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AN OVERVIEW ON PHYTOCHEMISTRY AND ETHNOMEDICINAL POTENTIAL OF *ACANTHUS ILICIFOLIUS* OF WEST BENGAL REGION

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Abstract

Mangroves are one among the most productive and biologically important ecosystem on this planet, providing vital ecosystem goods and services. *Acanthus ilicifolius* generally known as Sea holy and holy mangrove. The genus *Acanthus*, belonging to the family Acanthaceae, is most common in both east and west coast of India including Andaman Islands and Nicobar Islands. Genus *Acanthus* comprises of over 30 species, However, in India only *A. ilicifolius* is known to occur in all mangrove habitats. *A. ilicifolius* is common in landward edges of mangroves just above the high tide mark, and also occurs in inner mangroves. Out of all the species, *A. ilicifolius* has a long history of use as a folklore and traditional remedy for treating various diseases in Ayurveda as well as in Thai medicine and Traditional Chinese Medicine. Furthermore, all the parts of *A. ilicifolius* plant have been used to cure a number of ailments in various traditional systems of medicine including Ayurveda. Thus, in the present review we aimed to describe and delineate on the geographical distribution, phytochemistry and ethnomedicinal properties of *A. ilicifolius.*

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Keywords: Mangroves, *Acanthus ilicifolius*, Phytochemistry, Ayurveda, Ethnomedicinal properties

Introduction

Acanthus ilicifolius generally known as Sea holy and holy mangrove. Mangroves are considered as one of the most specialized ecological assemblages of halophytic plants acting as a transient zone between land and ocean. They comprise of taxonomically diverse shrubs and trees, distributed along tropical and sub-tropical environments having specific habitats such as shores, estuaries, tidal creeks, backwaters, lagoons, marshes, mudflats and even at upstream points where water remains saline.[1] Mangrove forests are unique functional ecosystems having much social, economic and biological importance. They are among one of the most productive ecosystems of the world as they provide important ecosystem supplies and services to human society as well as coastal and marine systems.[2,3] These habitats interact with a wide array of aquatic or terrestrial flora and fauna, enabling their growth and establishment. Considering their value for the environment and coastal communities, mangrove conservation should become a priority and efforts must be invested to find new and successful methods for conserving mangrove ecosystems.[4]

The genus *Acanthus*, belonging to the family Acanthaceae, comprises of over 30 species, mostly shrubs or perennial herbs, native of tropics and subtropics, many of which are found from India to southern China, tropical Australia and the Western Pacific islands, throughout Southeast Asia.[5] In India, it is common in both east and west coast including Andaman Islands and Nicobar Islands. The name '*Acanthus*' is derived from a Greek word meaning 'spiny' and the genus is also known as 'Bear's Breeches' due to the spiny nature of the plant. The genus comprises of mangrove species *viz. Acanthus ebracteatus* Vahl., *A. ilicifolius* L., *A. volubilis* Wall., *A. latisepalus*, *A. montanus* and *A. xiamenensis* that are known to sustain in the most hostile atmosphere making this genus a unique taxon among all true mangrove genera that represent both terrestrial and true mangrove species.

A. xiamenensis is endemic to China and all the other species are common in Indo-West Pacific region. However, in India only *A. ilicifolius* is known to occur in all mangrove habitats except Lakshadweep, whereas *A. ebracteatus* and *A. volubilis* have very restricted distribution. *A. ilicifolius* is common in landward edges of mangroves just above the high tide mark, and also occurs in inner mangroves. In ancient times, *Acanthus* leaves were employed as a decorative motif in architecture of the Mediterranean countries. In the late 1960s, the founders of The Arts Society chose the *Acanthus* leaf as the Society's emblem. Out of all the species, *A. ilicifolius* has a long history of use as a folklore and traditional remedy for treating various diseases in Ayurveda as well as in Thai medicine and Traditional Chinese Medicine.[6,7] Hence, this genus represents medicinally as well as economically important plants.[8] With this scenario, in the present review we aimed to describe and delineate on the geographical distribution, phytochemistry and ethnomedicinal properties of *A. ilicifolius.*

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Taxonomy of *A. ilicifolius*

Class: Dicotyledones
Subclass: Gamopetalae
Series: Bicarpellatae
Order: Personales
Family: Acanthaceae
Genus: *Acanthus*
Species: *ilicifolius*

Environment and Geographical Distribution of *A. ilicifolius*

A. ilicifolius is regular in estuaries all through Asian tropics from India to Polynesia and northern Australia. Asia and Australia have the best assortment and conveyance of mangrove species known to mankind. In India, it is reported from the east (the largest area of mangrove forest, the Sunderbans), the West seashore, Andamans and a North eastern state, Meghalaya as depicted in Figure 1.[9] It typically develops on waterway banks or tidal channel sides or low swampy zones in mangrove woodlands and regions.[10]

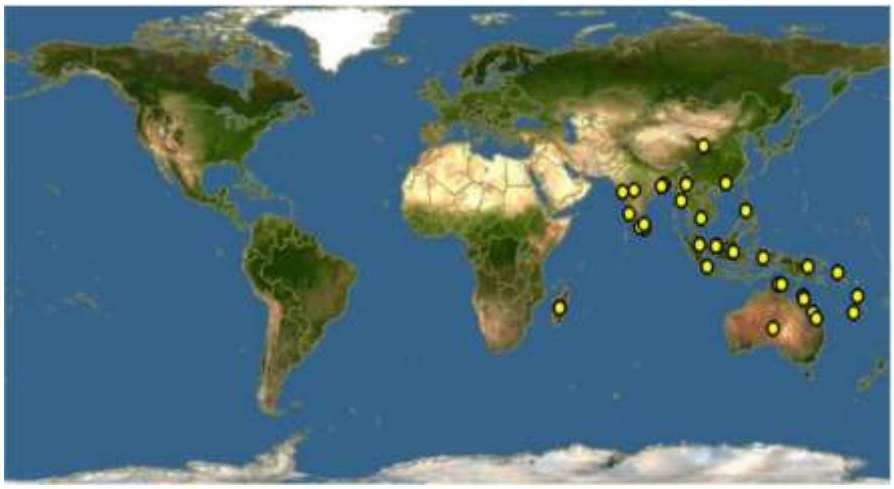

Figure 1: Showing geographical distribution of *A. ilicifolius*

Morphology of *A. ilicifolius*

A. ilicifolius is a shrub grows up to 2 meter tall in robust mangrove areas, Aerial roots-stilt roots; Leaves-simple, opposite, lanceolate, narrowed at base, serrate margins armed with spines; spines longer in flowering season; petiole short, 5 to 6 mm in length, slightly winged with two sharp spurs at the base; color dark green when fresh, yellowish-brown on drying. Odor-indistinct, taste bitter. Flowers-sessile, 4 cm long, spike inflorescence, terminal, corolla light blue or violet; Fruit-capsule, ovoid–oblong, up to 3 cm long, compressed, apiculate, brown, shining (Figure 2).[7,11]

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Figure 2: Showing *A. ilicifolius* plant

Microscopic Characteristics of *A. ilicifolius*

Leaf can be characterized by important features like presence of salt glands with a unicellular stalk and multicellular head in adaxial side; median vein with numerous irregular collateral vascular bundles; the lateral vein bundles somewhat near to median bundle with continuous layer of sclerenchyma sheath; the two layered palisade tissue being confined on abaxial side only; glandular trichomes and deeply sunken stomata intermittently seen in the abaxial region.[11] Stem shows single layered thick epidermis; outer cortex with collenchyma cells and inner cortex consisting of parenchyma with air cavities; solitary sclereids embedded in peripheral phloem cells; pith made up of small parenchymatous cells that contain numerous calcium oxalate crystals and water-storing large parenchymatous cells. The diagnostic features of powdered drug include glandular trichomes with 2 to 10 celled salt secreting head either sessile or with 1 to 2-celled stalk; lower epidermis with plenty of diacytic stomata; transversely cut fragments of lamina exhibiting upper epidermis with sunken pits embedded with glandular trichomes; groups of long pericyclic fibres with thick pitted wall and narrow lumen; and pitted lignified parenchymatous cells.[12]

Phytochemistry of *A. ilicifolius*

Studies on phytochemical investigation of the genus *Acanthus* indicated that phytochemical study has been extensively done on the true mangrove species; *A. ilicifolius*, beside this work no phytochemical isolation has been performed on this genus.[13] Through several phytochemical studies, *A. ilicifolius* has been explored for the presence of various classes of bioactive compounds namely alkaloids, benzoxazinoids, lignans, flavonoids, triterpenoids and steroids.[14] The phytochemicals reported in various parts of *A. ilicifolius* are described as below:

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Phytochemistry of leaf

The alkaloids reported in leaves of *A. ilicifolius* are as follows:

- Acanthicifoline, a 1-methyl-1,2,3,4-tetrahydro-5-methoxy-2,7-napthyridin-3-one[15]
- Trigonellin[16]
- 2-benzoxazolinone[17,18]
- Acanthiline A (pyrido[1,2-a] indole); 4-hydroxybenzoxazole-2-one[19]
- Indole alkaloids like 1H-indole-3-carboxylic acid, 1H-indole-3-carboxaldehyde and 1H-indole-3-acetic acid[20]
- Betaine[21]

The Benzoxazinoids reported in leaves of *A. ilicifolius* are as follows:

- Benzoxazin-3-one, benzoxazinoidglucosides[22]
- 4-benzoxazin-3(4H)-one, megastigmane 2-benzoxazolinone, 5,5'-bis-benzoxazoline-2,2'-diaone[12]

The lignans reported in leaves of *A. ilicifolius* are as follows:

- A coumaric acid derivative called acancifoliuside[23]
- Acteoside[24]
- Isoacteoside[25]
- Acanthaminoside[26]
- (+)-syringaresinol-O-β-D-glucopyranoside, (+)-lyoniresinol-3α-O-β-glucopyranoside[27]
- (-)-lyoniresinol are isolated from the methanolic extract of leaf; (+)-lyoniresinol 3α-O-β-D-galactopyranosyl-(1→6)-β-D-glucopyranoside[28]
- (+)-lyoniresinol-2α-O-β-D-galactopyranosyl-3α-O-β-D-glucopyranoside have been reported from aerial parts[29]
- (Z)-4-coumaric acid glycosides like (Z)-4-coumaric aci-4-O-β-D-glucopyranoside and (Z)-4-coumaric acid-4-O-β-D-apiofuranosyl-(1'→2')-O-β-D-glucopyranoside[5]
- Phenylethyl-O-β-D-glucopyranosyl-(1→2)-β-D-glucopyranoside, phenylethyl-O-β-D-glucopyranoside, benzyl-O-β-D-glucopyranoside and vanillic acid[21]
- 411-epoxymegastigmane glucoside and megastigmane glucosides [(6S, 9S)-roseoside)] have also been reported from *A. ilicifolius* growing in China[5]
- The phenylethanoids reported in the plant are blepharin, acteoside, isoverbascoside[30]
- Martynoside and crenatoside[31]

The flavonoids reported in leaves of *A. ilicifolius* are as follows:

- Quercetin, quercetin-3-O-β-D-glucopyranoside[32]
- Apigenin-7-O-β-D-glucuronide, vitexin[33]
- Luteolin 7-O-β-D-glucuronide, apigenin-7-O-β-D-glucuronide, methylapigenin-7-O-β-D-glucuronate[33]
- Catechin/epicatechin, galatechin/epicatechin and amphicin/epigalin[3]

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The aliphatic glycosides reported in leaves of *A. ilicifolius* are as follows:

- Ilifolioside B[33]
- Ilicifolioside C[34]

The triterpenoids reported in leaves of *A. ilicifolius* are as follows:

- Pentacyclic triterpenes, β-amyrin, α-amyrin[35]
- Lupeol, oleanolic acid and ursolic acid[16]

The steroids reported in leaves of *A. ilicifolius* are as follows:

- β-Sitosterol[35]
- Cholesterol, campesterol, stigmasterol[36]
- Stigmast-7-en-3-β-ol, octacosyl alcohol, stigmasteryl β-D-glucopyranoside[37]
- Daucosterol and 3-O-β-D-glucopyranosyl-stigmasterol[30]

The hydrocarbons reported in leaves of *A. ilicifolius* are as follows:

- 24-Methylene cycloartenol, cycloartenol, 19-Norlanost-5-en-3-ol, 24-methylenelanost-9-en-3β-ol, 4-methyl-cholesta-7-ene-3β-ol, phytol, octadeconate, tetracosanol and octacosanol[36,38]

The fatty acid derivatives reported in leaves of *A. ilicifolius* are as follows:

- Palmitic acid and octadecanoic acid[36]

Other phytochemicals reported in leaves of *A. ilicifolius* are as follows:

- Amino acids like glutamic and aspartic acids and organic acids like malic, citric, oxalic glycolic and succinic acids[39]
- Uridine and uracil[40]

Phytochemistry of roots

The major phytochemicals reported in roots of *A. ilicifolius* are as follows:

- Triterpenoids[41]
- 2-benzoxazolinone (acanthosides A-D)[42]

Phytochemistry of pods

The major phytochemicals reported in pods of *A. ilicifolius* are as follows:

- 1,4-Benzoxazinone[5]

Phytochemistry of stems

The major phytochemicals reported in stems of *A. ilicifolius* are as follows:

- Homologous series of 15 saturated odd and even fatty acids[43]
- Lignan and cycloligan glycoside[29,44]
- Phenylethanoid glycoside (ilicifolioside A), an aliphatic alcohol glycoside-ilicifolioside B[23]

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- Lignin glucosides, (+)-lyoniresinol-3α-[2-(3,5-dimethoxy-4-hydroxy)-benzoyl]-O-β-glucopyranoside and dihydroxymethyl-bis (3,5-dimethoxy-4-hydroxyphenyl) tetrahydrofuran-9(or 9')-O-β-glucopyranoside; and benzoxazinoidglucosides[12,15]

Ethnomedicinal Properties of *A. ilicifolius*

The pharmacological study has been extensively performed on *A. ilicifolius* among the species of this genus. This study revealed that *A. ilicifolius* has significant bioactivities like, antioxidant and cytotoxic activity,[45] antinociceptive activity,[46] anti-inflammatory activity,[47] anti-osteoporotic activity,[35] hepatoprotective activity,[47] chemopreventive activity; leishmanicidal, tumour reducing and anticancer activities;[24,25,47,48] antileishmanial, antiulcer, antimicrobial, and osteoblastic, activities.[47] Moreover, Firdaus et al. found in their study that flower extract of the plant also has good cytotoxic effects;[45] Smitha et al. showed the anticancer activity of ethyl acetate extract of on two cell lines PA-1 and MCF-7.[49] The major ethnopharmaceutical activities of *A. ilicifolius* described in details herein:

Anti-inflammatory

The methanolic fraction of leaf extract of *A. ilicifolius* is reported to produce significant inhibition of rat paw oedema, when administered both prior to and after carrageenan administration, in a manner similar to BW755C, a synthetic cyclooxygenase (COX) and lipoxygenase (LOX) inhibitor. The extract is shown to decrease protein exudation and leukocyte migration in the peritoneal fluid, thereby indicating its effectiveness towards inhibiting peritoneal inflammation and also significant inhibition of COX (1 and 2) and 5-LOX activity. Moreover, pre-incubation of the extract is shown to inhibit the production of proinflammatory cytokines (TNF-α and IL-6) in lipopolysaccharide (LPS)-stimulated peripheral blood mononuclear cells (PBMCs). It is also reported to possess significant free radical (DPPH, ABTS, superoxide and hydroxyl radical) scavenging activity.[50]

Antioxidant and Cytotoxic

The methanol extract of *A. ilicifolius* contains phenolic substances grouped as cancer prevention agent compounds.[51] The limit of antiradical proficiency of *A. ilicifolius* flowers can be as medium. The extract was not in unadulterated structure; be that as it may, it may very well be arranged as a decent and potential antioxidant agent. The LC_{50} of extracts of *A. ilicifolius* or pure compounds on salt water shrimp or cell line under 100 μg/mL is ordered as a potential cytotoxic and dangerous substance.[52] The ethanol leaves extract of *A. ilicifolius* was seen as cytotoxic towards lung fibroblast (L-929) cells in 72 h MTT test and the focus required for half-cell passing was 18 μg/mL,[25] in the interim the methanol extract of *A. ilicifolius* was cytotoxic to Hela and κB cell line.[53] Wostmann and Liebezeit detailed that this mangrove contained cancer prevention agent substances.[54] The most noteworthy cancer prevention agent and cytotoxic activity were found on methanol extract. Methanol has been known progressively powerful to break up dynamic mixes in cells. Henceforth, it was simpler to infiltrate the cell film to extract the intracellular fixings from plant materials. Tiwari et al. expressed that few dynamic mixes will be gotten if methanol utilized as dissolvable in the extraction strategy for example anthocyanins,

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saponins, tannins, flavones, and polyphenols.[55] These mixes have known as free radical scavenger, responsive species quencher, hydrogen donor, cancer prevention agent chemicals activator, detoxification inducer, ordinary normal cell differentiation promoter and expansion cell inhibitor, and apoptosis inducer.[56-60]

The cytotoxicity of methanol extract of *A. ilicifolius* can be related to the antioxidant activity and synergism impact of multi-part in separate. Triterpenoid saponin demonstrated its cytotoxicity in HeLa cells through both mitochondrial brokenness and ER stress cell passing pathways, while saponin stifled tumor obtrusive and relocation by hindering MMP-2 and MMP-9 activation.[61] Imai et al. established that flavonoid adequately smothered the multiplication of a human colon carcinoma cell line, COLO 201, through apoptosis acceptance while phenolic indicated anticancer action on disease colon cell by capturing the cell cycle.[62] All in all, the methanol concentrate of *A. ilicifolius* flower is potential as antioxidant (cancer prevention agent) substances and cytotoxic compounds.[45]

Furthermore, Firdaus et al., analyzed the cytotoxic of the flower extracts of *A. ilicifolius* on the brine shrimp lethality. The results exhibited methanol extract has lowest LC_{50} value (22 µg/ml) while water extract showed the highest value at 10 µg/ml among the extracts.[45] Dey et al. have tested the cytotoxic activity of a methanolic crude extract of the plant where it has found that the extract exhibited a significant cytotoxic activity with the LC_{50} value at 60 µg/ml and LC_{90} value at 120 µg/ml.[63]

Antimicrobial

Antimicrobial activity of alcohol, butanol and chloroform extract (10 mg/ml) of both leaves and roots of the *A. ilicifolius* exhibited significant activity against all microbes, *B. subtilis, P. vulgaris, P. aeruginosa, S. aureus, C. albicans, A. niger*, and *A. fumigatus*. The experiment was followed by agar cup plate method that unveils the leaves were more active than that of roots where ampicillin used as a standard for bacteria and clotrimazole for fungi. Chloroform extract of leaf showed the highest zone of inhibition that was measured ~26 mm against the fungus *C. albicans*. But butanol extract of leaf extract displayed lowest ~08 mm against the bacterium *S. aureus*.[64]

Govindasamy and Arulpriya studied antimicrobial activity of *A. ilicifolius* against seven skin infection causing microbes, methicillin resistance *S. aureus* (MRSA), *L. plantarum, S. pyogenes, S. epidermis, C. albicans, P. aeruginosa,* and *T. rubrum*. In this test four extract of the leaf has been examined where chloroform extract showed the highest activity against all microbes (except *S. epidermis* and *L. plantarum*).[49]

Antiviral

The ethanol extracts (50%) of the leaf, flower and root of *A. ilicifolius* have been shown to possess in vitro antiviral activity against Tobacco Mosaic Virus.[65,66] Blepharin, acteoside, isoverbascoside, daucosterol and 3-O-β-D-glucopyranosyl-stigmasterol isolated from the leaf when investigated for anti-influenza virus activities by measuring the neuraminidase activity of

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influenza virus, the phenylethanoids (blepharin, acteoside, isoverbascoside) exhibited significant antiviral activities.[30]

Anti-leishmanial

2-Benzoxazolinone (BOA) isolated from the leaf (40 µg/ml) of *A. ilicifolius* is shown to have anti-leishmanial activity against *Leishmania donovani* when compared with pentamine in in vitro experiments. BOA (i.p.) in the doses ranging from 0.25 to 1 g/kg is shown to be safe in mice.[65,67]

Antinociceptive

The methanolic extract of *A. ilicifolius* is reported to exhibit antinociceptive effects, due to its flavonoids and tannins, and is mediated by inhibition of lipooxygenase and/or cyclooxygenase in peripheral tissues induced by acetic acid, thereby reducing PGE2 synthesis and interfering with the mechanism of transduction in primary afferent nociceptor.[68,69]

Anticancer

Smitha et al. studied the anticancer activity of ethyl acetate extract of leaf and root extract of *A. ilicifolius* on two cell lines, MCF-7 and PA-1. *A. ilicifolius* is more effective on PA-1 and the result has recommended that at 50 µg/ml ratio is adequate to inhibit the cancer cells. Moreover, the result has also unveiled that the extract is slightly cytotoxic to both of the cell lines.[70] Benzoxazolinone-type alkaloids, acanthosides A-D yielded from the root of *A. ilicifolius* are reported to possess significant cytotoxicity against the HepG2, HeLa, and A-549 cancer cell lines with IC_{50} 7.8 to 26.6 µM, due to the presence of substituted benzoyl moiety in their structures.[71]

Hepatoprotective

The alcoholic extract (250 and 500 mg/kg, p.o.) of *A. ilicifolius* has shown significant hepatoprotective activity in rats in carbon tetrachloride-induced hepatotoxicity model, that was comparable with curcumin (100 mg/kg, p.o.), as evaluated from the serum and tissue activity of marker enzymes.[24]

Antidiabetic

A single oral dose of 200 and 400 mg/kg of ethanolic extract of root is shown to significantly decrease blood glucose levels in alloxan-induced diabetic rats after 5 h and 3 h respectively in an acute study and on first day in a sub-acute study. It is reported to improve regeneration of β-cells of pancreas.[72]

Osteoblastic

Osteoblasts are the bone-framing cells of the skeleton; they incorporate, direct and regulate the mineralization of the extra-cell grid of the bone. MC3T3-E1 cells, an osteoblast-like cell line, have been accounted for to hold their ability to separate into osteoblasts, and may give valuable data on the impacts of phytochemicals on the separation of osteoblasts.[73] Acancifoliuside, a coumaric acid derivative isolated from the methanolic leaf extract of *A. ilicifolius*, when tested for its effects on the functions of osteoblastic MC3T3-E1 cells, significantly increased the growth and differentiation of osteoblasts, indicating that *A. ilicifolius* leaf may help to prevent osteoporosis.[35]

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Anti-ulcer

The anti-ulcer activity of methanolic leaf extract of the *A. ilicifolius* (at 100 to 200 mg/kg) produces significant inhibition of gastric lesions induced by pylorus ligation and ethanol-induced gastric ulcers in Wistar albino rats. The extract is shown to cause significant reduction in the gastric volume, free acidity and ulcer index as compared to control, probably due to anti-secretary action.[66]

Conclusion

The world's tropical and subtropical regions are home to a large dispersion of *Acanthus* plants. The ethnomedicinal applications *Acanthus* in health care management have received remarkable recognition as a result of systematic pharmacological studies on the species. A true mangrove plant, *A. ilicifolius* is found throughout the world's tropical and subtropical regions. *A. ilicifolius* botanical research offers scientific data on morphological and anatomical traits.

The phytochemical studies revealed different bioactive compounds from the various parts of *A. ilicifolius*. Numerous pharmacological studies done using different types of extracts of *A. ilicifolius* revealed various pharmacological properties such as antimicrobial, anti-inflammatory, antiviral, antidiabetic, antioxidant, cytotoxic and anticancer activities, antinociceptive, hepatoprotective, leishmanicidal and osteoblastic activity which encouraged the use of *A. ilicifolius* in ethnomedicine. Thus, more research on *A. ilicifolius* is advised in order to cover the advantages of this mangrove plant and uncover hidden areas to support clinical applications for improved health.

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