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Pharmacological Activities Of Sonneratia alba Mangrove Plant : A Review

Andita Fitri Mutiara Rizki*[1,2], Wihda Aisarul Azmi[1,2,] Muhaimin[3], Melva Louisa[2], I Made Artika[1,4], and Josephine Elizabeth Siregar[1]

[1]Eijkman Research Center for Molecular Biology, National Research and Innovation Agency, Jalan Raya Bogor KM. 46, Cibinong, Bogor 16911, Indonesia.
[2]Master's Programme in Biomedical Sciences, Faculty of Medicine Universitas Indonesia, Jalan Salemba Raya No. 6, Central Jakarta 10430, Indonesia.
[3] Faculty of Pharmacy, Padjadjaran University, Jatinangor, 45363, Indonesia.
[4]Department of Biochemistry, Faculty of Mathematics and Natural Sciences, Bogor Agricultural University, Darmaga Campus, Bogor 16680, Indonesia.

ABSTRACT

Indonesia is a country with a high amount of diverse natural resources. Various plants have important roles in supporting human medicinal needs due to their availability in providing various medicinal resources. One of the natural resources is Sonneratia alba, a species of mangrove plant known with high adaptive ability and tolerance to extreme environmental conditions such as high saline stress, light intensity exposure, and free radicals. This review summarized the findings on pharmacological activities of S. alba. Several studies reported the adaptive ability of S. alba with its various pharmacological activities such as antimalarial, antioxidant, antimicrobial, and anticancer. These activities are strongly correlated with its bioactive constituents such as terpenoid, alkaloid, tannin, quinone, phenolic, and flavonoid. The mechanism of each pharmacological activity has been suggested in several studies. These findings could be beneficial in drug discovery for several infectious and degenerative diseases and in the development of drugs at industrial stage.

Keyword : *Anticancer, antimalaria, antimicrobial, antioxidant, Sonneratia alba*

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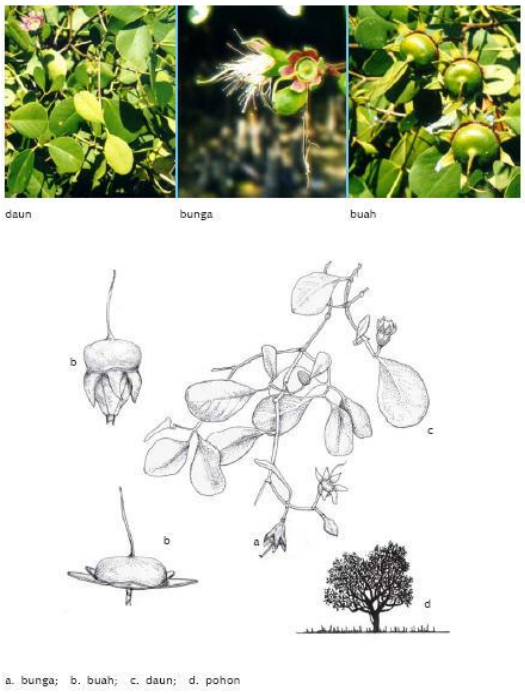
INTRODUCTION

The high level of biodiversity in Indonesia provides natural resources for drug discovery. Plant diversity has an essential role in supporting human medicine due to its availability to provide various kinds of therapeutic sources. Plants have self-defense mechanisms to protect themselves from predators and microbial infection by producing and synthesizing some phytochemical compounds (Newbold et al., 1997). There are many kinds of biochemical compounds contained in plants that have pharmacological activities. However, considering the country's wide range of plant biodiversity, there are still many plants that have yet to be explored and may have hidden medicinal potency. The exploration and further research on medicinal plants for drug discovery and development are required for treatment of various diseases.

The tropical climate in Southeast Asia regions, such as Indonesia provides a suitable unique ecosystem of mangrove plant growth, a wetland composed of halophytic trees, trees, and shrubs. Indonesia is the home of approximately 20% of mangrove plant species worldwide, with a large proportion of the mangrove ecosystem (Friess, 2016). Mangrove plants have high adaptability to the low-nutrient soil environment and still produce biochemical compounds to support their life (Reef et al., 2010). These characteristics may help mangrove plants to grow and synthesize biochemical compounds. Several pharmacological activities have been found in mangrove plants, such as antioxidant, antimalarial, antimicrobial, and anticancer (Assaw et al., 2020; Rahayu & Sunarto, 2020).



Picture 1 (Source: Wetlands International Indonesia Programme, 2008) Mangrove plant *Sonneratia alba.* The picture shows each parts of *S.alba* plant such as: a.) flower, b.) fruit, c.) leaf, d.) bark. Different parts of the plant exhibit different pharmacological effects, due to different types and levels of biochemical constituents.

Sonneratia alba is one of the mangrove plant species known with its pharmacological activities such as antioxidant, antimalarial, antibacterial, and anticancer (Muhaimin et al., 2019; Saad et al., 2014). This review summarized the pharmacological activity of *S.alba* with its biochemical compounds and their possible mechanism of action. This study could be beneficial in providing knowledge and information of *Sonneratia alba* as a new candidate for drug discovery and development against several infectious and/or degenerative diseases.

METHOD

In this study, criteria of data source included original articles on human, animal, bacteria, parasites, pharmacological activity, antibacterial, antimalaria, antioxidant and anticancer.

Data excluded in this study were article reviews, opinions and systematic reviews. The research journal data sources provided in this study was collected from two databases: PubMed and Google Scholar. Search strategy applied in this study was performed by using manual search with keywords: *Sonneratia alba* pharmacological activity, *Sonneratia alba* antioxidant, *Sonneratia alba* antibacterial, *Sonneratia alba* antimalarial, and *Sonneratia alba* anticancer.

DISCUSSION

The pharmacological activity of the mangrove plant *S. alba* against several diseases strongly correlates with several biochemical compound leads which belong to secondary metabolites such as terpenoid, flavonoid, alkaloid, tannin, quinone, phenolic, saponin, oleanolic acid, and glycosides (Muhaimin et al., 2019). These compounds contribute to *S. alba* pharmacological effects such as antimalarial, antioxidant, antimicrobial (bacteria and fungi), and anticancer (Poonam Gawali & B. L. Jadhav, 2011) as described below.

Antimalarial Activity

One of the pharmacological activities of *S. alba* is as an antimalarial. This potential antimalarial activity of *S. alba* has been explored by Muhaimin et al., 2019. The study involved antimalarial testing of methanolic extract of *S.alba* leaf extract performed using *ex vivo* assay against *Plasmodium berghei* ANKA parasite. The methanol extract of *S. alba* leaf was shown to suppress parasitemia levels of *P. berghei* ANKA during 24-hour assay test. This antimalarial activity correlates to its biochemical compounds, such as quinone, alkaloid, flavonoid, phenolic, and terpenoid. There is limited study on pharmacological activity of *S.alba* as an antimalarial, therefore further research needs to be conducted.

Antioxidant Activity

Several studies have been performed on the pharmacological effects of *S. alba* such as its antioxidant activity. Kaewpiboon et al. (2012) conducted *in vitro* cytotoxic analysis and 2,2-diphenyl-1-picryhydrazyl (DPPH) radical scavenging assay using *S. alba* leaf extracts. This study reported that the ethanol extracts of *S.alba* leaves showed effective DPPH radical scavenging activity with EC_{50} values of 3.27 ± 0.53, and its crude water extract has EC_{50} values of 6.43 ± 2.29. These results indicated that *S. alba* extracts have potential antioxidant activity.

The *S. alba* leaf extracts have been incorporated into an active packaging film in a study conducted by Nurdiani et al., 2022. The antioxidant activity of the active packaging was determined by using the DPPH radical scavenging activity method. The active film packaging incorporated with *S. alba* leaf extracts substantially increased the scavenging value from 12.36% to 60.98%. These results suggested that incorporation of S. *alba* extracts into film packaging enhanced antioxidant ability due to bioactive compounds of the plant, such as phenolic-based compounds (Hanani et al., 2019).

A study conducted by Kaleh et al. (2022) reported that the antioxidant effects of *S. alba* plant are related to endophytic rhizobacteria, *Bacillus* sp., which have symbiotic association with the plant and produce antioxidant enzymes.

Another study by Suh et al. (2014), reported that methanol root extracts of *S. alba* have radical scavenging activity of 80.0% measured using the DPPH method. This high antioxidant activity was strongly correlated with the phenolic compounds contained in the plant. Wang et al. (2013) cloned and expressed a gene of *S. alba*, which encodes iron superoxide dismutase (FeSOD), an enzymatic antioxidant. This

gene was hypothesized to be associated with high saline tolerance of mangrove plants such as *S. alba*. This gene plays an important role as a first-line defense to extreme free radical threat. The gene was expressed in *Escherichia coli* cells and then characterized. Results showed that in comparison with FeSODs from other plant species, all iron-binding sites (His 27, His 80, Asp 164 and His 168) of *S. alba* FeSOD were conserved. In addition, it was found that the FeSOD of *S. alba* has good pH stability and was active when incubated at 50^{o}C for 1 h. Further molecular analysis revealed that *S. alba* FeSOD was expressed in leaf, stem, flower, fruit, and root tissues with the highest expression in leaf tissues.

Similarly, Yang et al. (2015) cloned and expressed a gene encoding cytosolic copper/zinc superoxide dismutase (SaCSD1) from the *mangrove* plant *S. alba* in *E coli* cells. It was demonstrated that the deduced amino acid sequence of SaCSD1 protein shows high similarity with superoxide dismutase (CSD) of some other plant species. The recombinant protein showed good activity and was stable. Molecular analysis indicated that the SaCSD1 gene is expressed in leaf, stem, flower, and fruit organs, with the highest expression in fruits. The SaCSD1 gene was suggested to have a similar function with iron superoxide dismutase (FeSOD) which reduced the oxidative stress of the plant caused by extreme salinity and temperature. High saline concentration on the environment restricts the growth of the plant due to a lack of H_2O adsorption and reduced assimilation process (Grattan & Grieve, 1998; Zhu, 2003). The SaCSD1 protein may protect *S. alba* from extremely high saline, temperature, and light exposure (Yang et al., 2015).

In a different study, the DPPH free radical scavenging activity of *S. alba* stem and leaf extracts was examined. It was found that the IC_{50} values for DPPH radical scavenging activity of the stem and leaves were 62.5 µg/mL and 87.5 µg/mL respectively. Phytochemical analysis showed that *S. alba* contains flavonoids, tannins, triterpenes, anthraquinones, alkaloids and saponins which may contribute to the antioxidant activity (Gawali & Jadhav, 2011).

The potential antioxidant activity-inducing compounds presence in the roots of *S.alba* have also been studied by Latief et al. (2019) and has identified compounds of stigmasterol and beta-sitosterol from ethyl acetate extract of *S.alba* roots using several methods such as UV-spectrophotometer, FT-IR, and NMR. The DPPH free radical scavenging activities of the ethyl acetate extract and a mixture of stigmasterol and beta-sitosterol were found to have IC_{50} values of 223.67 ppm and 439.71 ppm respectively. It was concluded that these compounds were less active but still have antioxidant potential (Latief et al. 2019).

Antimicrobial Activity

Pharmacological effect on antibacterial activity of *S.alba* plant was found in a study conducted by Kaewpiboon, et al. (2012). This study reported that aqueous extract of *S. alba* leaves inhibits the growth of Gram-negative bacteria *Pseudomonas aeruginosa* and Gram-positive bacteria *Micrococcus luteus*.

The incorporation of *S. alba* extract to the active packaging film used in food and beverage industrial products has been conducted by Nurdiani et al. (2022). This study showed that the gelatin fish-based active packaging incorporated with *S.alba* leaf extract (0.35% concentration) has higher inhibition zones against Gram-positive and Gram-negative bacteria compared to other film packaging without incorporation of *S. alba* extract. The highest inhibition zone against Gram-positive bacteria *Bacillus subtilis* was obtained with inhibition zone 2.42 mm, meanwhile inhibition value 2.22 mm was obtained against Gram-negative bacteria

Escherichia coli. This antibacterial activity value was considered to be stronger than that of the film packaging without incorporation of *S. alba* extract.

Another study reported by Manilal, et al. (2015), tested *S. alba* leaf extract against human and shrimp pathogens. *S. alba* extract with each different solvent, ethyl acetate, methanol, and ethanol, showed antibacterial activity against human pathogenic bacteria based on the inhibition zone against bacteria *Staphylococcus aureus* of 308.85±10.9 mm^2, and inhibition zone value of 143.83±7.4 mm^2 against human pathogenic yeast *Candida albicans*. The antibacterial effects exhibited against human pathogens may be contributed by the bioactive compounds in mangrove plant *S. alba* such as triterpenoid.

The antibacterial activity of *S. alba* leaf against human pathogenic bacteria was also investigated in the study conducted by Sahoo et al. (2012). In this study, ethanol and aqueous extracts of *S. alba* leaf were challenged against Gram-positive bacteria (*Staphylococcus aureus* and *Streptococcus* sp.) and Gram-negative bacteria (*Proteus vulgaris* and *Proteus mirabilis*) using disc method antibacterial assay and the inhibition zone around tested disc was measured. The ethanol extract of *S. alba* leaf plant exhibited antibacterial activity against both Gram-positive and Gram-negative bacteria, with highest inhibition zone performed against Gram-negative bacteria *Salmonella typhi* with value 17 mm categorized as strong antibacterial. Activity of antibacterial performed in *S. alba* leaf ethanol extract indicates strongly related to its biochemical constituent with phenolic-based compounds such as flavonoid, terpenoid, and alkaloid.

In a study conducted by Saad, et al. (2012), antimicrobial test was performed by using minimum inhibitory concentration (MIC) against Gram-positive bacteria (*Staphylococcus aureus* and *Bacillus cereus*), Gram-negative bacteria (*Escherichia coli*), and yeast *Candida neoformans*. Inhibition zone test showed that the antibacterial activity against Gram-negative bacteria *Escherichia coli* has the strongest antibacterial effect with inhibition zone diameter value of 17.5 mm. The phytochemical compounds contained in *S. alba* considered to be related with the antibacterial activity include flavonoid, tannins, alkaloid and phenolic.

Potential antibacterial phenolic compounds were isolated from endophytic associated fungi *Alternaria* sp. in *S. alba* mangrove plant in a study conducted by Kjer, et al. (2009). These compounds, xanalteric acid I and II, alternarian acid (altenusin), were tested against several multidrug-resistance pathogens such as *E. coli, S. aureus, S. pneumonia, P. aeruginosa, etc*. The compounds xanalteric acid I and II showed weak response to *S. aureus*. Meanwhile altenusin exhibited broad antibacterial activity against several multidrug-resistance pathogens.

Isolation of triterpenoid compounds from *S. alba* stem plant was conducted by Harizon et al. (2015). Antibacterial test of all triterpenoid compounds against Gram-positive bacteria *Staphylococcus aureus* ATCC 6538 and *Staphylococcus mutans* ATCC 25175 using minimum inhibitory concentration (MIC) method, exhibited the antibacterial activity against pathogen tested with minimum inhibitory concentration value range of 15-55 μg/mL. The highest antibacterial activity was shown by the lupeol with MIC against *S. mutans* and *S. aureus* of 40.5 and 15.6 μg/mL, respectively.

A study of the potential of alkaloid compounds as antibacterial isolated from ethanol extract of *S. alba* roots was also conducted by Latief et al. (2021). Purified alkaloid compounds were tested using disk antibacterial assay against Gram-positive bacteria *S. aureus* and Gram-negative bacteria *E. coli*. Presumably, the alkaloid compound isolated was an alkaloid indole group and exhibited antibacterial activity to

all tested bacteria by producing a similar inhibition zone compared to the positive control chloramphenicol 50 ppm.

Anticancer Activities

Study of potential anticancer activity from *S. alba* root extract was reported by Latief et al. (2020). In this study, *S. alba* root was extracted, isolated and purified to determine the potential compounds as anticancer. The characterization of potential compounds was conducted using several methods such as UV-Vis and FTIR methods. From this analysis, compounds were identified to be steroids. These compounds were tested in cytotoxicity assays at various concentrations and the LC_{50} value was 10.04 µg/mL and presumably has a potential use for anticancer. The LC_{50} of the extract was 23.98 µg/mL.

Extracts of the *S. alba* leaf plant were tested on HeLa cell viability. In this study, *S. alba* leaf ethyl acetate extract was tested using cytotoxicity on HeLa cells. Cytotoxicity test showed that the ethyl acetate extract of *S. alba* was cytotoxic against HeLa cell viability with IC50 value of 478.630 µg / mL. This result shows that ethyl acetate *S. alba* leaf extract has potency as an anticancer. The biochemical compounds of the plant identified using the Liquid Chromatography Mass Spectrometry (LC-MS) method were diosmetin, caffeine, and turmeron and may contribute to the anticancer activity (Suryaningrum, 2021).

Suggested Mechanism of Action

The proposed mechanism of action of *S. alba* pharmacological activity was summarized in Table 1.

Table 1. Proposed mechanism of action on *S. alba* plant pharmacological activity

Pharmacological Effect	Suggested Mechanism of Action	Reference
Antimalaria	Biochemical compounds contained in the *S. alba* plant (flavonoid, terpenoid, quinone, alkaloid, and phenolic) have strong correlation with antimalarial activity against *Plasmodium* sp. parasite.	(Muhaimin, et al., 2019)
Antibacterial	Phenolic-based biochemical compounds presence in plants strongly related to antibacterial activity. Triterpenoid compounds of *S. alba* such as lupeol presumably play an essential function as antibacterial agent.	(Sahoo et al., 2012; Harizon et al., 2015)
Antioxidant	Flavonoids contained in *S. alba* have roles as an antioxidant and protect plants from high temperature and UV light. Symbiotic association with halotolerant endophytic rhizobacteria produces antioxidant enzymes in response to high salt content exposure. Iron superoxide dismutase (FeSOD) gene has an essential role in preventing plant tissue oxidation from extreme high saline exposure.	(Ghasemzadeh et al., 2010; Kaewpiboon et al., 2012; Kaleh et al., 2022; Wang et al., 2013)

Pharmacological Effect	Suggested Mechanism of Action	Reference
Anticancer	Biochemical compounds of *S. alba* extract are linked with anticancer activity.	(Suryaningrum, 2021)

Based on several studies, antioxidant effects on *S. alba* were provided by flavonoids contained in plants that grow in areas with massive resources of phenolic. This flavonoid compound protects the organism from extreme conditions such as high temperature and saline and UV light protection. In another study, the antioxidant activity of *S. alba* was shown to be associated with endophytic rhizobacteria that are halotolerant by producing antioxidant enzymes to protect its symbiotic plant from high salt content exposure (Kaleh et al., 2022).

A study by Wang et al. (2013) reported that the iron superoxide dismutase (FeSOD) gene was found in several parts of *S. alba* mangrove as a high salt tolerant plant. The presence of this gene indicates an essential role in oxidation prevention of plant tissue from extreme environmental conditions such as high saline concentration. Production of enzymes encoded by the FeSOD gene may protect the plant tissues from toxicity of superoxide radicals caused by high stress levels of radiation exposure, saline, and temperature (Wang et al., 2013; Su et al., 2021). In general, plants have several SOD isoforms. Fe SODs are found in the chloroplast, Mn SODs are located the mitochondrion and the peroxisome, and Cu-Zn SODs are found in the chloroplast, the cytosol, and possibly the extracellular space (Alscher et al., 2002; Stephenie et al., 2020).

Additional Potential Use of *S. alba* Extract

Several genes were also found in *S. alba* with their function as a defense for an oxidant and extreme conditions such as high salt concentration and light exposure. These genes, namely iron superoxide dismutase (FeSOD) and cytosolic copper/zinc superoxide dismutase (SaCSD1), have an essential role in preventing plant tissue from free radical exposure and extreme high saline environmental conditions. FeSOD and SaCD1 genes showed enzyme activity with stable acidic and neutral pH that could be beneficial for industrial product use (Wang et al., 2013; Yang et al., 2015).

High antioxidant activity of *mangrove* plant *S. alba* to inhibit free radical has been reported in several studies. Considering high antioxidant potency and biochemical constituents, *S. alba* leaf could be useful in food and beverage industries. Functional tea could be a useful industrial product, for which *S. alba* leaf is processed with several methods to produce tea products (Mandang et al., 2021).

Another potential use of *S. alba* is in active fish gelatin packaging food and nutrition aspects, due to high antioxidant and antibacterial activity (Nurdiani et al., 2022).

CONCLUSION

Several studies reported that *S. alba* extracts exhibit several pharmacological activities such as antioxidant, antimalaria, antimicrobial and anticancer. Mangrove plant *S. alba,* known as high saline tolerant, can adapt to extreme environmental conditions such as high salt, UV light intensity exposure, and free radicals. This adaptive ability makes *S. alba* produces several functional bioactive compounds as self-defense mechanisms. Suggested mechanism in several studies indicates that bioactive compounds contained in *S. alba* are strongly correlated with pharmacological effects and could be beneficial in drug discovery and development. In addition, various pharmacological activities of *S. alba* could also be useful in industrial aspects. Further

research on *S. alba* should be conducted in order to earn other potency for medicinal cure and treatment to various diseases. Detailed studies on the mechanism of action of bioactive compounds with potential pharmacological activity are also required.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIAL

Not applicable

COMPETING INTEREST

The authors declare that there is no conflict of interest regarding the publication of this paper.

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AUTHOR'S CONTRIBUTION

AFMR: conceptualizing, writing the original draft, and reviewing

WAA: writing, reviewing, and editing

ML: writing, reviewing, and editing

MM: conceptualizing, writing, reviewing, and editing

IMA: conceptualizing, writing, reviewing, and editing

JES: conceptualizing, writing, reviewing, and editing

All authors have read and approved the manuscript

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