasingly threatened by human activities and climate change, necessitating urgent conservation efforts to protect their integrity and the myriad of life forms they support.

### ***Avicennia* Genus: A Key Mangrove Species**

The genus *Avicennia* belongs to the family Acanthaceae and comprises several species of mangroves widely distributed in tropical and subtropical coastal regions. The most common species include *Avicennia marina*, *Avicennia officinalis*, and *Avicennia germinans*, which are found along the coasts of Asia, Africa, Australia, and the Americas (Thatoi *et al.*, 2016). These species dominate intertidal zones, where they thrive in estuarine and coastal environments with fluctuating salinity levels. The ability of *Avicennia* to colonize such habitats is attributed to their physiological and morphological adaptations that enable them to withstand high salinity, tidal inundation, and anaerobic soil conditions (Asaf *et al.*, 2021). Their widespread distribution makes them ecologically significant, as they play a crucial role in stabilizing coastal areas and providing habitat for marine and terrestrial species.

One of the most remarkable adaptations of *Avicennia* to saline environments is its specialized salt-exclusion mechanism. Unlike other mangrove species that excrete salt through leaf glands, *Avicennia* primarily relies on salt filtration at the root level. The roots selectively absorb freshwater while blocking the uptake of excess salts, allowing the plant to maintain a balanced internal salinity (Taffouo *et al.*, 2006). *Avicennia marina*, possess salt glands on their leaves that excrete excess salt, which crystallizes and can be washed away by rain or wind (EIDohaji *et al.*, 2020). This dual mechanism enables *Avicennia* to survive in hypersaline conditions where few other plant species can thrive. Another key adaptation of *Avicennia* is its specialized root system, which includes pneumatophores—vertical aerial roots that protrude above the soil surface to facilitate gas exchange in oxygen-deficient mudflats (Figure 1). These roots contain specialized lenticels that allow the uptake of atmospheric oxygen, compensating for the anoxic conditions of waterlogged soils. Additionally, *Avicennia* exhibits viviparous seed germination, meaning seeds begin to develop into seedlings while still attached to the parent tree (Yan *et al.*, 2015). Once mature, these propagules detach and float until they find a suitable substrate for establishment. This reproductive strategy increases the chances of successful colonization in dynamic coastal environments, ensuring the persistence of *Avicennia* populations despite harsh conditions.



**Figure 1.** *Avicennia* mangrove.

This adaptation enhances survival rates and plays a crucial role in stabilizing shorelines and providing habitat for diverse marine life, contributing to the overall health of coastal ecosystems. The ability of *Avicennia* to thrive in saline conditions further underscores its importance as a keystone species in mangrove ecosystems, supporting biodiversity and coastal resilience (Triest *et al.*, 2021). The intricate relationship between *Avicennia* and its environment highlights the need for conservation efforts to protect these vital ecosystems from threats such as climate change, pollution, and urban development (Luna *et al.*, 2018). Effective conservation strategies must focus on restoring degraded mangrove habitats and implementing sustainable management practices that ensure the long-term survival of *Avicennia* populations and the myriad species they support.

### **Mangroves Natural Products and Their Potential**

Marine natural chemistry is a branch of natural product chemistry that studies bioactive compounds derived from marine organisms such as bacteria, fungi, mangroves, algae, sponges, and corals. The marine environment is characterized by extreme conditions, including high salinity, variable pressure, and unique ecological interactions, which drive the evolution of structurally diverse and biologically active secondary metabolites. (Sahu *et al.*, 2022). These natural products often possess novel chemical scaffolds that differ from those found in terrestrial organisms, making them a valuable source for biomedical research and pharmaceutical development (Marrero, 2016). Over the past few decades, mangrove-derived compounds have attracted significant attention for their potential applications in medicine, agriculture, and biotechnology. Mangroves are a type of salt-tolerant plant that form distinctive ecosystems and communities to survive in a harsh environment. There is evidence to suggest that mangroves produce a number of phytochemicals. Mangrove-derived natural products have garnered significant attention due to the unique chemical diversity in these coastal ecosystems, characterized by their saline and anaerobic environments. These conditions have led to the evolution of distinctive bioactive compounds with promising pharmaceutical and industrial applications. Various mangrove species have been reported to produce a wide range of secondary metabolites, including alkaloids, flavonoids, tannins, terpenoids, and phenolic compounds, exhibiting antimicrobial, antioxidant, anti-inflammatory, and anticancer properties. Such discoveries highlight mangroves as a valuable and underexplored reservoir of novel natural products with potential therapeutic benefits, paving the way for more focused studies on specific genera like *Avicennia* to uncover unique bioactive molecules.

In addition to their ecological significance, *Avicennia* mangroves play a crucial role in coastal protection and biodiversity conservation. These salt-tolerant plants create vital habitats for marine species, including fish, crabs, and mollusks, which thrive in their detritus-rich environments (Fajri *et al.*, 2023). Furthermore, the unique phytochemical profiles of *Avicennia* species contribute not only to their resilience against harsh environmental conditions but also to their potential medicinal applications; extracts from these mangroves have been shown to



exhibit antimicrobial and anti-inflammatory properties, highlighting their value beyond mere ecosystem services (Beniwal *et al.*, 2024). As such, preserving these mangrove ecosystems is essential for maintaining ecological balance and harnessing future pharmaceutical advancements that could emerge from their bioactive compounds.

*Avicennia* is a promising source of bioactive compounds due to its rich phytochemical profile, which includes various secondary metabolites with potent biological activities (Thatoi *et al.*, 2016). This genus of *Avicennia* contains flavonoids, alkaloids, tannins, saponins, and terpenoids, which have been reported to exhibit antimicrobial, antioxidant, anti-inflammatory, and anticancer properties. Studies have shown that *Avicennia* species, such as *Avicennia marina* and *Avicennia officinalis*, produce unique bioactive compounds that can inhibit the growth of pathogenic bacteria and fungi (Mahera *et al.*, 2013). These antimicrobial properties make *Avicennia* a potential candidate for developing natural alternatives to synthetic antibiotics, especially in addressing the growing issue of antibiotic resistance.

In addition to its antimicrobial potential, *Avicennia* has demonstrated strong antioxidant activity, which is essential in preventing oxidative stress-related diseases such as cancer, cardiovascular disorders, and neurodegenerative conditions (Sadoughi and Hosseini, 2020). The presence of phenolic compounds and flavonoids in *Avicennia* contributes to its ability to neutralize free radicals, reducing cellular damage and inflammation (Cheniti *et al.*, 2022). Furthermore, research indicates that some bioactive compounds derived from *Avicennia* possess cytotoxic effects against cancer cells, suggesting potential applications in cancer therapy. These findings highlight the significance of *Avicennia* in pharmaceutical research and its potential for drug development.

Beyond human medicine, the bioactive compounds in *Avicennia* also have applications in aquaculture and environmental biotechnology. Extracts from *Avicennia* have been explored as natural antifouling agents to prevent biofilm formation in aquatic systems, reducing the risk of infections in fish farming. (Ramzi *et al.*, 2023) Additionally, the plant's antibacterial properties could control pathogenic bacteria in aquaculture, minimizing the dependence on synthetic antibiotics, contributing to antimicrobial resistance (Hudecová *et al.*, 2023). The diverse pharmacological potential of *Avicennia* makes it a valuable natural resource for developing bio-based therapeutics, contributing to both human health and sustainable environmental management.

### Antibacterial Resistance and the Need for Novel Compounds

Antibiotic resistance has become a major global health challenge, threatening the effectiveness of existing treatments for bacterial infections. The overuse and misuse of antibiotics in human medicine, animal husbandry, and agriculture have accelerated the evolution of drug-resistant bacteria, rendering many conventional antibiotics ineffective. Pathogens such as *Methicillin-resistant Staphylococcus aureus* (MRSA), *Carbapenem-resistant Enterobacteriaceae* (CRE), and *Multidrug-resistant Pseudomonas aeruginosa* have emerged as significant threats, leading to increased morbidity, mortality, and healthcare costs (Bobbarala *et al.*, 2009). The World Health Organization (WHO) has classified antibiotic resistance as one of the top global public health concerns, emphasizing the urgent need for new antimicrobial agents to combat resistant pathogens (Aslam *et al.*, 2021).

Natural products have historically played a crucial role in discovering new antibiotics, as many of the most effective antibacterial agents, including penicillin, streptomycin, and tetracyclines, were originally derived from microorganisms (Alrubaye *et al.*, 2024). Unlike synthetic compounds, natural products often exhibit unique structural diversity and complex mechanisms of action, making them valuable in the fight against resistant bacteria. Marine ecosystems, in particular, have emerged as a promising source of novel bioactive compounds with antibacterial properties. Many marine organisms, such as sponges, fungi, and mangroves like *Avicennia* genus, produce secondary metabolites that have evolved as chemical defenses against microbial competition in their environments (Srinivasan *et al.*, 2021). Avicennones A & C, stenocarproquinone B, avicennones E & F isolated from the twigs of *A. marina* showed significant antimicrobial activities against *Mycobacteria* species, *Staphylococcus aureus*, and *Candida albicans* (EIDohaji *et al.*, 2020). These natural compounds have the potential to be developed into new antibiotics with novel mechanisms of action to overcome bacterial resistance.

*Avicennia* species have gained attention in antibacterial research due to their production of diverse bioactive compounds with potent antimicrobial activity. Extracts from *Avicennia marina* and *Avicennia officinalis* have been shown to exhibit inhibitory effects against both Gram-positive and Gram-negative bacteria, including drug-resistant strains. The presence of flavonoids, tannins, alkaloids, and terpenoids in *Avicennia* contributes to its antibacterial properties by disrupting bacterial cell membranes, inhibiting protein synthesis, or interfering with quorum sensing (Alrubaye *et al.*, 2024). Given the growing demand for alternative antimicrobial agents, further

exploration of *Avicennia* and other marine-derived natural products could lead to new antibiotics capable of addressing antibiotic resistance.

To fully harness the potential of natural products in antibacterial drug discovery, interdisciplinary approaches integrating marine biology, organic chemistry, pharmacology, and biotechnology are essential. Advances in genome mining, metabolomics, and synthetic biology have enabled researchers to identify and optimize bioactive compounds for pharmaceutical development. (France *et al.*, 2023) Sustainable sourcing methods, such as microbial fermentation and genetic engineering, can help scale up the production of promising antimicrobial compounds while minimizing environmental impact. As antibiotic resistance continues to rise, exploring natural products, particularly from marine ecosystems, remains a vital strategy in developing novel antibiotics to safeguard global health.

## PHYTOCHEMISTRY OF GENUS *AVICENNIA*

### Bioactive Compounds in *Avicennia*

Mangrove plants, including those from the *Avicennia* genus, are rich in secondary metabolites that play a significant role in their ecological adaptation and pharmacological properties. These bioactive compounds, including flavonoids, tannins, saponins, and terpenoids, have been widely studied for their antimicrobial, antioxidant, and anti-inflammatory effects (Habib *et al.*, 2018). Secondary metabolites serve as chemical defenses against microbial infections, herbivory, and environmental stress, making *Avicennia* a promising source of novel bioactive compounds for pharmaceutical applications (Miclea, 2022). Among the various bioactive classes, flavonoids are known for their antioxidant and antimicrobial properties, tannins exhibit astringent and antibacterial activities, saponins disrupt bacterial membranes, and terpenoids interfere with bacterial quorum sensing and biofilm formation.

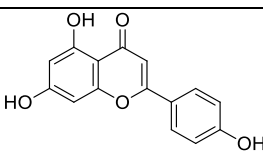
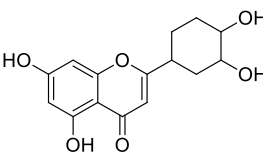
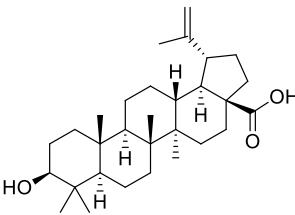
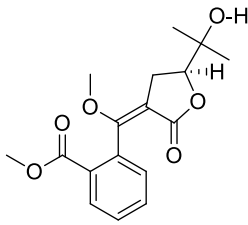
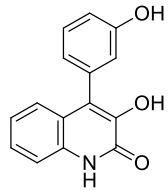
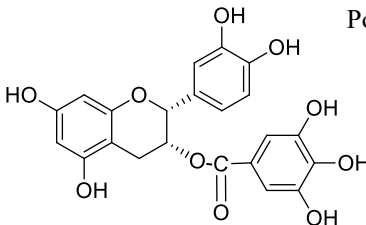
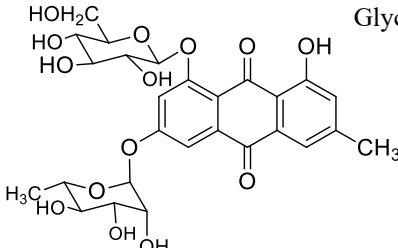
Several specific bioactive compounds have been isolated from different *Avicennia* species, demonstrating significant antibacterial activity (Al-Mur, 2021). For example, flavonoids such as apigenin and luteolin have been extracted from *Avicennia marina* and have shown inhibitory effects against pathogenic bacteria. Alkaloids and tannins identified in *Avicennia officinalis* have exhibited broad-spectrum antibacterial properties, particularly against drug-resistant *Staphylococcus aureus* and *Escherichia coli* (Qin *et al.*, 2023). Additionally, terpenoids such as betulinic acid and avicenone have demonstrated strong antimicrobial potential by targeting bacterial cell walls and membranes. These compounds highlight the potential of *Avicennia* as a natural source for developing novel antibiotics and antimicrobial agents (Salin *et al.*, 2010). Table 1 overviews some key bioactive compounds isolated from *Avicennia* species and their reported antibacterial activities.

These findings demonstrate the antibacterial potential of *Avicennia* species and underscore their relevance in drug discovery efforts. Further research into the isolation, characterization, and mechanism of action of these compounds could contribute to developing new antimicrobial agents, addressing the urgent need for alternatives to conventional antibiotics.

### Variability in Chemical Composition

The chemical composition of *Avicennia* species is highly variable and influenced by environmental factors such as salinity, geography, temperature, and nutrient availability. Mangrove ecosystems exist in dynamic and often harsh coastal environments, where fluctuations in these factors drive plant metabolic adaptations. High salinity can enhance the production of osmoprotective compounds like flavonoids and tannins, which help *Avicennia* tolerate salt stress while exhibiting antibacterial properties (Riseh *et al.*, 2021). Similarly, geographical differences, such as variations in soil composition and climatic conditions, can lead to differences in the types and concentrations of secondary metabolites produced by different populations of *Avicennia* (Karimi *et al.*, 2020). Studies have shown that plants growing in high-salinity environments tend to produce higher concentrations of phenolic compounds than other metabolites, such as terpenoids, which contribute to their defense against microbial infections and herbivory (Table 2).

**Table 1.** The bioactive compounds isolated from *Acivennia*.

Bioactive Compound	Chemical Structure	Compound Class	Source Species	Antibacterial Activity
Apigenin		Flavonoid	<i>Avicennia marina</i>	Demonstrated inhibitory activity against <i>Escherichia coli</i> and <i>Staphylococcus aureus</i> . The MIC values for <i>Pseudomonas aeruginosa</i> , <i>Bacillus subtilis</i> , <i>S. aureus</i> , and <i>E. coli</i> were $10.8 \pm 0.78$ mg/mL, $6.1 \pm 0.27$ mg/mL, $2.3 \pm 0.08$ mg/mL, and $6.3 \pm 0.28$ mg/mL, respectively (Okla et al., 2021).
Luteolin		Flavonoid	<i>Avicennia marina</i>	Exhibited antimicrobial activity against Gram-positive bacteria. The MIC values were 0.064–0.128 mg/mL for <i>S. aureus</i> and 1.0 mg/mL for <i>E. coli</i> (Devi et al., 2016).
Betulinic Acid		Terpenoid	<i>Avicennia officinalis</i>	Acts by disrupting bacterial cell membranes. The MIC values against <i>E. coli</i> , <i>P. aeruginosa</i> , and <i>S. aureus</i> were each 256 µg/mL (Oloyede et al., 2017)
Avicenone A		Terpenoid	<i>Avicennia alba</i>	Inhibits bacterial biofilm formation. The inhibition zone diameters for high, medium, and low concentration groups were $26.72 \pm 0.36$ mm, $21.84 \pm 0.57$ mm, and $14.82 \pm 0.19$ mm, respectively (Tao et al., 2021).
4-chlorophenylbiguanide		Alkaloid	<i>Avicennia officinalis</i>	Demonstrated broad-spectrum antibacterial activity. EB and EL extracts showed stronger antibacterial effects against <i>P. aeruginosa</i> (MIC: 100 µg/mL) compared to <i>B. subtilis</i> , <i>E. coli</i> , and <i>S. aureus</i> (MIC: 200 µg/mL) (Das et al., 2018).
Epigallocatechin ester		Polyphenol	<i>Avicennia marina</i>	Demonstrated effective antibacterial activity against <i>Staphylococcus aureus</i> and <i>Escherichia coli</i> . The MIC values for <i>Pseudomonas aeruginosa</i> , <i>Bacillus subtilis</i> , <i>S. aureus</i> , and <i>E. coli</i> were $10.8 \pm 0.78$ mg/mL, $6.1 \pm 0.27$ mg/mL, $2.3 \pm 0.08$ mg/mL, and $6.3 \pm 0.28$ mg/mL, respectively (Okla et al., 2021).
Kaempferol-3-O-rutinoside.		Glycoside	<i>Avicennia marina</i>	Disrupts bacterial cell walls (Aderiye and Oluwole, 2015).

The study by Rahmania et al. (2024) emphasizes the remarkable diversity of bioactivities and medicinal uses among various *Avicennia*, shaped by their geographical distribution and unique phytochemical profiles. *Avicennia bicolor*, endemic to the Pacific coasts of Central and South America, contains bioactive compounds such as quercetin, kaempferol, triterpenoids, and alkaloids with antimicrobial and antioxidant properties, traditionally used

for treating wounds and skin infections. *Avicennia alba*, distributed across Asia and northern Australia, is rich in flavonoids and diterpenes that exhibit antiviral, larvicidal, and cytotoxic effects, suggesting its potential in research on herpes simplex virus (HSV) therapies and mosquito control products. *A. officinalis*, prevalent in Asia and northern Australia, is known for its content of naphthoquinones, gallic acid, and phenolics with hepatoprotective, anti-tumor, and radioprotective activities, making it a promising candidate for liver disease and cancer treatment development. *Avicennia schaueriana*, native to the Caribbean, contains vitexin and taraxerol, which show cardioprotective and anti-inflammatory effects; vitexin is currently under investigation for ischemic injury therapies.

**Table 2.** Antibacterial potential of genus *Avicennia* and their bioactive compounds.

Species	Key Bioactive Compounds	Environmental Influence	Antibacterial Activity
<i>Avicennia marina</i>	Flavonoids (apigenin, luteolin), saponins, tannins (Sharaf <i>et al.</i> , 2000)	High salinity enhances flavonoid production	Inhibits <i>E. coli</i> , <i>S. aureus</i>
<i>Avicennia officinalis</i>	Alkaloids, tannins, betulinic acid (Yi <i>et al.</i> , 2014)	Nutrient-rich environments increase alkaloid content	Effective against drug-resistant <i>S. aureus</i> , <i>E. coli</i>
<i>Avicennia alba</i>	Terpenoids (avicenone), flavonoids (Zheng <i>et al.</i> , 2016)	Warm coastal regions promote terpenoid synthesis	Disrupts bacterial biofilm formation
<i>Avicennia germinans</i>	<i>Avicennia germinans</i> Phenolics, tannins, steroids (Spinaci <i>et al.</i> , 2019)	Muddy, low-oxygen environments increase tannin levels	Broad-spectrum antibacterial activity

Several other species also offer unique pharmacological potential. Australian endemics such as *A. balanophora* and *A. integra* produce distinctive triterpenoids with antimicrobial, antioxidant, UV-protective, and nematocidal properties. *A. germinans*, found in the Americas and West Africa, contains iridoids, lupeol, betulinic acid, and flavonoids; it is traditionally used for treating malaria and snakebites, while betulinic acid is currently in clinical trials for melanoma therapy. The most widespread species, *Avicennia marina*, spanning from Asia to the Middle East, is known for its naphthoquinones (e.g., avicenone C), limonoids, and quercetin, offering antimicrobial, antioxidant, and antidiabetic benefits. This species is used in traditional and modern medicine, including as a diabetes supplement (via  $\alpha$ -glucosidase inhibition), UV-protective cosmetic ingredient, and nutraceutical. Overall, the chemical diversity across the genus *Avicennia* underscores their strong potential as a plant-based source for mangrove-derived bio-pharmaceutical innovations.

These findings emphasize that environmental conditions and geographical distribution play a crucial role in shaping the chemical composition of *Avicennia* species. Understanding these variations can help optimize the extraction of specific bioactive compounds for pharmaceutical and industrial applications, ensuring a sustainable approach to utilizing mangrove-derived natural products.

## ANTIBACTERIAL ACTIVITY OF *AVICENNIA* EXTRACTS

### Methods for Evaluating Antibacterial Activity

The antibacterial activity of *Avicennia* extracts is commonly evaluated using standardized microbiological assays that measure their effectiveness against bacterial pathogens. One of the most frequently used methods is the disk diffusion assay, where filter paper disks soaked with plant extracts are placed on an agar plate inoculated with bacteria. The formation of a clear zone around the disk, known as the inhibition zone, indicates antibacterial activity. Another widely used method is the microdilution method, which determines the lowest concentration of an extract that inhibits bacterial growth (Tiwari *et al.*, 2022). The minimum bactericidal concentration (MBC) test further assesses the ability of an extract to kill bacteria rather than just inhibiting growth. These methods provide quantitative and qualitative data on the potency of *Avicennia* extracts as natural antibacterial agents (Alsaadi *et al.*, 2022).

Various bacterial species are used as model organisms in antibacterial studies to evaluate the broad-spectrum activity of *Avicennia* extracts. Gram-negative bacteria such as *Escherichia coli* and *Pseudomonas aeruginosa* are commonly tested due to their intrinsic resistance mechanisms, such as efflux pumps and outer membrane barriers, which make them challenging to treat with conventional antibiotics (Davin-Regli *et al.*, 2021). Gram-positive bacteria, including *Staphylococcus aureus* and *Bacillus subtilis*, are also frequently studied since their simpler cell



wall structure often makes them more susceptible to antibacterial compounds. Including Gram-positive and Gram-negative bacteria in experimental studies ensures that the extracts are tested against a wide range of bacterial targets, improving their potential for future pharmaceutical applications.

Recent studies on the genus *Avicennia* have demonstrated significant antibacterial activity against both antibiotic-sensitive and drug-resistant bacterial strains (Manilal et al., 2016; Mitra et al., 2021). Methanolic and ethanolic extracts of *Avicennia marina* have been found to exhibit strong inhibitory effects against *S. aureus* and *E. coli*, with large inhibition zones observed in disk diffusion assays (Karthi et al. 2020). Similarly, alkaloid-rich extracts from *Avicennia officinalis* have shown potent bactericidal activity against *P. aeruginosa*, a pathogen known for its resistance to multiple antibiotics (Yan et al., 2021). The mechanism of action of these extracts varies depending on the bioactive compounds present, with some targeting bacterial cell walls, while others interfere with protein synthesis or disrupt biofilm formation.

Evaluating *Avicennia* extracts using well-established antibacterial assays is crucial for identifying promising candidates for further pharmaceutical development. Advances in bioassay techniques, such as microdilution assays and time-kill studies, are improving the accuracy and reliability of antibacterial screening. Additionally, combining plant extracts with existing antibiotics in synergy studies has shown potential in enhancing bacterial susceptibility, reducing the likelihood of resistance development. As research into *Avicennia* and other mangrove-derived bioactive compounds continues, refining these methods will be essential for translating laboratory findings into clinical and industrial applications.

Several methods have been employed to evaluate the antibacterial activity of *Avicennia* extracts, each offering specific insights into their efficacy. One commonly used technique is the disk diffusion assay, where filter paper disks impregnated with plant extracts are placed on agar plates inoculated with bacteria. The resulting zone of inhibition, measured in millimeters, indicates antibacterial activity, and this method has been applied against organisms such as *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Bacillus subtilis* (Mansur-Azzam et al., 2014). Another method is the minimum inhibitory concentration (MIC) assay, typically performed using broth microdilution techniques. This approach determines the lowest concentration of extract that can inhibit visible bacterial growth, with MIC values expressed in µg/mL or mg/mL. Studies using this method have tested bacteria including *E. coli*, *S. aureus*, *P. aeruginosa*, and *Salmonella* spp. (Shin et al., 2016). The minimum bactericidal concentration (MBC) test is purposed to assess bactericidal properties. This method identifies the lowest concentration of extract that kills bacteria by plating treated cultures and observing bacterial viability, commonly targeting *E. coli*, *S. aureus*, and *P. aeruginosa* (Bindu et al., 2014). The time-kill assay offers a dynamic view by measuring the reduction in colony-forming units (CFU/mL) over time after exposure to the extract, typically involving *E. coli* and *S. aureus* (Bolotsky et al., 2020). Lastly, the biofilm inhibition assay is employed to examine the ability of extracts to prevent or disrupt bacterial biofilms. This method measures the percentage of biofilm reduction and is particularly useful against *P. aeruginosa* and *S. aureus* (Idir et al., 2022).

### Key Findings from Recent Studies

Recent studies have demonstrated that *Avicennia* extracts possess significant antibacterial activity against both Gram-positive and Gram-negative bacteria (Table 3). Various bioactive compounds, including flavonoids, alkaloids, tannins, and terpenoids, contribute to this antibacterial potential by targeting bacterial cell walls, inhibiting protein synthesis, or disrupting biofilm formation. Extracts from *A. marina*, *A. officinalis*, and *A. alba* have been widely studied, with promising results against multiple bacterial pathogens. Research has shown that methanolic and ethanolic extracts exhibit stronger antibacterial effects than aqueous extracts, likely due to the better solubility of active compounds in organic solvents.

A comparison of antibacterial activity between Gram-positive and Gram-negative bacteria reveals notable differences. In general, *Avicennia* extracts tend to be more effective against Gram-positive bacteria, such as *Staphylococcus aureus* and *Bacillus subtilis* (Mitra et al., 2022). This is primarily due to the simpler peptidoglycan layer in Gram-positive bacterial cell walls, allowing for easier bioactive compound penetration. Studies using disk diffusion and MIC assays have reported significant inhibition zones and low MIC values for Gram-positive strains, indicating high susceptibility to *Avicennia* extracts.

On the other hand, Gram-negative bacteria, including *Escherichia coli* and *Pseudomonas aeruginosa*, tend to be more resistant due to their outer membrane, which acts as a barrier to many antimicrobial agents. However, certain extracts from *Avicennia* species have shown promising results against these bacteria. For example, alkaloid-rich extracts from *Avicennia officinalis* and terpenoid compounds from *Avicennia alba* have demonstrated

bactericidal effects against *P. aeruginosa*, a pathogen known for its multidrug resistance. Additionally, biofilm inhibition assays have indicated that *Avicennia* extracts can disrupt biofilm formation in both Gram-positive and Gram-negative bacteria, which is crucial in overcoming antibiotic resistance (Ratha et al., 2021).

**Table 3.** Antibacterial activity of *Avicennia* species extracts against gram-positive and gram-negative bacteria.

Species	Extracted Part	Extraction Solvent	Gram-Positive Bacteria ( <i>S. aureus</i> , <i>B. subtilis</i> )	Gram-Negative Bacteria ( <i>E. coli</i> , <i>P. aeruginosa</i> )	Source
<i>Avicennia marina</i>	Leaves	Ethanol	Inhibition zone against <i>S. aureus</i> : 12.20 ± 2.12 mm (1,000 mg/mL) Positive	Inhibition zone against <i>E. coli</i> : 8.13 ± 0.42 mm (1,000 mg/mL) Positive	(Alhaddad et al., 2019)
<i>Avicennia marina</i>	Leaves	96% Ethanol	antibacterial activity against <i>S. aureus</i> : 20,25 ± 2.25 mm Positive	antibacterial activity against <i>E. coli</i> : 19 ± 0 Positive	(Putri, 2024)
<i>Avicennia marina</i>	Leaves	30% Ethanol	antibacterial activity against <i>S. aureus</i> : 23 ± 1	antibacterial activity against <i>E. coli</i> : 19,75 ± 0,25	(Putri, 2024)
<i>Avicennia alba</i>	Leaves and Stem	Not reported	Inhibition zone against <i>S. aureus</i> : 5.13 ± 0.50 mm (100% concentration)	Inhibition zone against <i>P. aeruginosa</i> : 5.05 ± 0.69 mm (100% concentration)	(Purba et al., 2022)
<i>Avicennia marina</i>	Young Leaves	NADES (Citric Acid:Glucose)	Inhibition zone against <i>S. aureus</i> : 28.69 mm Positive	Inhibition zone against <i>E. coli</i> : 30.99 mm Positive	(Kartikaningsih et al., 2024)
<i>Avicennia marina</i>	Leaves	n-Hexane, Ethyl Acetate, Ethanol	antibacterial activity; Ethyl acetate extract: <i>S. aureus</i> : 16.97 ± 1.15 mm	antibacterial activity; Ethyl acetate extract: <i>E. coli</i> : 14.40 ± 0.46 mm	(Alhaddad et al., 2019)
<i>Avicennia marina</i>	Bark	Methanol	Inhibition zone against <i>S. aureus</i> : 7.56 mm	Inhibition zone against <i>E. coli</i> : 25.28 mm	(Renaldi et al., 2018)

Overall, these findings highlight the potential of *Avicennia* as a natural source of antibacterial agents, particularly against Gram-positive pathogens. However, the ability of certain *Avicennia* compounds to target drug-resistant Gram-negative bacteria suggests that further research into their mechanisms of action is warranted. Optimizing extraction techniques and exploring synergistic effects with conventional antibiotics could enhance the therapeutic applications of *Avicennia* extracts in combating bacterial infections. Table 3 summarizes key findings from recent studies on the antibacterial activity of *Avicennia* extracts against Gram-positive and Gram-negative bacteria. Table 3 highlights that *Avicennia* extracts, particularly from *A. marina*, exhibit antibacterial activity against Gram-positive bacteria such as *Staphylococcus aureus* and Gram-negative bacteria such as *Escherichia coli*. The effectiveness of the extracts varies depending on the plant part used and the solvent employed for extraction.

### Mechanisms of Action

The antibacterial activity of *Avicennia* extracts is attributed to the presence of bioactive compounds that interfere with essential bacterial processes. Several proposed mechanisms explain how these extracts exert their effects, including cell wall disruption, inhibition of protein synthesis, and interference with bacterial metabolic pathways. One of the primary mechanisms is cell wall disruption, where bioactive compounds such as flavonoids, tannins, and terpenoids destabilize the bacterial cell membrane. This disruption leads to increased permeability, loss of essential intracellular components, and cell lysis. Polyphenolic compounds, such as tannins, have been

reported to form complexes with bacterial proteins, affecting membrane integrity and inhibiting bacterial growth (Virtanen *et al.*, 2023).

Another significant mechanism involves inhibiting protein synthesis, where bioactive compounds interfere with bacterial ribosomes, preventing the translation of essential proteins. For example, flavonoids are known to bind to bacterial ribosomes, disrupting the elongation phase of protein synthesis. This inhibition leads to impaired bacterial growth and replication (Donadio *et al.*, 2021). Additionally, specific compounds in *Avicennia* extracts play crucial roles in antibacterial activity. For instance, alkaloids and saponins have been found to interfere with bacterial enzyme systems, affecting metabolic pathways necessary for bacterial survival. Terpenoids and essential oils, commonly found in *Avicennia* species, exhibit antimicrobial activity by disrupting quorum sensing, a bacterial communication process essential for biofilm formation and virulence (Alsaadi *et al.*, 2022).

## APPLICATIONS AND POTENTIAL

### Pharmaceutical Applications

The increasing threat of antibiotic resistance has intensified the search for new antimicrobial agents, and natural products from mangrove plants, particularly *Avicennia* species, have shown promising potential in this regard. The bioactive compounds found in *Avicennia*, such as flavonoids, tannins, alkaloids, terpenoids, and saponins, exhibit strong antibacterial properties and could serve as the foundation for novel antibiotic development. These compounds have demonstrated efficacy against Gram-positive and Gram-negative bacteria, including drug-resistant strains like *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

One of the key advantages of *Avicennia* compounds is their diverse mechanisms of action, which differ from conventional antibiotics. For instance, flavonoids and tannins disrupt bacterial cell walls, while alkaloids interfere with protein synthesis. This diversity in antibacterial action makes *Avicennia* extracts a valuable resource for overcoming resistance mechanisms developed by pathogens (Djeussi *et al.*, 2013). Additionally, the specific terpenoids found in *Avicennia* species have been shown to inhibit biofilm formation, which is a major factor in bacterial resistance to existing antibiotics.

Further research and clinical studies are necessary to isolate and optimize these bioactive compounds for pharmaceutical applications. Advances in biotechnology, such as nanotechnology-based drug delivery systems and synthetic modifications of natural molecules, could enhance the efficacy and stability of *Avicennia*-derived antibiotics. If successfully developed, these compounds could contribute to a new generation of antimicrobial drugs, addressing the global antibiotic resistance crisis while utilizing sustainable natural resources (Table 4).

### Ecological and Environmental Applications

The application of *Avicennia* extracts in aquaculture has gained significant interest due to their potent antibacterial properties. In aquaculture, bacterial infections are caused by pathogens such as *Vibrio spp.*, *Aeromonas spp.*, and *Pseudomonas spp.* can lead to high mortality rates, reduced production, and economic losses. The bioactive compounds found in *Avicennia*, including flavonoids, tannins, alkaloids, and terpenoids, exhibit strong antimicrobial activity, making them a promising natural alternative to conventional antibiotics. The use of *Avicennia* extracts could help reduce dependency on synthetic antibiotics, thereby minimizing the risk of antibiotic resistance development in aquatic environments (Ramasubburayan *et al.*, 2024).

Beyond direct antibacterial effects, *Avicennia* extracts may also serve as immunostimulants in fish and shrimp. Studies have shown that plant-derived bioactive compounds can enhance the immune responses of cultured species, increasing their resistance to infections. This natural approach aligns with sustainable aquaculture practices by improving the overall health of aquatic organisms without introducing harmful chemical residues into the environment. Additionally, plant-based treatments reduce the risk of antibiotic contamination in aquaculture products, ensuring food safety for consumers.

Aside from disease control, *Avicennia* species also contribute to bioremediation, a process that uses natural organisms to remove pollutants from aquatic environments (Mondal *et al.*, 2019). Mangroves, including *Avicennia*, play a crucial role in absorbing and filtering heavy metals, excess nutrients, and organic pollutants from water bodies. Extracts from *Avicennia* have been studied for their ability to break down harmful microbial populations and organic waste in aquaculture ponds, thus improving water quality. This function is particularly important in intensive aquaculture systems, where high organic matter accumulation can lead to poor water conditions and disease outbreaks.

**Table 4.** Challenges in drug development.

Challenge	Description	Potential Solutions
Toxicity	Some bioactive compounds from <i>Avicennia</i> may exhibit cytotoxic effects on human cells, limiting their therapeutic use (Butala et al., 2021).	Conduct thorough toxicity screening, adjust dosages, and modify chemical structures to enhance safety.
Bioavailability	Poor solubility and absorption of plant-derived compounds in the human body can reduce their effectiveness (Hu et al., 2022).	Improve formulation using nanotechnology (e.g., nanoparticles, liposomes) and enhance solubility through chemical modifications.
Stability	Specific secondary metabolites may degrade quickly, losing their bioactivity over time.	Utilize encapsulation techniques, optimize storage conditions, and develop more stable synthetic analogs.
Extraction and Purification	Obtaining pure bioactive compounds from <i>Avicennia</i> is complex and requires advanced techniques (Jenner et al., 2011).	Develop efficient extraction and purification methods, such as chromatography and bioengineering approaches.
Drug Resistance	Bacteria may eventually develop resistance to <i>Avicennia</i> -derived antibiotics, reducing long-term efficacy (Brandt, 2022).	Use combination therapies with existing antibiotics and explore synergistic effects with other natural compounds.
Regulatory Approval	New drug candidates must undergo extensive, time-consuming, costly clinical trials.	Strengthen preclinical research, secure funding, and collaborate with pharmaceutical companies for development.
Sustainability	Overharvesting <i>Avicennia</i> for drug development may impact mangrove ecosystems.	Promote sustainable cultivation, use biotechnological methods like plant tissue culture, and encourage conservation efforts.

The sustainable harvesting of *Avicennia* is essential to ensure the long-term availability of these beneficial resources. Overexploitation of mangroves for medicinal and aquaculture purposes could lead to habitat degradation, affecting biodiversity and ecosystem stability. To address this, cultivation methods such as controlled mangrove plantations, tissue culture, and sustainable harvesting guidelines should be implemented. Encouraging community participation in mangrove conservation programs can also promote responsible resource utilization while protecting coastal ecosystems.

Overall, using *Avicennia* extracts in aquaculture represents a promising strategy for combating bacterial infections, enhancing aquatic health, and maintaining environmental balance. The industry can reduce its ecological footprint by integrating these natural compounds into sustainable aquaculture and bioremediation practices while ensuring long-term productivity. However, further research is needed to optimize extraction methods, assess long-term effects, and develop standardized formulations for commercial use.

## CHALLENGES AND FUTURE DIRECTIONS

Despite the promising antibacterial potential of *Avicennia* extracts, there are significant limitations in current research. One of the major gaps is the incomplete understanding of the comprehensive chemical profile of *Avicennia* species. Although many studies have identified several bioactive compounds, many secondary metabolites remain unexplored or uncharacterized (Maithani et al., 2022). The chemical composition of *Avicennia* is influenced by environmental factors such as salinity, temperature, and geographic location, leading to variations in bioactive compound concentrations. A more comprehensive investigation of these variations is necessary to standardize the use of *Avicennia* extracts for antibacterial applications.

Another critical limitation is the lack of in vivo studies and clinical trials. Most research on *Avicennia* has been conducted in vitro, focusing on antibacterial activity against specific pathogens (Roberts et al., 2015). While these studies provide valuable insights, they do not fully reflect how these compounds behave in living organisms. Factors such as bioavailability, toxicity, and potential side effects must be evaluated through animal model studies and clinical trials. Without these validations, the practical application of *Avicennia*-derived antibacterial agents remains uncertain, limiting their integration into pharmaceutical and aquaculture industries.

There are numerous opportunities for future research, particularly in exploring understudied *Avicennia* species. Most studies have focused on *Avicennia marina* and *Avicennia officinalis*, but other species within the genus may also contain novel bioactive compounds with potent antibacterial properties. Investigating these lesser-known species could expand the library of natural antimicrobial agents and lead to the discovery of new therapeutic candidates. Furthermore, comparative studies across different *Avicennia* species could help determine which ones offer the most consistent and potent antibacterial effects.

Another promising direction is the integration of omics technologies, such as genomics, metabolomics, and proteomics, to enhance compound discovery. These advanced techniques allow for high-throughput screening of bioactive compounds and provide deeper insights into their biosynthetic pathways. Genomic studies can help identify key genes responsible for metabolite production, while metabolomics can analyze the chemical diversity of *Avicennia* extracts in different environmental conditions. By leveraging these technologies, researchers can optimize extraction methods, enhance compound yields, and improve the comprehensive understanding of *Avicennia*'s medicinal potential. This multidisciplinary approach could accelerate the development of novel antibacterial agents and broaden the applications of *Avicennia*-derived products in medicine, aquaculture, and environmental management.

## CONCLUSION

*Avicennia* mangrove species exhibit significant antibacterial potential, offering promising avenues for novel drug discovery, particularly in combating antibiotic-resistant pathogens. The diverse bioactive compounds found in these mangroves highlight their crucial role in marine natural product research. Preserving mangrove ecosystems is essential not only for maintaining biodiversity but also for sustaining future biomedical advancements. The degradation of these habitats could lead to the loss of valuable bioactive resources before their full potential is realized. To harness the antibacterial properties of *Avicennia* mangroves effectively, interdisciplinary collaboration between marine biologists, microbiologists, chemists, and pharmacologists is necessary. A holistic approach integrating biotechnology, ecological conservation, and sustainable utilization of mangrove resources will pave the way for innovative therapeutic discoveries.

## CONFLICT OF INTEREST

There is no conflict of interest in this article.

## AUTHOR CONTRIBUTION

YM: Conceptualization, Methodology, Software; AA: Data Analysis, Manuscript Drafting; Yu.M: Supervision; AA: Manuscript Review and Editing.

## DECLARATION OF GENERATIVE AI

During the preparation of this work the authors used in order to Artificial Intelligence (AI) tools (specifically, ChatGPT by OpenAI, GPT-5 model) were utilized solely to assist in language refinement, paraphrasing, and grammar correction. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

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