REVIEW ARTICLE

A review on a lesser known Indian mangrove: *Avicennia officinalis* L. (Family: *Acanthaceae*)

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Abstract

Introduction: The genus of *Avicennia* consists of total eight species which survive at intertidal zones from tropical and temperate regions of world, the foremost species being *Avicennia officinalis* and *Avicennia marina*. The plants belonging to this genus have both therapeutic and economic (industrial) benefits. Among all the species, *A. officinalis* is an important Indian mangrove differentiated greatly by its antibacterial and anticancer activities. This article is an effort to compile all the essential information of *A. officinalis* in a comprehensive manner, including pharmacognostic features, traditional and ethnomedicinal uses, phytochemistry, and pharmacological activities of the plant. **Materials and Methods:** All the information regarding traditional aspects and modern studies of *A. officinalis* were gathered through a massive literature survey of traditional and Ayurvedic books along with scientific resources. **Results and Discussion:** Different parts of *A. officinalis* have traditional medicinal applications for the treatment of various diseases such as cancer, rheumatism, diarrhea, ulcer, Alzheimer and bacterial, fungal, and viral infections. Laboratory investigations so far have resulted in isolation and identification of more than fifty bioactive compounds from different parts of the plant majorly targeting antibacterial activity. The phytochemicals reported as characteristic constituents of this plant are flavanoids, steroids, terpenoids with polyisoprenoids, and tannins. Further, records appertaining pharmacological evaluation have revealed significant activities such as antioxidant, anticarcinogenic, antidiabetic, antiviral, and many more. **Conclusion:** The article summarizes the diversity and distribution of *A. officinalis,* in addition to in-depth coverage of traditional medicinal usage and phyto-pharmacological investigations done on this medicinal plant so far, highlighting the need for further studies on the phytoconstituents responsible for the validated traditional and folklore claims of its enormous medicinal usage.

Key words: *Avicennia officinalis*, Indian mangrove, phytochemicals, pharmacological activities

INTRODUCTION

The mangroves are taxonomically diverse group of halophytic plant community found in tropical and sub-tropical regions across the globe.[1,2] They can endure extreme temperature, high salinity, and other abnormal natural conditions. Their contribution in enhancing biodiversity and stabilizing coastal environments is widely accepted.[3] The genus *Avicennia* is the lone mangrove genus that occurs throughout the world. Along with *Rhizophora*, it forms the dominant plant communities of mangrove forests.[4] Unlike other mangroves, *Avicennia* grows in a very wide range of salinities and intertidal topographic positions. Based on the concurrence of phylogenetic evolution, the Royal Botanic Gardens, Kew and Missouri Botanical Garden states that the genus *Avicennia* consists of eight species, namely, *A. officinalis* L., *A. balanophora* Stapf & Moldenke, *A. bicolor* Standl, *A. germinans* (L.) L., *A. integra* N.C. Duke., *A. marina* (Forssk.) Vierh., *A. schaueriana* Stapf and Leechm. ex Moldenke, and *A. tonduzii* Moldenke.[5] Out of these, *A. officinalis* is an important yet lesser known

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Received: 26-05-2020
Revised: 07-01-2021
Accepted: 25-01-2021

mangrove, the importance of which is highlighted in this article.

A. officinalis (sometimes also referred as *A. tomentosa* and *A. alba*) is majorly found in salt marshes and tidal creeks of tropical and sub-tropical regions of India, Bangladesh, Brunei, Myanmar, Sri Lanka, Thailand, and the Philippines.[6-8] It is generally known by various names in different languages that include White Mangrove, Indian Mangrove (English) as it is found in most coastal states of India; Sagarodbhutah, Tuvara (Sanskrit); Baen, Bina (Hindi); Tivar (Gujarati); Bani (Bengali); Ipati, Uppati (Kannada); Upati (Konkani); Kandal, Upattam (Siddha/Tamil); Orayi (Malayalam); and Tavir (Marathi).[6,7,9] Polyisoprenoids in particular dolichols are observed to be of chemotaxonomic significance for the mangrove.[10] *A. officinalis* is documented to show presence of the salts of iridoid acids and their cinnamic acid esters. Avicennioside, a C_9-iridoid, has been found only in *A. officinalis* and not in *A. marina* that was not considered separate species earlier.[11]

MATERIALS AND METHODS

A literature search was conducted using the keywords "*Avicennia*," "Indian mangrove," "white mangrove," "phytochemicals," and "biological activities" on electronic databases (Web of Science, PubMed, Scopus, Science Direct, Google scholar, Springer Link, ACS Publications) and traditional and Ayurvedic books were thoroughly referred to compile published research works till April 2020. Moreover, bibliographies of the cited articles were also tracked to document total literature.

Botanical Description

A. officinalis grows as a fairly big tree of 12–18 m height and 3.6–4.5 m girth with smooth lenticels and light colored bark that is not fissured. Depending on the color of the bark, it is differentiated from other species (black and mottled). The wood of *A. officinalis* is very brittle and coarse grained.[6] The leaf is coriaceous having salt crystals in the surface, especially in dry weather,[1,12] leathery, opposite, elliptic oblong or obovate-oblong, glabrous above, and tomentose beneath and 5.0–7.5 cm long.[6] Flower is 1 cm in diameter and is the largest among all the species of its genus.[1,13] It is orange-yellow present in small globular heads or in trichotomous corymbs, ovoid, compressed,[6] distinctly zygomorphic and broken with 3–7 flowers in each head with petals that are hairy inside, scarcely 5–6 mm in diameter, expanded, and with rancid or fetid smell. The corolla sometimes has yellow throat, hence named bicolor. Distinctive feature of the flower is the inequality of the stamens, formed inside at the same level as in the flower. The filaments of outer pair are at least 1 mm long compared with the inner pair, which is 0.5 mm.[1] The fruit is an ovoid capsule, 2.5–4 cm long and contains a single seed which completely fills the capsule. A grown up tree has 8–20 cm long, pencil-like pneumatophores, and aerial stilt roots. There are numerous upright air-filled roots that rise above the soil from long horizontal thin roots beneath the soil.[1,12,13] *A. officinalis* tree growing in its natural habitat along with its flowering twig is represented in Figure 1.[14]

DISTRIBUTION AND HABITAT

Avicennia members are densely distributed mangrove species found in both coastal river and sea-beds of tropical as well as temperate regions worldwide.[1] *A. officinalis* is reported to have varied distribution in tropical and subtropical regions of both North and South America including Colombia, Costa Rica, Mexico; Panama, Brazil, Chile; coast of Africa; Middle East, South, and South-East Asia which include Coast of India, Bangladesh, Malaysia, Vietnam, Thailand, Indonesia; and coast of Trans Asia countries, Australia, and New Zealand.[6,15]

Taxonomic Ambiguity

The genus *Avicennia* (L.) is named after *Avicenna* or Abdallah Ibn Sina (980–1037 AD), a Persian physician.[16] This genus is kept in the division of Tracheophyta, subdivision Spermatophytina, class Magnoliopsida, and order Lamiales.[17,18] The allocation of family to the genus *Avicennia* has long been a controversial subject. There are different opinions concerning the systematic rank of *Avicennia* as a monotypic family Avicenniaceae, as a subfamily Avicennioideae, or as a tribe Avicenniae; the phylogenetic relationship of *Avicennia* to the Verbenaceae, Santalales, Celastrales, Dipterocarpaceae, and Ancistrocladaceae; and the subdivision of the genus into sections and the definition of the species.[13,17,18] Over the years, botanists across the globe have tried to exemplify the taxonomical classification of the genus through their classical investigations, accounting its proximity to the family Avicenniaceae.[12,19,20] Morphologically, *Avicennia* differs from the typical Verbenaceous plants in its incomplete four-celled ovary with a free central placenta, the orthotropous ovules, fruits with endosperm, a viviparous embryo, wood anatomy, and pollen morphology.[21] On the contrary, modern molecular studies and phylogenetic relationships indicate that the genus has closer proximity towards the family Acanthaceae.[20]

Figure 1: Avicennia officinalis (a) plant in its natural habitat and (b) a flowering twig

Ethnomedicinal Uses

The *Avicennia* species are traditionally used throughout the world as medicine. The local community inhabiting the mangrove forest mainly uses *A. officinalis* for the treatment of various diseases. The whole plant is generally used in treatment of tumor, rheumatoid arthritis, ulcer, and diabetes.[22,23] People of South-East Asia use the flowers to produce some of the best honey in the world possessing antibacterial and antioxidant properties. Resin oozing out from the bark is mentioned to be useful as a contraceptive in Java.[24,25] In Arabia, the root of *A. officinalis* is used as an aphrodisiac and unripe seeds are used as poultice to hasten suppuration of boils and abscesses. In Indo-China, the bark is used for skin application especially in curing scabies. In India, the mangrove plant has been used in folklore medicines for management of various complications such as rheumatism, paralysis, asthma, snake-bites, and ulcers.[6,26] Fruits and immature seeds are used as natural cicatrizant of abscesses and ulcers. The pulp of unripe fruits of *A. officinalis* was earlier used to heal skin lesions of smallpox. In Sundarbans of India, warm juice extracted from skin of fruits is used in treatment of sores, while plant decoction along with sugar is used in dyspepsia accompanied with acid eructation.[7,18] The plant is commonly used in India in the form of herbal preparations for treatment of scabies, boils, tumors, hepatitis, and leprosy. It is also prescribed as an aphrodisiac, contraceptive, and diuretic.[26-28]

Other Economic Uses

The tannins of the bark of *A. officinalis* are commonly employed in dyeing and leather industries. The wood is utilized as a fuel and construction material. It is also used for cheap beams, door frames, rice pounders, boats, and in oil mills. Wood ash is employed for washing clothes in Tamil Nadu and also mixed with paints to make the latter adhere more firmly.[6] Branch is fed to cattle as fodder as well as used for the preparation of doors and mats. The pneumatophores of this plant are used for production of bottle stoppers and floats. Seeds are soaked in water overnight, then boiled and used as famine food in Celebes. The fruits are used as an insect-repellent and are also edible and consumed by fishermen in Java. The bitter fruits and seeds are occasionally eaten after baking or steaming.[6,26,28] *A. officinalis* is considered as potential accumulator of trace metals (Iron, Manganese, Zinc, Copper, Lead, Nickel, Chromium, Cobalt, Arsenic, Cadmium, and Mercury).[29,30] Bio-accumulation of vanadium, niobium, and tantalum that are recognized as technologically critical elements of high demand for industrial development, have also been observed in the mangrove.[31]

A Source of Potential Endophytes

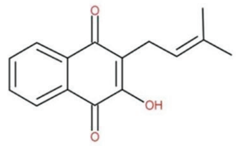
Endophytes include a group of microorganisms associated with healthy plant tissues of a host plant. Their biological diversity is large and noticeable, mainly in temperate and tropical rainforests.[32,33] Endophytic fungi, especially from mangrove plants, are rich source of secondary metabolites which play a major role in various pharmacological actions, preferably in cancer and bacterial infections. Several reports on different potentially active endophytes of *A. officinalis* are recorded that produce many compounds and may prove to be suitable sources of new natural products.[34] The mangrove and its predominant endophytic fungus *Aspergillus flavus* are shown to possess antioxidant activity in various *in vitro* assay systems (such as iron chelating capacity, reducing power and hydroxyl radicals/hydrogen peroxide/1-Diphenyl-2-picryl-hydrazyl radical scavenging activities, and inhibition of lipid peroxidation using the *β*-carotene-linoleate model system). This represents mutual associations of the plant and endophyte against various biotic and abiotic stresses.[35]

Seven endophytic fungal strains have been isolated and identified from the leaves of *A. officinalis*, of which *Irpex hydnoides* demonstrates substantial cytotoxic effect against Hep2 cell lines with 125 μg/mL IC_{50} value. The bioactive metabolite responsible for this effect is suggested to be tetradecane by GC-MS analysis.[36] A study on evaluation of crude extract of a novel strain *Alternaria longipes* VITN14G obtained from *A. officinalis* for *in vitro* antidiabetic activity by assessment of *α*-glucosidase and *α*-amylase inhibitory activities has led to 2,4,6-triphenylaniline showing no significant difference in *α*-amylase inhibition rates and a significant difference of 10% in *α*-glucosidase inhibition rates than that of the standard drug acarbose. Moreover, it is shown to result in a cell viability of 73.96% on L929 cell lines. Further, the binding energies of the isolate with glycolytic enzymes have been calculated by molecular docking studies and the *in silico* studies indicate that 2,4,6-triphenylaniline produces a stronger binding affinity toward the glycolytic enzyme targets, thus supporting the outcome of antidiabetic activity for type 2 diabetes.[37]

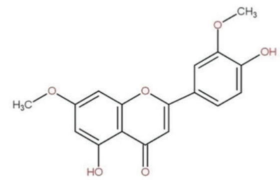
Phytochemistry

In genus *Avicennia*, the first investigation on chemistry was done back in 1913, when Bournot isolated and detected lapachol with anti-tumor activity from *A. officinalis* growing in West-Africa and India.[7,38] Further studies have led to the chemical profiling of *A. officinalis* indicating the presence of wide class of bioactive compounds such as terpenoids, steroids, alkaloids, flavonoids, polyphenols, phenolic acids, saponins, and tannins.[39-45] The chemical structures of some of the important constituents are shown in Figure 2.

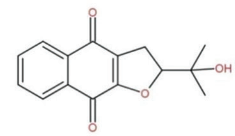
Chrysoeriol 6’’-(3’’’,5’’’-dimethoxycoumaroyl)-7-O-β-D-glucopyranoside, luteolin 7-O-β-D-glucopyranoside, 3’-methylluteolin-4’-O-βD-glucopyranoside, flavogadorinin, and astaxanthin are isolated and identified from the leaves of *A. officinalis*.[46,47] Naphthofuranquinones reported in the twigs of the plant include avicenol C and



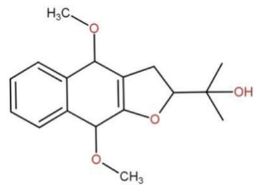
Lapachol



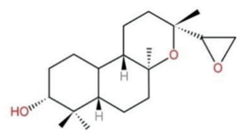
Velutin



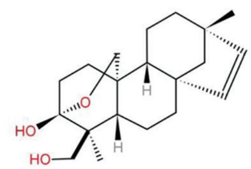
Avicequinone



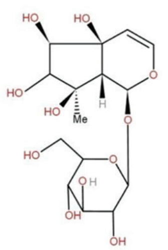
Avicenol C



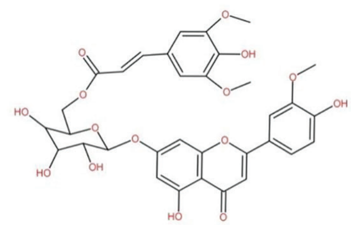
Rhizophorin-B



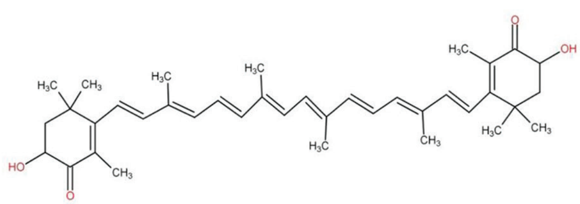
Excoecarin A



Avicennioside



Chrysoeriol 6"-(3"',5"'-dimethoxycoumaroyl)-7-O-β-D-glucopyranoside



Astaxanthin

Figure 2: Chemical structures of some important constituents of *Avicennia officinalis*

stenocarpoquinone B.[48,49] Aviridoid (1S,5R,8S,9R)-2'-(E-coumaroyl) mussaenosidic acid, velutin, α-tocopherol, a mixture of 6-methoxynaphtho(2,3-b)-furan-4,9-quinone, and 7-methoxynaphtho(2,3-b)-furan-4,9-quinone, Avicequinone C, along with iridoids, avicennioside, 7-cinnamoyl-8-epiloganic acid, geniposidic acid, and 2'-cinnamoylmussaenosidic acid have also been isolated and characterized from the *A. officinalis* leaves.[11,50,51] The leaves are also reported to contain 8-O-cinnamoylmussaenosidic acid, officinosidic acid [5-hydroxy-10-O-(p-methoxycinnamoyl) adoxosidic acid], known iridoids loganin, and 10-O-(5-phenyl-2,4-pentadienoyl) and geniposidic acid along with a disaccharide acteoside as peracetates.[52] The methanol extract of plant is reported to yield 1,2,3-benzene triol and 4, 4'-(1-methylethyldiene)bis-2-methyl. Diterpenoids such as ent-16-hydroxy-3-oxo-13-epi-manoyl oxide, rhizophorin-B, triacontan-1-ol, ribenone, excoecarin A, ent-15-hydroxy-labda-8,13E-dien-3-one, ent-3,15-dihydroxy-labda-8,13E-diene, and ent-(13S)-2,3-seco-14-labden-2,8-olide-3-oic acid have been isolated and identified in the roots. Lupeol, betulinic acid, ursolic acid, and betulin have been isolated from the hexane extract, while 4',5-dihydroxy-3',7-dimethoxyflavone and 8-O-acetylharpagid iridoid are isolated from the ethyl acetate extract of this plant.[53] The triterpenoids isolated from chloroform-methanol extract of fresh mangrove leaves include *α*-amyrin, *β*-amyrin, lupeol, oleanolic acid, and ursolic acids and the reported sterols are cholesterol, campesterol, stigmasterol, sitosterol, and stigmast-7-en-3-β-ol.[39,54] Taraxerol, β-amyrin, taraxerone, betulin, betulinic acid, and triacontanal have been isolated from bark and leaf of *A. officinalis*. The light petroleum extract of aerial parts, on further processing, is noted to yield lupenone, friedelin, lupeol, β-sitosterol, betulinic acid, ursolic acid, and its methyl ester and methyl ester acetate.[7,55]

Phytochemical investigation of the aerial roots of *A. officinalis* of Krishna estuary, India, also revealed the presence of three pentacyclic triterpenoids-betulin aldehyde, betulinic acid, and betulin.[56]

Pharmacological Activities

Numerous pharmacological studies of *A. officinalis* have been performed so far that correlate well with the folklore and traditional uses of this plant. The medicinal potential of its extracts and the bioactives is discussed in detail to uncover therapeutic value of this species.

Anti-cancer and Cytotoxic Activity

Crude ethanolic extract of leaves of *A. officinalis* showed cytotoxic effects in brine shrimp lethality bio-assay carried out against *Artemia salina* using vincristine sulfate as positive control, where the LC_{50} of the extract was found to be 131.2 μg/mL.[57]

The cytotoxic effect of *A. officinalis* leaf methanolic extract (at 200 and 400 mg/kg doses) was also evaluated for cancer management, using Ehrlich ascitic carcinoma (EAC) cell lines for inducing cancer in mice. The LD_{50} value of the extract administered to mice was found to be greater than 4 g/kg. Its effect on cancerous cell growth and host survival was estimated by evaluating cell count and percentage increase in lifespan of the tumor hosts and drug treated groups. The extract reversed the hematological changes induced by the cell lines and the mean survival time of EAC transplanted mice was found to increase from 22.33 days of EAC control group to 29.32 days (for 200 mg/kg) and 33.66 days (for 400 mg/kg) in treated groups, which was found significant when compared 5-flourouracil (20 mg/kg) treated group.[58]

Antidiabetic Activity

The ethanolic extract of *A. officinalis* bark is reported to exert significant hypoglycemic activity at 200 mg/kg dose in streptozotocin (STZ)-induced diabetic mice by inhibition of α-amylase and α-glucosidase, the carbohydrate metabolizing enzymes. Besides, the blood glucose level, it has also shown to lower the total cholesterol, triglyceride, liver toxicity markers (SGOT and SGPT), and urea levels.[59] The petroleum ether and aqueous extracts of leaves were also evaluated for *in vitro* antidiabetic activity by α-amylase and α-glucosidase assays, where aqueous extract (1 mg/mL) was found to be more effective than crude petroleum ether extract.[60]

Antidiarrheal Activity

The methanolic extract of *A. officinalis* leaf exhibits noticeable antidiarrheal activity in castor oil-induced diarrhea in mice. The extract causes significant increase in the mean latent period and reduces the frequency of defecation at an oral dose of 500 mg/kg when compared to the standard drug loperamide (50 mg/kg). The effect is attributed to the saponins, steroids and alkaloids present in *A. officinalis* and the mechanism is proposed to be inhibition of autocoids and prostaglandins release, which, in turn, inhibits motility and secretion induced by castor oil.[61,62]

Anti-inflammatory Activity

The methanolic extract of leaves (200 and 400 mg/kg) is shown to possess remarkable dose-dependent anti-inflammatory activity in carrageenan-induced acute, formalin-induced sub-acute, and Freund's adjuvant-induced chronic arthritis inflammatory models in rats. The activity was reported to be comparable to the standard drugs indomethacin and diclofenac sodium. Betulinic acid, a triterpenoid, was suggested to be responsible for the effect and the inhibition of prostaglandins was proposed to be the mechanism behind it.[63,64]

Antimicrobial Activity

Hexane, chloroform and methanol extracts of mature leaves and bark are shown to exhibit antimicrobial activity against various human and plant pathogenic bacteria and fungi, using agar well-diffusion method.[57,65,66] In an experimental study, different diterpenes isolated from *A. officinalis* roots collected from Andhra Pradesh (India) were evaluated for antimicrobial activity. The study revealed moderate antifungal activities of Excoecarin A, ent-16-hydroxy-3-oxo-13-epi-manoyl oxide and ent-15-hydroxy-labda-8(17),13E-dien-3-one against *Rhizopus oryzae* and *Aspergillus niger*, along with antibacterial activity of rhizophorin-B1 against *Bacillus subtilis*.[67] In a bioactivity-guided fractionation study for active antibacterial metabolites from *A. officinalis* twigs collected from Malaysia, strong inhibitory effect was observed on Gram-positive bacteria (*Bacillus subtilis*, *Staphylococcus aureus,* and *S. epidermidis*), the minimum inhibition concentration values being in the range of 0.156–5.0 mg/mL. On the contrary, Gram-negative bacteria (*Enterobacter cloacae*, *Vibrio cholera,* and *Escherichia coli*) were not affected by the plant extracts. Two naphthofuranquinones, avicenol C, and stenocarpoquinone B, isolated from the active fractions using chromatographic techniques, were suggested to be responsible for the antibacterial action.[48]

Fruit extracts of *A. officinalis* in ethyl acetate, acetone, ethanol and methanol solvents, and the bioactive principles isolated thereof, namely, 1,2,3-benzenetriol and 4,4'-(1-methylethyldiene)bis2-methyl, also exhibited antibacterial activity against *Enterobacter cloacae*, *Proteus vulgaris*, *Bacillus cereus,* and *Enterococcus faecalis*.[68]

Various extracts of *A. officinalis* leaf in different solvents showed promising effects when examined for antimicrobial activity against pathogenic organisms such as *Agrobacterium tumefaciens, Streptococcus mutans, Staphylococcus aureus, Trichophyton rubrum, Aspergillus flavus, Klebsiella pneumoniae, Pseudomonas aeruginosa, Bacillus subtilis, Escherichia coli,* and *Serratia marcescens*. The ethyl acetate extract being the most potent extract was found to contain a mixture of diethyl phthalate, hydroxyl-4-methoxy benzoic acid and oleic acid as the active principles, through a GC-MS analysis.[40,69-71]

Anti-nociceptive, Analgesic, and Antipyretic Activities

The ethanol and methanol extracts of dried leaves are shown to produce 64.67% writhing inhibition in acetic acid-induced writhing test in mice at the oral dose 500 mg/kg, the effect was comparable to the standard drug diclofenac sodium that showed 85.95% inhibition at 25 mg/kg dose. The presence of polyphenolic compounds such as flavonoids and tannins along with pentacyclic triterpenes in the leaf extracts is indicated to be possibly responsible for pain inhibition in mice.[57,62,72]

On investigation of methanolic extract of aerial parts (at 100 and 200 mg/kg doses) for analgesic activity using tail immersion and radiant heat methods, it was noted to possess central and peripheral mechanisms for pain inhibition. The mechanism was suggested to be initiated by the effect of the extract on modulation of action potential and signal transmission generated from the sensory mediators such as delta and C fibers sensory neurons to relive pain. The same extract on oral administration at 200 mg/kg dose exhibited antipyretic effect similar to acetyl salicylic acid in brewer's yeast-induced fever model, through possible mechanisms of prostaglandin inhibition by blocking cyclooxygenase enzyme activity.[73]

Antioxidant Activity

A. officinalis fruit and leaf extracts possess profound antioxidant potential as proven by 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid), that is, ABTS, chromium peroxide (CrO_5), and Ferric reducing antioxidant power (FRAP) assay methods. Out of the various tested extracts, ethanol and methanol extracts exhibited highest activity, while ethyl acetate and aqueous extracts demonstrated lowest activity.[13,74] The ethanol bark and leaf extracts exhibit a dose-dependent scavenging potential against ABTS, DPPH, and superoxide radicals with IC_{50} values ranging from 82 to 207.6 μg/mL,[66] the petroleum ether and aqueous extracts of leaves also demonstrate antioxidant capacity in DPPH, superoxide, and hydrogen peroxide scavenging assays with IC_{50} values ranging from 0.17 to 0.27 mg/mL for the extracts.[57,59,60]

Antiulcer Activity

The ethanolic extract of *A. officinalis* leaves was examined for ulcer-protective effect by employing aspirin and pylorus ligation (APL) and indomethacin-induced acute gastric ulcer models in albino rats. The study revealed notable decrease in the ulcerative lesion index on oral administration of the extract at the doses of 250 and 500 mg/kg, comparable to the standard drug omeprazole (30 mg/kg). The potential anti-secretory and antiulcer effects were shown to be mediated through reduction in free acid and total acid by the leaf extract. In another experiment, antiulcerogenic, and gastro-protective effects of aqueous leaf extract, attributed to the presence of polyphenols and hydrolyzable tannins, was highlighted using non-steroidal anti-inflammatory drugs (NSAID)-induced, pylorus-ligated induced, and ethanol-HCl induced ulcer model in rats.[45,75]

Anti-HIV Activity

In reverse-transcriptase inhibition assay and glycoprotein gp120 binding inhibition assay methods, petroleum ether and aqueous extracts prepared from *A. officinalis* leaf powder exerted strong *in vitro* antiviral effect. The mode of action derived was especially the interference with gp120/CD4 interaction by binding to both gp120 and CD_4 (T-cell) ligand.[76]

CNS activity

The leaf extracts (at the doses of 250 and 500 mg/kg) are documented to reduce the time of onset of sleep and potentiate the sleeping-time in pentobarbital-induced hypnosis test in mice, suggesting its CNS depressant activity. Furthermore, the probable tranquilizing effect has been confirmed by decrease in the responses of mice in exploratory behavior tests (hole cross, head dip, and open field tests).[61,77] Through another study, the ethyl acetate extract of leaf was verified to possess CNS depressant activity by neuropharmacological experiments conducted for the assessment of locomotion and muscle coordination ability in mice. It was revealed that different doses of the extract (250, 500, and 1000 mg/kg, orally) reduced the locomotor activity in rota rod and forced swim tests in a dose-dependent manner. The sedative effect was further confirmed by promotion of diazepam-induced sedation by all the three doses of the extract.[78]

The methanolic extract of leaves produced cholinesterase inhibitory activity at concentration <2 mg/mL when evaluated through an *in vitro* assay method. Various concentrations of the extract when incubated with total cholinesterase and butyryl cholinesterase produced 50% inhibition of both the enzymes as assessed by Ellman's colorimetric method and the effects were found to be comparable to the standard drug donepezil. The study suggested that this effect of *A. officinalis* can be taken into account for development of safe and effective medicine for neurodegenerative disorder like Alzheimer's disease.[79]

Diuretic Activity

The methanolic leaf extract exerts marked diuretic effect on Swiss-albino mice, as evident from its effect on Na^+/K^+ excretion ratio of 1.52 and 1.33 at 200 and 400 mg/kg doses, respectively. The extract, through its effect on rate of glomerular filtration and direct inhibitory effect on the reabsorption mechanism of salt, initiated the diuretic action by increasing urine volume along with Na^+ and Cl^- load, with lesser potassium-related side effect. The effect was comparable to that of the standard loop diuretic drug furosemide and diuretic agent urea.[77]

Other Potential Biomedical Uses

Phytoremediation capacity

A. officinalis demonstrates strong metal retention capacity by adopting the phyto-extraction and phyto-stabilization strategies. In various experimental studies, different trends of accumulation of trace metals (Cobalt, Chromium, Copper, Iron, Manganese, Nickel, and Zinc) and heavy metals (Lead, Arsenic, Mercury, and Cadmium) by the pneumatophore, leaves, and bark are determined. The pneumatophore tissues are shown to accumulate maximum concentration of the metals, thereby illustrating immense potential for removing pollutants from large area of abiotic milieu (soil, water, and sediments) without affecting the ecosystem adversely.[29-31,80]

Biosynthesis of Silver Nanoparticles

Studies have reported that mangrove plants such as *A. officinalis* and *A. marina* provide are highly efficient for the synthesis of biologically active silver nanoparticles which could be exploited by pharmaceutical industries for prevention of several dreadful diseases. The terpenoids and polyphenolic compounds found in *A. officinalis* leaves extract which are proven to be potential reducing agents in the synthesis of the silver nanoparticles. This biological approach would be cost effective for large-scale production and would serve as best alternative to conventional chemical and physical methods of silver nanoparticles synthesis.[81,82]

CONCLUSION

Mangroves are considered to be the most productive ecosystems in the world. Reintroduction of mangrove vegetation needs be prioritized not only in the context of predicted consequences on global warming, sea level rise, coastal erosion, and other natural as well as man-made disturbances but also due to the huge therapeutic potential of this plant according to the traditional claims and scientific studies. The review discusses about botanical identification, distribution, potential secondary metabolite composition, and bioactivities of *Avicennia officinalis* in a comprehensive manner. It has been noted that mangrove can be used an accumulator of hazardous metals and thus can serve as useful tool as phyto-extractor of the toxic metals. In addition, potential endophytes from *A. officinalis* are noted that could serve to yield bioactive lead molecules. Through tracking of the literature for this study, we could verify the available literature for validation of most of the traditional and folkloric claims pertaining to the medicinal usage of this plant. Further, it is evident that most of the chemical constituents of *Avicennia officinalis* remain unknown and have not even been studied so far. Therefore, this review strongly recommends bringing forward the scientific information on this potential mangrove for its sustainable use as a source of valuable medicinal compounds.

ACKNOWLEDGMENT

The authors are thankful to L. M. College of Pharmacy, Ahmedabad, Gujarat, for providing necessary facilities for the literature survey and access to online resources to gather comprehensive information for the review article.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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Source of Support: Nil. **Conflicts of Interest:** None declared.