ETHNOMEDICINAL, PHYTOCHEMICAL, AND PHARMACOLOGICAL ASPECTS OF GENUS ACANTHUS

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ABSTRACT

Acanthus (family Acanthaceae) is a genus of the major group angiosperms (flowering plants) comprising more than 29 species widely distributed in the tropical and subtropical region. The aim of this review is to offer thorough scientific information on ethnomedicinal uses, phytochemical, and pharmacological activities of the plant species belonging to the genus Acanthus. Numerous traditional uses of the genus have been supported in this article from the results, and executed by the extracts and/or pure compounds obtained from pharmacological studies will provide a single platform to help future researches on the genus Acanthus. Furthermore, ethnomedicinal evaluation using fractions or isolation of medicinal principles was extensively explored by databases like Google, Google Scholar, and Science Direct at the same time.

Keywords: Acanthus, Acanthaceae, Ethnomedicinal uses, Phytochemistry, Pharmacology, Medicinal principles

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INTRODUCTION

The word ‘Acanthus’ is originated from the Greek word ‘Acantha’ meaning thorn or thistle signifies sensitive leaves [1]. Most of the species are shrubs or perennial herbs with terminal or axillary, uninterrupted spikes; flower with lower lip only; calyx 4-lobed with larger posterior and anterior lobes; corolla tube short, horny; elongate 3-lobed lip and with 4 exerted stamens, inserted at top of corolla tube [2]. The genus exhibits some mangrove species which are known to survive in the most antagonistic environment which makes this genus as inimitable taxa among all true mangrove genera that represent both terrestrial species and true mangrove. Thus, researchers grow attractive reason to assemble attention for the study of the genus Acanthus. Furthermore, ethnomedicinal evaluation using fractions or isolation of medicinal principles was extensively explored by databases like Google, Google Scholar, and Science Direct at the same time.

Description of the genus

The genus Acanthus L. is consist of about 29 representative species geographically distributed mostly in the tropical and subtropical region of the world [3]. Total 20 genera from 20 families represent c. 70 true mangroves species among these the genus Acanthus represents five mangrove species e. g. A. ebracteatus, A. illicifolius, A. volubilis, A. latifolius and A. montanus [4-5]. However, Tomlinson and Yang et al. reported only three mangrove species and c. a. 27 terrestrial species [6-7]. In India, only 6 species of the genus are
available; A. ebracteatus Vahl, A. ilicifolius L., A. leucostachyus Wall. ex Nees, A. carduaceus Griff., A. mollis L., A. volubilis Wall. Out of these 6 species A. ilicifolius and A. leucostachyus are extremely medicinal and A. leucostachyus Wall. ex Nees, A. carduaceus Griff., A. mollis L. are terrestrial species [8]. Asia and Australia represent the paramount variety and distribution of mangrove species [1]. Therefore, the genus is unique among all true mangrove genera were both true mangrove and terrestrial members are obtainable. The two sub species A. ebracteatus subsp. ebracteatus and A. ebracteatus subsp. ebracteatus of A. ebracteatus which are endemic to Australia [1]. Moreover, both subspecies are detached by few key morphological features i.e. leaf shape, stem spines, flower color and hairiness etc [1]. In our previous study, the genus was reported with one known species; A. leucostachyus from North East India which was originally established by Wallich in his Numerical List of Dried Specimens (Cat. No. 2512) on the basis of the collection made by F. De Silva from Sylhet District of Bangladesh [8]. But in the worksheet [9], higher plant diversity in Pakke Wildlife Sanctuary and Tiger Reserve in East Kameng District of Arunachal Pradesh revealed another member of the genus. A. ilicifolius L., a shrub was available in those areas, medicinal use still unknown and least concern at the which has the same geographical distribution and same habitat and ecology. Grow shady places association with other plants like Thottea tomentosa (Blume) Ding Hou and Borerria hispida (L.) K.Schm. etc. [8].

Phenology: March-September

Species examined: Specimens of A. leucostachyus Wallich examined in the Bhutan and North East India by various workers in different times [8, 12, 13].

Status: The plant was reported wrongly as endemic to Eastern Himalaya [13-14].

A. ilicifolius L.

Common names: Holv leaved acanthus, holy mango, dense leaved acanthus and sea holy (Eng.), Harkulanta (Hind.), Harkucha kanta (Beng.), Holechudi (Kan.), Payinachulli (Mal.), Kahudaimulli (Tam.), Alasyakampa, Alchi (Tel.).

The plant is a shrub, height up to 3 m green, light green or purple, stem thick, branched, roots rarely above ground leaves simple, opposite, lanceolate to broadly lanceolate, leaf margin spiny/dentate, leaf tip acute, petiole low length 0.5-2 cm long, inflorescences terminal [15].

Distribution: A. ilicifolius true mangrove species distributed in tropical Asia and Africa, through Malay to Polynesia grown in the many of the foreshore areas [1, 16]. The plant is also reported to grow in Bangladesh [17, 18]. In India, it is reported from the east (the large area of mangrove forest, the Sunderbans) and west seashore and Andamans and a northeastern state, Meghalaya [1, 17].

Habitat and Ecology: Generally it is found on river banks or low mainland areas of mangrove forests and its surroundings above the high tide mark [1].

Phenology: February-May.
Specimen examined: India, Andaman and Nicobar Islands, South Andaman, Shoal Bay Creek (P. Ragavan, PBL 30965 and 30966) [15].

*A. ebracteatus* Vahl-Vahl

It is a shrub up to 2 m tall, branched, axial spines downward facing, stem thick, grey tint, roots rarely above ground, broadly elliptic to lanceolate, ~10-20 x 3-5 cm; leaves simple, opposite, leaf tip acute to obtuse with or without spiny; petiole length low ca ~0.5-1.5 cm; inflorescence terminal; ovary bilocular; style surrounded by stamens [15].

Distribution: India, to tropical Australia, Southeast Asia, and the western Pacific islands. In Southeast Asia plant has found in Cambodia, Myanmar, the Philippines, Vietnam, Malaysia, Singapore, Indonesia and Papua New Guinea; in India, it has recorded in Kerala, Puducherry, and ANI [15].

Habitat and Ecology: Grow in landward ends of mangroves over the high tide mark and in inner mangroves.

Phenology: Throughout the year.

Specimen examined. India, Andaman and Nicobar Islands, South Andaman, Sippighat (P. Ragavan, PBL 30969 and 30970) [15].

*Acanthus volubilis* wall

Plant is a twisted shrub up to ~2-4 m tall; stem slim, soft, green, branched, axial spines lacking; roots rarely above ground/prop roots on lower parts of reeling stem; leaves simple, opposite, spines absent, juicy, elliptic/oblong-lanceolate; leaf tip acute to obtuse with spin; leaf margin spines lacking, petiole low length ca 0.5-2 cm long; green; inflorescence terminal; style surrounded by stamens; ovary bilocular [15].

Distribution: South to Southeast Asia i.e. Sri Lanka and the Andaman Islands, to Myanmar, Indonesia, Cambodia, Malaysia, Singapore, Thailand and Papua New Guinea; in India, the plant has found in Odisha, ANI, and Sundarbans [15].

Habitat and Ecology: Grown in landward ends of mangroves up to the high tide mark.

Phenology: March-June.

Specimen examined: India, Andaman and Nicobar Islands, South Andaman, Shoal Bay Creek (P. Ragavan, PBL 30969 and 30970) [15].

*Acanthus mollis* L.

Synonyms: A. Hispiancus Lou., A. latifolius E. Goez., A. longifolius Poir., A. hustinianus Auct., A. niger Mill., A. platyphyllus Murb., A. spinossimum Host.

Traditional uses

*A. ilicifolius* also named as “Holy Mangrove” is used as an ethnomedicinal plant in many countries. In Malaysia the plant leaf used to heal rheumatism, neuralgia and poison arrow wounds; in India, the fresh bark is applied as an antiseptic [19]. The pharmacological study has been extensively performed on this genus. Besides these diverse classes of phytochemicals such as triterpenoids, alkaloids, saponins, glycosides, flavonoids, steroids etc. Ralf and Gerd [39] study also specify the presence of terpenoids, alkaloids, flavonoids, phenols, coumarins. Flower extracts disclose the occurrence of alkaloids, terpenoids, saponins, phenolics, flavonoids, tannins but the absence of steroids [40].

Phytochemistry

Phytochemical study of *A. ilicifolius* done by Raut and Khan [38] emphasized the presence of some important chemical constituents like triterpenoids, alkaloids, saponins glycosides, flavonoids, steroids etc. Ralf and Gerd [39] study also specify the presence of terpenoids, alkaloids, flavonoids, phenols, coumarins. Flower extracts disclose the occurrence of alkaloids, terpenoids, saponins, phenolics, flavonoids, tannins but the absence of steroids [40]. The pharmacological study has been extensively performed on this genus. Besides these diverse classes of phytochemicals such as alkaloids, fatty acids, glycosides, lignans, triterpenoid, coumaric acid etc. various derivatives have been isolated and characterized from different extracts like Hexane, chloroform, ethanol, methanol of *A. ilicifolius*. Illustrated in table 2 with their structures, pubchem ID’s and relevant citations.

Compound isolation

**Pharmacology**

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 [26, 55], antinociceptive activity [56], anti-inflammatory activity [23, 26], anti-osteoporotic activity [57], hepatoprotective activity [26, 59], chemo preventive activity [21]; leishmanicidal tumour reducing and anticanicar activities [26, 58, 59, 60]; antileishmanial, antiulcer, antimicrobial, and osteoblastic activities [26]. Moreover, Firdaus et al. found in their study that flower extract of the plant also has good cytotoxic effects [40]; Smitha et al. showed the anticancer activity of ethyl acetate extract of on two cell lines PA-1 and MCF-7 [61].
| Class of Phytochemicals | Name of the Phytoconstituents | Compound structure | PubChem ID | References |
|------------------------|-------------------------------|--------------------|------------|------------|
| Alkaloids              | Acanthicifoline               | ![Structure](image1) | 442503     | [46]       |
|                        | Trigonellin                   | ![Structure](image2) | 5570       | [44]       |
|                        | 2-benzoxazolinone             | ![Structure](image3) | 6043       | [47, 48]   |
|                        | Benzoxazin-3-one              | ![Structure](image4) | 72757      | [49]       |
|                        | 5,5'-bis-benzoxazoline-2,2'-dione | ![Structure](image5) | NF         | [50]       |
|                        | Benzoxazinoid glucosides      | ![Structure](image6) | NF         | [51]       |
|                        | 4-O-β-D-glucopyranosyl-benzoxazolin-2(3H)-one | ![Structure](image7) | NF         | [52]       |
|                        | 2-hydroxy-4H-1,4-benzoxazin-3-one | ![Structure](image8) | 322636     | [48]       |
| Flavonoids             | Quercetin                     | ![Structure](image9) | 5280343    | [44]       |
|                        | Quercetin-3-O-β-D-glucopyranoside | ![Structure](image10) | 15959354   | [44]       |
| Steroids | Compound      | Chemical Structure | CAS Numbers   | Reference |
|----------|---------------|--------------------|---------------|-----------|
|          | acacetin 7-O-α-L-rhamnopyranosyl-(1”\n|           | 6”)-O-β-D-glucopyranoside (Linarin) and vitexin | ![Linarin](image) | 5317025 & 5280441 | [53] |
|          | Linarin      | ![Linarin](image)  |               |           |       |
|          | Vitexin      | ![Vitexin](image)  |               |           |       |
| Steroids | Cholesterol  | ![Cholesterol](image) | 5997          |           | [49] |
|          | campesterol  | ![Campesterol](image) | 173183        |           |       |
|          | stigmasterol | ![Stigmasterol](image) | 5280794       |           |       |
|          | β-sitosterol | ![β-Sitosterol](image) | 222284        |           | [44] |
Antioxidant activity

Firdaus et al. [40] have scrutinized the antioxidant properties of *A. ilicifolius* by the DPPH scavenging assay. The assay was conducted on total five extracts (acetone, methanol, acetone 70%, methanol 80% and water) of flowers and found that methanol extract showed highest antiradical efficiency (141.30%), while water extract of showed lowest (0.0037%) among the extracts. Dey et al. [27] confirmed the antioxidant effects of the methanol extract of the plant. DPPH assay has been adopted for evaluation of the free radical scavenging activity of the extract by preparing ten different concentrations starting from 500 μg/ml to 0.98 μg/ml using serial dilution technique where IC_{50} was recorded to be 5.1 μg/ml. Moreover, the antioxidant activity of the fractions and isolated compounds of the plant has also been reported [58-60].

Polysaccharides isolated from the plant also showed significant radical scavenging activity [62]; flavonoids and phenolic compounds of *A. ilicifolius* displayed their good antioxidant activity on the animal model [63].

Cytotoxic activity

Firdaus et al. [40] 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. Dey et al. [27] 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.

Antimicrobial activity

Antimicrobial activity of alcohol, butanol and chloroform extract (10 mg/ml) of both leaves and roots of the plant 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 [41] studied antimicrobial activity of 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*).
Three extracts, ethanol, methanol and aqueous of leaf, stem, and root of the plant has used for the activity. The cube plate method used to detect the efficiency of the plant against the eleven bacterial strains Escherichia coli, Bacillus, megaterium, Lactobacillus plantarum, Salmonella paratyphi B, Shigella dyentroze, Streptococcus mutans, Klebsiella pneumoniae, Aspergillus flavus, Staphylococcus albus, and Lactobacillus acidophilus and one fungus C. albicans. Ethanol and methanol extract showed more or less same activity and methanol extract indicated significantly more effective than the aqueous extract. Maximum zone of inhibition noticed on aqueous extract of root and methanol extract of the leaf as 17 mm against the same bacterium, S. albus [26].

Rao et al. [65] examined the antimicrobial activity of methanol, ethanol, and ethyl acetate extracts of flower, seed, leaf, and root of the plant by the well-diffusion method. Microbes like Vibrio harveyi, Aeromonas hydrophila, and E. coli were taken for the test, results direct the highest activity observed on ethyl acetate seed extract against V. harveyi. Dey et al. [27] observed the antibacterial activity of a methanolic crude extract of the plant by ten gram-negative and sixgram positive bacteria, unfortunately, no activity was witnessed for the crude methanol extract.

Anticancer activity

Smitha et al. [61] studied the anticancer activity of ethyl acetate extract of leaf and root extract of the plant on two cell lines, MCF-7 and PA-1. The plant 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. The antimicrobial and antioxidant activity of A. ilicifolius is depicted in table 3.

### Table 3: Antimicrobial and antioxidant activity of Acanthus ilicifolius

| Plant parts   | Solvent used for extraction/isolated compound | Activity against                         | Reference |
|--------------|-----------------------------------------------|-----------------------------------------|-----------|
| Leaf and root | Hexane, chloroform, and methanol              | Antibacterial, antifungal                | [66]      |
| Leaf and root | Benzoino and phenethylidone derivatives       | Antimicrobial                           | [67]      |
| Leaf and root | 2-Benzoxazolinone 4 and benzoxazinium derivatives | Antimicrobial, antifungal and insectidal | [22, 43, 68] |
| Leaf and root | Methanol                                       | Antibacterial                           | [27]      |
| Flower       | Acetone and methanol                          | DPPH                                    | [55]      |

### CONCLUSION

The plants from the genus Acanthus are broadly scattered in the tropical and subtropical regions of the world. The systematic pharmacological studies on the genus have given remarkable recognition to their ethnomedicinal uses in health care management. The phytochemical studies of the genus Acanthus revealed, isolation of a total of 21 bioactive compounds from A. ilicifolius and were identified with their structures and their respective PubChem ID’s were mentioned in this review. Hence, the existence of these bioactive compounds may be explored from other sister species and their different pharmacological properties may also be compared. Numerous pharmacological studies using different types of extracts or pure phytochemicals of Acanthus species well justified their practice as an ethnomedicine; for example, antioxidant, antimicrobial, cytotoxic and anticancer activities besides its well-known antinociceptive, hepatoprotective, leishmanicidal and osteoblastic properties. Furthermore, scanty and limited toxicity reports on the animal model are presently available, which suggests that detailed toxicological evaluation is needed for different extracts from the various species. Consequently, the biological effectiveness should be carried out for the isolated secondary phytochemicals as well, which would definitely authenticate the medicinal claims of the Acanthus genus.

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### CONFLICTS OF INTERESTS

All authors have no conflicts of interest to declare.

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