Journal of Applied Pharmaceutical Science Vol. 0(00), pp 001-011, 2024
Available online at http://www.japsonline.com
DOI: 10.7324/JAPS.2024.181289
ISSN 2231-3354

A review of botany, phytochemistry, and pharmacology of the mangrove apple *Sonneratia alba* J. Sm.

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ARTICLE HISTORY
Received on: 14/12/2023
Accepted on: 23/01/2024
Available Online: XX

Key words:
Antimicrobial, ethnomedicine, pharmacognosy, *S. alba*, pedada, perepat.

ABSTRACT

Mangroves are salt-tolerant plants that form distinctive communities and ecosystems. To survive in a harsh environment, mangroves are believed to produce numerous phytochemicals. *Sonneratia alba* J. E. Smith is a true type of mangrove plant belonging to the family Lythraceae. This evergreen tree has been widely distributed in the Indo-West Pacific region and is a common species along both the east and west coasts of India. It is the maiden mangrove species in India that has received recognition as the state mangrove plant by the state of Maharashtra. This mangrove has been widely used in traditional medicine for treating skin disorders, bleeding injuries, diarrhea, and so on. Its bioactivity can be attributed to its phytochemical content, which is rich in phenolics, steroids, tannins, terpenoids, and so on. This review is an attempt to compile various phytochemical and bioactivity investigations done on *S. alba*. Results indeed showcase its therapeutic prospects as indicated by the wide range of secondary metabolites and biological activities.

INTRODUCTION

Plants and products derived from them have tremendous pharmacological importance. They produce a number of phytochemicals, many of which have ethnomedicinal applications and have also found a place as lead molecules for discovering new drugs [1,2].

Mangroves are special plants that have been used in folklore medicine for a long time. They have developed unique adaptations and several novel metabolites to tolerate and thrive in harsh, salty waters. Distributed in over 120 countries globally, they form unique and extremely productive communities with other mangroves and associated flora and fauna. They are also of ecological, economical, and medicinal importance. No wonder there exist numerous reports that establish the therapeutic potential of mangroves [3–6].

Sonneratia alba J. E. Smith is a true mangrove species. This evergreen tree is a core mangrove occurring in the Indo-West Pacific region of the globe [7]. Inspite of having numerous applications, a dedicated review on *S. alba* could not be found. Therefore, an attempt has been made to compile up-to-date information available on this plant to highlight its significance.

MATERIALS AND METHODS

Globally recognized databases such as Google Scholar, Scopus, PubMed, Scilit, ResearchGate, and Science Direct were screened to gather the reported work done on *S. alba*. The specific keywords included *Sonneratia alba*, *S. alba*, phytochemistry, pharmacognosy, antibacterial, mangrove, pedada, perepat, bioactivity, phytomedicine, pharmacological activity, and ethnobotany. While the focus has been on articles dated 2013 to 2023 (the last 10 years), few published before 2013 have been also included to avoid missing out on some important observations on the study plant. Relevant references cited in these articles were also considered to make this narrative review as complete as possible.

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RESULTS AND DISCUSSION

Classification and taxonomy

The name of genus *Sonneratia* has been conferred in honor of a French explorer and botanist, Peirre Sonnerat whereas the name of the species *alba* was given owing to the presence of peculiar white-colored stamens and petals in this species (*Alba* meaning white in Latin) [8]. Earlier this species used to be classified into the Sonneratiaceae family but phylogenetic studies using molecular markers have shown that Sonneratiaceae happens to be a sub-set of the family Lythraceae [9]. The Lythraceae family includes more than 30 genera having 620 plus species; the majority of which are widespread in tropical regions and few in temperate regions of the world [10].

Earlier, *Sonneratia* genus was represented by five main species viz. *S. alba* Sm., *Sonneratia ovata* Backer, *Sonneratia apetala* Banks, *Sonneratia griffithii* Kurz, and *Sonneratia caseolaris* (L.) Engler [11,12]. However, it was improved by the inclusion of *Sonneratia lanceolata* Blume [13], making it a total of six species that can be distinguished from each other on the morphological characters such as size and shape of the fruit and leaf, the color of the flowers, and so on. In the overlapping regions, these species often hybridize naturally, resulting in *Sonneratia* × *hainanensis*, *Sonneratia* × *gulngai*, and *Sonneratia* × *urama* [12]. The hybrids, however, exhibit reduced genetic fitness than their true parent species with a large number of sterile pollens [14,15].

English botanist Sir James Edward Smith in the year 1816 first described *S. alba* in Cyclopedia with a typified name of *Sonneratia acida* var. *mucronata*. Other synonyms for *S. alba* include *S. acida* Benth., *Sonneratia iriomotensis* Masam., *Sonneratia mossambicensis* Klotzsch *ex* Peters, and *Chiratia leucantha* Montr. *Sonneratia griffithii* Watson is now a synonym of *S. alba* Sm. [12,15].

This mangrove species is taxonomically classified as follows:

Kingdom: Plantae
Sub-kingdom: Viridiplantae
Infra-kingdom: Streptophyta
Phylum: Tracheophyta
Sub-phylum: Spermatophytina
Class: Magnoliopsida
Super-order: Rosanae
Order: Myrtales
Family: Lythraceae
Genus: *Sonneratia*
Species: *Sonneratia alba*

Sonneratia alba is most commonly identified as "mangrove apple" or "sweet-scented mangrove apple" for the apple-like fruits it produces. This mangrove is also known by several region-specific names as mentioned in Table 1 [12,14–22].

Botany

Sonneratia alba (Fig. 1) usually grows to a height of 10–15 m. However, shrub-like specimens of 3 m tall and huge trees growing to 30 m have also been occasionally found. The tree is branched and the creamish/brownish bark is characterized by longitudinal fissures. This mangrove is surrounded by thick, short, blunt pneumatophores having an average size of 25–30 cm. Leaves are glabrous, leathery, stalked, simple, opposite having elliptic to obovate shape. At the apex, they become sub-orbicular obtuse. Leaves are normally 5–12 cm in length having a breadth of 4–6 cm. The base of the leaf is narrowed into a short petiole of just 3–5 mm long. This mangrove produces bisexual, white-colored flowers (3–6 cm) which are usually present singly or at times, in groups of three. The petals are small and white. Six to eight lobes are present inside the calyx tube which resembles a cup. Sepals are long and have a green color outside and a red color inside. Stigma is capitate, style is around 4 cm long whereas the ovary is globose. Every flower has long, attractive, 5–8 cm long, white stamens which are many in number. Flowers are nocturnal; they open in the late evening and last only for that one night. The calyx is filled with large amounts of nectar, attracting insects (such as Hawk moths), birds, and mammals (bats) that facilitate its pollination [14,15]. Flowering season has been observed to vary from country to country having different geographical and climatic conditions. In general, it usually flowers from February to July. Fruits are hard, around 4 cm in diameter, have a smooth surface, and are green in color. Around 150 small-sized, curved seeds are produced inside each fruit. The fruiting season depends upon the region-specific flowering season and in general, the fruiting is observed from August to February [15,23].

Global distribution

The species has a widespread global distribution in tropical and sub-tropical countries ranging from East Africa to northern tropical Australia (passing through India and South East Asia), the west Pacific Islands, and southwest Oceania. *Sonneratia alba* has been reported in more than 23 countries in

Table 1. Common and Vernacular names of *S. alba.*

Bengali: *Sadachak keora*	Kannada: *Karpu*	Sinhala (Sri Lanka): *Kirilla*, *Kirala*
Chinese: *Bei e hai sang*	Konkani: *Pandhari Chipi*	Swahili (East Africa): *MLilana*
Khmer (Cambodia): *Ampouthmar*, *Rompea-chheu*	Marathi: *Karpu*, *Chipi*	Telugu: *Pedda Kalinga*
English: *Mangrove apple*	Malayalam: *Chakkarakantal*, *Nakshathrakandel*	Tagalog/Filipino (Philippines): *Bunayon*, *Patpat*, *Bungalon*, *Palalan*, *Ilukabban*, *Payan*
Indonesian: *Perepat*, *Posi-posi*, *Bidada*, *Pidada*, *Pedada*, *Bogem*, *Tamindao*	Malay: *Perepat*, *Pidada*, *Pedada*	Thai: *Lampoo thale*, *Lampoo talay*
Japanese: *Mayapushiki*	Odia: *Orua*	Vietnamese: *Ban dang*

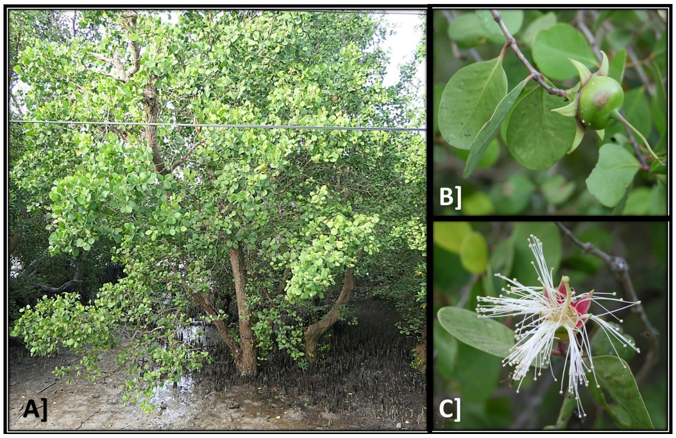

Figure 1. *Sonneratia alba* with its important parts. (A) Tree with spike-like pneumatophores. (B) Close-up of the leaves and fruit. (C) White flower (stamens) with pink colored base.

Africa, Asia, and Australia continents. Being a quite commonly seen species through most of its global range, it is categorized with the "Least Concern" tag in the IUCN's Red List Book of Threatened Species [24].

Habitat

It is a pioneer species which means that it prefers higher salinities of 18%–30% and is generally present on the seaward side (away from the mainland). It is unable to tolerate much of freshwater. It has been often found thriving in sandy clay habitats or on the recently developed mud flats but at times, has been also seen growing along rocky coastal shores [15,25].

Local and ethno-medicinal uses

Sonneratia alba is well-known by the locals for its edible fruit which is often consumed. In the Goa state of India, ripe fruits of *Sonneratia* sp. are used for making curries while unripe ones are used in making jellies [25]. They are also used in making pickles and vinegar. Tribals of Bhitarkarnika Wildlife Sanctuary in Odisha state, India have been preparing a vegetable using it [18]. Cakes are also made for eating [26]. The bark is used for the extraction of tannins and as a source of fuel whereas honey is also gathered thanks to its nectar-producing flowers [23]. Wood is utilized for making boxes, as a packing material as well as in the building material. In the Sulawesi province of Indonesia, boats and houses are constructed using the timber of *S. alba*. There are reports of bridges, cabinets, wharfs, furniture, floorings, and musical instruments being made from wood. Tribal folks from Papua New Guinea have been making use of pneumatophores in making floats and corks [15]. Fishing communities of East African coastal countries have been using *S. alba* wood for making ribs and keels of large watercraft (dhows) and also in oars, paddles, and masts [20,27]. Bark extract has been regularly used by natives in Indonesia to delay the fermentation and thereby preserve the alcoholic, palm tree-based drink [28].

Traditional healers and tribes have been using this plant for treating health ailments. Extracts or pulp from the fruit are used as a poultice for treating muscular swellings and sprains. A compression is made using the fruit pulp and is applied to stop hemorrhage. It is also used to cure various skin disorders [15]. The plant is believed to have antiseptic properties. *Sonneratia alba* is commonly used in Indian and Indonesian folklore medicine for treating injuries (sprains and wounds), diarrhea, and fever [18,21,23].

Phytochemistry

Plants produce phytochemicals in the form of primary and secondary metabolites. The former is involved in metabolic activities, while the latter is involved in protecting the plant from the attack of herbivores by playing a crucial role in the defense mechanisms [1]. Members of the genus *Sonneratia* are rich sources of phytochemicals [29]. Primary metabolites in *S. alba* include various carbohydrates and sugars, proteins and amino acids, lipids and fatty acids whereas a wide range of secondary metabolites belonging to classes such as triterpenoids, phenolics, steroids, and so on, have also been documented.

Several reports are available involving qualitative as well as quantitative analyses, showing the presence of all major phytochemical classes such as alkaloids, phenolics, flavonoids, saponins, tannins and terpenoids, quinones, and steroids in *S. alba* leaf, fruit, bark samples indicating it produces a wide range of primary as well as secondary metabolites [30–35].

Table 2 depicts the proximate elemental content in different parts of *S. alba* [36–41]. Values seem to vary in different parts. Analyzing ion concentrations of Na^+, Cl^-, and K^+ is essential in the case of mangroves such as *S. alba* that grow in a harsh, saline habitat. Stress experienced from such abiotic factors acts as inducers in mangroves leading to the production of novel metabolites [5].

The composition of natural saturated, monounsaturated, and polyunsaturated fatty acids was studied in the freshly collected leaves and stems. Results indicated that *S. alba* can act as a rich alternative source of natural essential fatty acids (EFAs), predominantly gamma linolenic acid (GLA). Higher percentages (36%) were found in leaf samples whereas stem had 11% GLA. EFAs are required in important metabolic reactions governing normal body functioning and are known to prevent the risk of heart attack and cancer [42].

From the elemental analysis of *S. alba* fruits and flour, it was evident that content and nutritional value in terms of carbohydrates and proteins increased when the flour was prepared from the fruits. On the contrary, fruits contain relatively higher fat content than those found in flour prepared from the fruits [38]. Owing to the presence of a higher vitamin content (294.26 ppm) and significantly higher antioxidant activity, it is suggested to use *S. alba* leaf tea as a nutritionally rich, healthier beverage [34]. Tannin content (hydrolysable type) in the bark of *S. alba* has been reported at 7.6% [43].

The floral scents of mangrove species found on the Iriomote Islands, Japan, were analyzed for chemical characterization [44]. *Sonneratia alba* floral scent was reported to have the presence of four main compounds viz. trans-β-ocimene (a mono-terpene), 2, 4-dithiapentane (an organo-sulfur), 2-heptanone (a ketone), and methyl-2-methylbutanoate (a fatty acid ester). Detection of 2, 4-dithiapentane in floral scent is attributed to the fact that nocturnal flowers of *S. alba*

Table 2. Proximate elemental composition in different parts of *S. alba.*

	Bark	Leaves	Fruits	Fruit flour
Water/moisture	38.23%	48.11%	30.71%	10.1%
Ash	6.21%	4.16%	5.06%	5.3%
Carbohydrates	37.16%	31.56%	52.16%	74.5%
Proteins	1.91%	2.78%	3.48%	8.5%
Fats	0.85%	1.04%	8.59%	1.49%
Fiber	15.64%	12.35%	------	------

	Young leaves	Old leaves
Low molecular weight carbohydrates (mol./m^3 plant water)		
Glucose	21.7	9.1
Fructose	25.4	7.0
Sucrose	5.8	10.1
Hexitols	199.7	79.1
Myo-inositol	1.7	1.1
Pinnitol	1.8	0.4
Nitrogenous compounds (mol./m^3 plant water)		
Total nitrogen	345.1	222.3
Total methylated oniun compounds	10.3	5.8
Total free amino acids	4.7	2.3
Proline	0.51	0.08
Glutamic acid	1.17	0.66
Aspartic acid	1.09	0.53
Alanine	0.37	0.24
Organic acids (equ./m^3 plant water)		
Malate	42.9	43.7
Citrate	12.0	9.4
Concentration of ions (equ./m^3 plant water)		
Chloride	472	745
Sodium	356	669
Potassium	128	36
Magnesium	139	106
Sulphate	32	53

are pollinated by bats. Other molecules are believed to help in attracting other pollinating insects and birds.

The composition of lipids in *S. alba* leaves and roots was studied [45]. Wax ester is the largest component comprising 19.3% of the total lipid, followed by sterol ester (16.8%) and polar lipids (11.7%). Similar to other mangroves, triterpenoid alcohols and phytosterols are commonly found in *S. alba*. Studying triterpenoids is crucial since they are known to play an important role in the adaptation process of several plants such as mangroves to the salt stress [46,47].

Table 3 and Figure 2 show a few important novel compounds and phytochemical classes isolated from the different parts of *S. alba*. Many of these have been reported to have bioactivities, and their pharmacological importance has been well-documented.

Pharmacological studies

Anti-bacterial

There are numerous reports highlighting the broad range of antibacterial potential of *S. alba* against both Gram-positive and negative bacteria [61].

Promising activity *in vitro* was reported by ethanol and aqueous leaf extracts against human bacterial pathogens *Staphylococcus aureus*, *Streptococcus* sp., multidrug-resistant *Salmonella typhi*, *Proteus vulgaris*, and *Proteus mirabilis* [62]. The antibacterial activity of crude methanol extract of bark showed promising activity against eleven tested bacteria. *Staphylococcus auerus*, *Salmonella typhimurium*, *Shigella flexneri*, and *Vibrio cholera* were found to be the most susceptible [63]. Carbon tetrachloride (CTC) fraction of methanol bark extract exhibited moderate inhibition of various

Table 3. Novel compounds/secondary metabolites isolated/identified from *S. alba.*

Sr. no.	Name of the compound and class	Part used and place of work	Bioactivity (if any)	Reference
1.	Lupeol, oleanolic acid, betulinic acid (triterpenoids); 2,6-dimethoxy-p-benzoquinone (quinone); a mixture of stigmasterol and β-sitosterol (phytosterol)	Twigs Thailand	Antimycobacterial Antimalarial	[48]
2.	Oleanolic acid, betulin, betulinic acid, alphitolic acid (triterpenoids); methyl gallate (phenolic compound) and 5-hydroxymethylfurfural (furan)	Leaves Vietnam	----------------	[49]
3.	Lupeol, oleanic acid (triterpenoids); β-sitosterol, β-stigmasterol (phytosterol); and sitost-4-en-3-one (steroid)	Leaves Bangladesh	Antioxidant Antibacterial Cytotoxic	[50]
4.	3,3'-Di-O-methylellagic acid (phenolic compound)	Bark Indonesia	Antioxidant	[51]
5.	3β-Hydroxy-lup-9(11),12-diene, 28-oic acid, lupeol, lupan-3β-ol (triterpenoids)	Bark Indonesia	Antibacterial	[52]
6.	Oleanolic acid, ursolic acid, α-, and β-amyrin cinnamate, lupeol (triterpenoids); β-sitosterol and stigmasterol (phytosterol); and squalene (lipid)	Fruits, twigs and leaves	----------------	[53]
7.	Lupeol (triterpenoids)	Leaves Indonesia	Antibacterial	[54]
8.	Lupeol (triterpenoids)	Leaves Indonesia	Anti-cholesterol	[55]
9.	Five novel sonneratiosides: A–E and β-D-glucopyranoside (sesquiterpene glycosides); ampelopsisionoside, lauroside A (megastigmane glycosides); alangionoside A (ionol glycosides); benzyl alcohol β-D-glucopyranoside; luteolin 7-O-rutinoside, isovitexin (flavone), arbutin (glycosylated hydroquinone)	Leaves Japan	Tyrosinase Inhibitory	[56]
10.	Mixture of the stigmasterol and β-sitosterol (phytosterol)	Roots Indonesia	Weak antioxidant	[57]
11.	β-Sitosterol (phytosterol)	Roots Indonesia	Cytotoxic	[58]
12.	Orientin, vitexin, luteolin (flavonoids); oleanolic acid (triterpenoid)	Leaves Indonesia	Anti-diabetic	[59]
13.	Luteolin, apigenin, and diosmetin (flavonoids)	Leaves Indonesia	Anti-diabetic	[60]

Gram-stain-positive bacteria viz. *Bacillus cereus*, *Bacillus subtilis*, *Sarcina lutea* as well as Gram-stain-negative bacteria viz. *Pseudomonas aeruginosa* and *Shigella dysenteriae* [64]. Another *in vitro* study done in Malaysia reported that the methanol leaf extract was found to be effective against Gram-stain-positive *S. aureus* and *B. cereus*, and the Gram-stain-negative *Escherichia coli* bacteria [65]. These bacteria were reported to be sensitive to methanol as well as ethanol extracts prepared from the leaves and bark but tolerant to chloroform extract [66]. Aqueous extracts prepared from leaves, fruits, and bark have been found active against *E. coli* and *S. aureus* [67].

Quorum sensing (QS) involves cell-to-cell communication, a life process controlling mechanism in bacteria (such as expression of pathogenicity and production of biofilms). Hence, disturbing QS can kill the bacteria. *Sonneratia alba* root extract is reported to have anti-QS activity *in vitro* against the bacteria *Chromobacterium violaceum* [68].

Flavonoids extracted from the *S. alba* fruits exhibited activity against pathogenic *Vibrio alginolyticus* whereas the isolated triterpenoid inhibited pathogenic *S. aureus*, *P. aeruginosa*, and *E. coli in vitro* [54,69]. Three lupane-type triterpenoids isolated from *S. alba* inhibited Gram-positive bacteria *S. aureus* ATCC 6538 and *Streptococcus mutans* ATCC 25175 [52]. Synthesized zinc oxide nanoparticles using *S. alba* leaf extract have shown excellent *in vitro* antibacterial activity against Gram +ve as well as −ve bacteria [70].

In an *in vivo study*, giant tiger prawn post-larvae were fed with Brine shrimps enriched with *S. alba* fruit extracts and later challenged with their common pathogen *Vibrio harveyi*. Treated larvae showed a significantly higher survival rate clearly indicating that *S. alba* extracts can have an important application in inhibiting *V. harveyi* infection in cultured prawns, ultimately increasing the commercial production [71]. Similar results have been reported of the protection conferred against *Saprolegnia* sp. [72]. *Sonneratia alba* ethanol leaf extract was highly antibacterial against a fish pathogen *Salmonella*

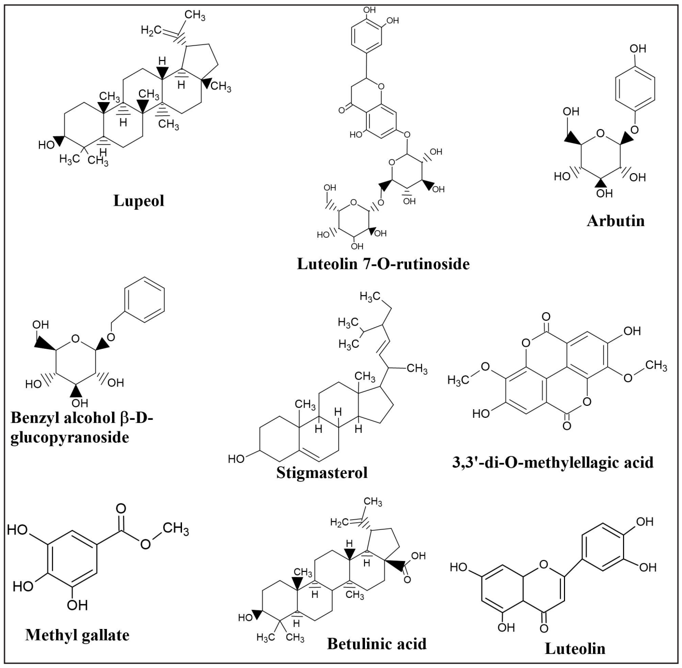

Figure 2. Representative bioactive compounds identified in *S. alba.*

arizonae with a zone of inhibitions comparable with those shown by standard antibiotics. Further testing *in vivo* showed a clear reduction and delay of the onset of goldfish mortality when infected with *S. arizonae* [73].

Anti-fungal

Extracts of *S. alba* fruits prepared in n-hexane, ethyl acetate, and ethanol exhibited moderate *in vitro* activity against the fungus *Candida albicans* whereas methanol fruit extracts inhibited the growth of the fungus *Helminthosporium* sp. which is known to cause corn leaf blight [74,75]. Methanol leaf extract was found to be effective against the fungus *Cryptococcus neoformans* [65]. CTC fraction of methanol bark extract showed mild antifungal activity against *C. albicans*, *Aspergillus niger*, and *Saccharomyces cerevisiae* when tested *in vitro* [64].

Anti-viral

Sonneratia alba leaf-synthesized silver nanoparticles tested *in vitro* at concentrations of 5–15 µg/ml were able to down-regulate the expression of the gene responsible for the envelope and a crucial protein in the dengue virus (serotype DEN-2) [76].

Insecticidal

In an *in vivo* study, methanol, ethyl acetate, and hexane extracts of *S. alba* fruits at 10% concentration exhibited 98%, 44.5%, and 28.4% mortality in *Nezara viridula* larvae. *Nezara viridula* commonly known as green stink or shield bug is a polyphagous plant eater and, therefore, needs to be controlled [77]. Silver nanoparticles synthesized using *S. alba* leaves were found to be lethal against the larvae and pupae of *Aedes aegypti* mosquitoes (LC_{50} of 3.15–15.61 ppm) *in vivo*. When treated with these *S. alba*-derived nanoparticles, adult guppy fish were found to predate mosquito larvae at an accelerated rate [76].

Antioxidant

Lipid peroxidation is known to be involved in aging, cancer, and so on [78]. Antioxidants are known to protect our body cells from harmful damage caused by free radicals. Therefore, studying antioxidant activity is considered to be important since it can lead to the identification of a bioactive molecule with therapeutic potential [79].

There are numerous *in vitro* studies that report the antioxidant potential of *S. alba*. Ethanol and methanol crude extracts of both leaves and bark along with the fractions partitioned in water showed IC_{50} values in the range of 0.019–0.038 mg/ml clearly indicating the antioxidant ability when compared with the IC_{50} value of 0.018 mg/ml by the standard vitamin C in the 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay [66]. Ethyl acetate fraction of methanol extract prepared using sepals was found to be a very strong antioxidant having an EC_{50} of 2.57 µg/ml and it also showed a strong lipid peroxide formation inhibition activity with IC_{50} of 0.84 µg/ml [80]. Nufus *et al.* [37] reported anti-oxidant activities at 9.83, 15.17, and 8.38 ppm for n-hexane, methanol, and ethyl acetate extracts prepared from *S. alba* fruits and described them as very strong since they were below 50 ppm. The chloroform bark extract showed the highest free radical scavenging activity with an IC_{50} value of 12 µg/ml in comparison with positive control butylated hydroxyl toluene (10 µg/ml). At the same time, the crude methanolic extract also exhibited strong antioxidant potential having an IC_{50} value of 14 µg/ml [64]. Methanol extract of stem and leaves showed an IC_{50} of 62.5 and 87.5 µg/ml whereas ethanol extract of bark and leaves showed an IC_{50} of 67.2 and 88.7 µg/ml [30,81].

It is well established that the total phenolic contents and antioxidant activities are positively correlated, flavonoids and other phenolic compounds contribute to antioxidant activity [82]. Scopoletin (a coumarin) along with other phenolics detected in the ethanol extract were suggested to be contributing to the activity. Extracts prepared from young leaves using soxhlet (in methanol) and by maceration (in ethanol) reported IC_{50} of 5.16 and 5.01 µg/ml, respectively, comparatively better than shown by standard ascorbic acid (5.21 µg/ml) indicating potent *in vitro* antioxidant activity [32]. Aqueous and methanol extract of *S. alba* bark showed almost double the concentration of total phenolic content than found in green tea and, therefore, exhibited potent *in vitro* DPPH radical scavenging activity [83]. Sumartini *et al.* [34] reported very strong *in vitro* antioxidant activity (average IC_{50} of 50 ppm) of the tea prepared using *S. alba* young and old leaves powder. 3,3’-di-O-methylellagic acid, an isolated phenolic compound, methanol bark extract, and ethyl acetate fraction all showed potent *in vitro* antioxidant activity when compared with L-(+)-ascorbic acid as standard by using DPPH assay. The samples tested exhibited significantly lesser IC_{50} values around 12 µg/ml than the standard which showed 17.64 µg/ml [51].

Thalassemia patients require antioxidant supplements to prevent oxidative stress. Ethanol leaf extract when tested *ex vivo*, was found to be a decent antioxidant and could be supplied as a natural antioxidant to anaemic thalassemia patients [84]. Ethyl acetate root extract and the isolated phytosterol, however, showed relatively weaker activity *in vitro* [57]. Silver nanoparticles synthesized from aqueous stem extracts and zinc oxide nanoparticles synthesized from leaf extract have also exhibited remarkable *in vitro* antioxidant activities [70,85].

Hypoglycemic/anti-diabetic

A polysaccharide isolated from the leaf extract of *S. alba* exhibited remarkable blood glucose attenuating activity *in vivo* as it lowered the blood sugar concentration by 19.2% during the first 6 hours and reduced it further to 66.9% post 12 hours of treatment [86]. In another *in vivo* study on STZ drug-induced hyperglycemic mice, a promising lowering of blood sugar levels (average being 39.6%) was observed post 6 hours after administration of *S. alba* nontoxic fraction separated from the leaf extract which further dropped to 56.4% 12 hours after the injection, clearly highlighting the presence of hypoglycemia-inducing principle present in the tannin-containing purified fraction [87]. Using *en silico* molecular docking studies, phytochemical compounds identified from methanol and ethyl acetate extract of leaves of *S. alba* were found to be α-glucosidase inhibitors and suggested to have a potential to be developed into anti-diabetic agents [59,60].

Analgesic

Methanol fraction of *S. alba* leaves extract was tested *in vivo* for its pain-relieving potential by observing formalin-induced hind foot/paw licking in Swiss albino mice. Mice that were pre-treated with methanol fraction (at 200 and 400 mg/kg) exhibited an encouraging dosage-dependent decrease in the hindfoot licking induced by formalin. Analgesic activity was comparable with the standard painkiller drug diclofenac but at a higher dose of 400 mg/kg suggesting further purification was warranted to enhance the activity [88].

Anti-inflammatory

Sonneratia alba extract at a dose of 150 and 300 mg/kg was found to be effective against inflammation (carrageenan-induced edema in albino mice). Results of this *in vivo* study, were highly promising when compared to the groups treated with the standard anti-Inflammatory drug Ibuprufen [88]. Silver nanoparticles synthesized from aqueous stem extracts and zinc oxide nanoparticles synthesized from leaf extract have also exhibited remarkable *in vitro* anti-inflammatory activities when tested for albumin protein denaturation inhibition and human erythrocytes membrane stabilization, respectively [70,85].

Acetyl cholinesterase inhibitory activity

Compounds with this ability can enhance the neuromuscular transmission process by increasing the levels and available time of the neurotransmitter enzyme acetylcholine in the central nervous system (CNS). A positive correlation has been reported between the % inhibitory activity and concentration of the *S. alba* leaf and bark extract prepared in methanol and dichloromethane when tested *in vitro* [89].

CNS depressant

Methanol faction of *S. alba* leaf extracts was tested *in vivo* to study the locomotor exercise, by employing gap cross and open-up field analysis tests in study mice. Results clearly showed that the samples tested were able to decrease the frequency and the degree of movement. Since the CNS plays a decisive role in regulating locomotor activity, the reduced activity is suggested to result from the sedation caused by the tested plant samples [88].

Tyrosinase inhibitory

Enzyme tyrosinase plays a pivotal role in melanin pigment production in the skin. Hence, anti-tyrosinase agents are being explored since they can help reduce melanin formation thereby skin darkening. Bark extract was found to have the highest anti-tyrosinase activity (82.4%), followed by leaf extract (72.5%). Root extracts exhibited relatively lower activity (40%). Results of this *in vitro* experiment suggest that purified products from bark and/or leaves could find a place in developing cosmetics [83]. Luteolin 7-O-rutinoside (a flavonoid), and arbutin (a hydroquinone) isolated from the leaves showed *in vitro* tyrosinase inhibitory activity in terms of IC_{50} at 387 ± 38.2 and 525 ± 77.4 µM, respectively [56]. Acetone leaf extract showed an IC_{50} of 0.55 mg/ml indicating potent anti-tyrosinase activity *in vitro* [90].

Polyphenol oxidase (PPO) inhibitory

It is studied since PPO inhibitors can control/delay the post-harvest browning of vegetables and fruits; increasing the shelf life and sale value. Promising inhibition of 82% of PPO in sweet potato was exhibited by *S. alba* extract in an *in vitro* investigation [91].

Anti-atherosclerotic

Atherosclerosis is defined as inflammation in blood vessels, specifically in the medium-sized arteries, it is a significant risk factor for cardiovascular disease. Masdar *et al.* [92] employed an *in vivo* rat model for the investigation of the anti-atherosclerotic potential of *S. alba* fruit extract. Atherosclerosis condition was induced in Wistar rats by administering a high-fat diet. *Sonneratia alba* fruit methanol extract showed an inhibitory effect on high-fat diet-induced atherosclerosis at the initial stage but did not affect the lipid profile in blood in Wistar rats [92]. In an *in vitro* study, a triterpenoid compound (lupeol) isolated from leaf methanol extract was shown to reduce cholesterol in a concentration-dependent manner from concentrations of 5 to 80 ppm at 13.7% to 77.0% indicating its potential [55].

Cytotoxic

There are *in vivo* cytotoxicity studies done against brine shrimps *Artemia salina*. *Sonneratia alba* leaf extracts prepared in three different solvents were found to be toxic against *A. salina*. LC_{50} values recorded were 3.59, 6.37, and 98.37 ppm for ethyl acetate, ethanol, and n-hexane extracts indicating ethyl acetate extracts to be most cytotoxic [91]. In another study, leaf methanol extract showed LC_{50} values of 817.5 and 515.8 ppm in the case of acute and chronic treatments with brine shrimps which indicate mild toxicity [86]. Cytotoxicity against *A. salina* exhibited by the CTC soluble partitionate of methanol bark extract was found to be promising [64]. Phytosterol isolated from the root extract was found to have an IC_{50} of 10.04 µg/ml clearly indicating its toxic nature and potential to be developed into an anticancer drug [58].

Anticancer

Leaf extract prepared in ethyl acetate was found to have moderate cytotoxicity *in vitro* against cervical cancer HeLa cells with an IC_{50} value of 478.63 µg/ml. If the extract is further purified, isolated compounds could exhibit potent anticancer activity [93]. In a recent *in vitro* study, gold nanoparticles synthesized from the fruits showed promising cytotoxic activity against A549 nonsmall cell lung adenocarcinoma [94].

Anti-malarial

In an *in vitro* experiment, 2, 6-dimethoxy-p-benzoquinone isolated from *S. alba* twigs has been reported to be a potent antimalarial compound with an IC_{50} of 3.08 µg/ml against a multidrug-resistant strain of *Plasmodium falciparum* [48]. Methanol leaf extract (rich in quinones) was found to be effective in reducing the parasitemia levels in mice erythrocytes infected by protozoan *Plasmodium berghei*. This *ex vivo* study reporting anti-plasmodial activity was noteworthy since the activity recorded was even better than the one exhibited by the standard anti-malarial drug pyremethamine [95].

CONCLUSION

Mangrove apple *S. alba* has a wide range of bioactivities such as antimicrobial, anti-oxidant, anti-diabetic, anti-viral, insecticidal, analgesic, cytotoxic, and so on. Having acetyl cholinesterase inhibitory activity can have numerous medicinal applications in the treatment of conditions such as myasthenia gravis, glaucoma, Alzheimer's disease, and so on. It is found to be a strong anti-oxidant, in addition to being nutritionally rich, edible, and cholesterol inhibitor, making it a good candidate to be developed as a food additive. Being a tyrosinase inhibitor, it can find applications in cosmetics for manufacturing creams that can control skin darkening. *In silico* studies have suggested that leaf extract of *S. alba* would have anti-diabetic potential. These activities are attributed to the presence of various phytochemicals such as terpenoids, phytosterols, flavonoids, coumarins, and so on. It is concluded that this mangrove can be an excellent natural resource for carrying out purification, isolation, and chemical characterization of bioactive principles to make the best of its therapeutic potential.

ACKNOWLEDGMENT

Authors are thankful to Shri. Dinesh Valke, a naturalist from Maharashtra state, India for kindly permitting to use the photograph of *S. alba* for educational purpose.

AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be an author as per the International Committee of Medical Journal Editors (ICMJE) requirements/guidelines.

FINANCIAL SUPPORT

There is no funding to report.

CONFLICTS OF INTEREST

The authors report no financial or any other conflicts of interest in this work.

ETHICAL APPROVALS

This study does not involve experiments on animals or human subjects.

DATA AVAILABILITY

All data generated and analyzed are included in this research article.

USE OF ARTIFICIAL INTELLIGENCE (AI)-ASSISTED TECHNOLOGY

The authors declares that they have not used artificial intelligence (AI)-tools for writing and editing of the manuscript, and no images were manipulated using AI.

PUBLISHER'S NOTE

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How to cite this article:
Kulkarnii CP, Manohar SM. A review of botany, phytochemistry, and pharmacology of the mangrove apple *Sonneratia alba* J. Sm. J Appl Pharm Sci. 2024. http://doi.org/10.7324/JAPS.2024.181289