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REVIEW ARTICLE

Sonneratia apetala: Its Ecology, Bioactive Compounds and Biological Activities Including its Nano-formulations

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Abstract

Plants have been the primary source of medications and are essential to maintaining human health. Despite significant advancements in the field of synthetic medications and antibiotics, plants continue to be essential in both traditional and modern medicine all over the world. It significantly increases soil fertility and has a variety of characteristics that make it an ideal founder restoration species. There has not been any evidence of an *Sonneratia apetala* natural invasion in the northern mangrove region yet. This tree is an evergreen species that is known for its rapid growth and natural occurrence. The main phyto-constituents present in *Sonneratia apetala* are betulinic acid, lupeone, lupeol, stigmast-5-ene 3beta, *β*-amyrin hexadecaneate, 5*β*-cholestane-3*α*,7*α*-diol, and physcoion. Some chemical constituents present in *Sonneratia apetala* are gibberellin, quercetin, caffeic acid, (-) catechin, and epicatechin. The fruits and bark have antioxidant, antidiabetic activity, antibacterial, hepatoprotective effect and astringent activity, anticancer activity, hypouricemic activity, and gastroprotective effects. The constituents of bark and leaf include flavonoids, alkaloids, tannins, glycosides (anthraquinone and cardiac), terpenoids, saponins, steroids, protein and amino acids, steroid and gums, carbohydrates, vitamins (thiamine, riboflavin) and certain minerals. This review also reported its ecological-, salt regulatory- and reproductive- features as well.

Keywords: Biological Activity, Nano Formulations, Natural Compound, Phytoconstituents, *Sonneratia apetala*

1. Introduction

Sonneratia apetala is a rapidly growing, evergreen tree species with a woody structure that is prevalent in the Sundarbans mangrove forest (Figure 1). It is also found in abundance in coastal regions of various countries such as India, Bangladesh, Malaysia, Myanmar, China, and New Guinea[1]. At maturity, the observed diameter at the breast height of this specimen can range from 20 to 30 cm, while its maximum height can reach up to 20m. This botanical specimen is known by various nomenclatures such as *motitavar*, *keora*, *kandal*, *chipi*, and *keruan*. The foliage of *S. apetala* is characterized by its simple, opposite arrangement, obtuse, oblong, and lanceolate shape, and the presence of a petiole that tapers towards the base of the leaf. The flowers exhibit bisexuality and are characterized by cymes and axillary inflorescence. The inflorescence is terminal and axillary, with cymas that are typically 1-2 flowered. The flowers are composed of 4 sepals and are yellowish or white, measuring approximately 1.5 to 2 cm in length. The most intriguing aspect of the flower is its style, comprising a curved, white stigma measuring 2 to 3 cm in length and flattened in the shape of a mushroom or umbrella. The fruit in concern is a berry that typically exhibits a rounded shape, possesses a dark green hue, and features a smooth texture. It is typically characterized by

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Figure 1. The plant of *Sonneratia apetala*.

a diameter of approximately 1 to 1.25 cm and contains numerous seeds. There are approximately 25-125 seeds that remain within a fruit[2]. Similarly, Chaudhuri and Choudhury reported that there are approximately 30-60 seeds that remain within a fruit[3]. According to Siddiqi *et al.*,[4] the average number of seeds found in 1kg of fruit is 8000. Approximately 93% and 63% of the seeds retained their viability after twenty and 40 days of storage, respectively. The roots of the plant possess pneumatophores that comprise parenchymatous tissue and a multitude of lenticels that ensnare atmospheric oxygen[5]. In regions characterized by a high sedimentation rate, mangroves generate a fresh set of cable roots, a significant quantity of pneumatophores[6], supplementary growth of pneumatophores[7], and an augmented number of lenticels on the pneumatophore, aerial root, and stems. During the initial phase, the bark exhibits a smooth texture, while in the later stages of maturity, it becomes rough and develops irregular fissures. The colouration of the bark varies between brown to dark hues, and it measures approximately 13 to 16 cm in thickness[8]. The branches are slender and drooping. Microscopically The leaf surface is cuticular are covered by waxy terete or hooked rodlets type of crystalloids, rodlets edges or less entire with irregular shape. Stomata sunken and stomata chimney may be present[9]. The terminal walls of xylem vessel elements are characterized by an oblique or transverse orientation and may exhibit a truncated or tailed morphology at one or both extremities. Additionally, the perforation plate is simple. The phenomenon of inter-vessel pitting is characterized by the presence of elliptical-shaped, crowded, and alternate pits with a diameter ranging from 3.75 to 17.56 µm. The pitting observed in Ray's vessels is characterized by a diameter ranging from 2.5 to 3.75 µm, exhibiting an alternate pattern and presenting a circular or oval shape. The fibres exhibit characteristics such as possessing thin walls, being septate, and having minute, simple, slit-like structures in their radial walls. The abundance of axial parenchyma is notably low. The rays exhibit homocellularity and possess a width ranging from 1 to 2 cells, while their height varies from 2 to 24 cells. Additionally, they contain gum deposits and crystals. To address the challenges posed by multi-drug-resistant bacteria and the problem of chemical drug abuse, it's imperative to explore novel strategies. As a result, microbial diseases will be easier to control. These herbal medications are less dangerous, have fewer adverse effects, and are also reasonably priced[10].

Mangrove plants have been extensively documented as dependable reservoirs of alkaloids, flavonoids, and saponins, which harbour distinctive anti-bacterial, anti-fungal, and anti-viral properties that can be extracted from them. In addition, these substances are rich in phytochemicals that have been shown to possess disease-preventive properties[11]. Food-based antioxidants are essential health-protective ingredients. According to scientific research, antioxidants reduce the risk of chronic illnesses like cancer, cardiovascular, and gastrointestinal ailments[12]. The plant's fruits have been employed in conventional medicinal practices to address diverse maladies such as gastrointestinal diseases, cough, intestinal parasites, bleeding, sprain, diarrhoea, bruises, otitis, and cataracts. In addition to their primary applications, these agents are also utilized for their vermifuge, anti-inflammatory, and hepatoprotective properties. Additionally, several plant parts are employed in the treatment of heart and hepatitis illnesses[13].

Even though there is a significant amount of review articles on *Sonneratia apetala* available on the internet, phytochemical analysis, pharmacological activities along with its nano-formulations and patents have not yet been reported in a single platform. Considering this, the study that is provided here describes information about the therapeutic potential of the *S. apetala* plant as well as its nanoformulations, patents, and some tentative conclusions.

1.1 Ecological Features

S. apetala is a species of mangrove that is indigenous to tropical and subtropical coastal regions. According to Robertson and Alongi's[14] findings, this species is typically located within the upstream estuarine zones of the low to mid-intertidal regions. According to previous studies[5,15], this species can establish a monophyletic stand. Additionally, it serves as a pioneer species during ecological succession in mangrove ecosystems[16]. According to Troup's[17] findings, the species tends to establish colonies on recently formed mudflats that exhibit moderate to high levels of salinity. The favourable ecological features of *S. apetala* are as follows. The plant thrives in nascent mudflat environments and exhibits a limited distribution primarily along the outward slope. The climate conditions are expected to range from normal to very humid, with a desirable precipitation level of 1337 to 2968 mm. The optimal temperature range for this particular entity is between 26.5 to 28.5 °C on an annual basis. Additionally, the mean minimum temperature during the coldest month required is 13.6°C. The plant's salinity tolerance threshold is reported to be between 3-8 parts per million (ppm) for soil and up to 44 ppm for water. Under optimal ecological conditions, the annual mean diameter increment is 0.60cm[18].

1.2 Salt Regulating Features of *S. apetala*

Sonneratia apetala has been identified as possessing the dual characteristics of salt exclusion and salt accumulation[19], as reported by Saenger in 1982 and Hutchings and Saenger in 1987. Like numerous other halophytes[20], *S. apetala* can amass various non-ionic[21] and ionic[22] solutes within its cellular structure, resulting in the creation of an osmotic pressure that surpasses that of seawater. Macnae documented an osmotic pressure range of 6 to 8.5 MPa[23], while the osmotic pressure of soil water was approximately 2.5 MPa in *S. apetala*. According to Scholander's observations, the elevated osmotic pressure within mangrove cells facilitates the extraction of water via oceanic sources through a mechanical ultra-filtration mechanism. After undergoing filtration, salt that enters the plant organism must be segregated from physiological processes. The process of isolation in *S. apetala* is achieved through the accumulation of isolating substances in various plant parts, including the senescent leaves and bark, and stem of pneumatophore. According to Banerjee's findings, leaves possess aqueous tissue as a means of adapting to elevated levels of salt concentration[24].

1.3 Reproductive Features

S. apetala is a plant species that undergoes pollination by various organisms such as moths[19], bats[25], honeybees, and other insects[3]. Birds were also identified as pollinators by Backer and Steenis in 1948. *S. apetala*'s flowers possess a significant amount of nectar, thereby serving as an attractant to these vectors. Pijl observed the spatial arrangement of flowers situated at the terminal portions of pendulous branches, which facilitate their conspicuousness and accessibility to bats[26]. The mode of dissemination for the fruits and seeds of *S. apetala* is hydrochory, as reported by Chapman[27] and Saenger[19]. The seeds possess a diminutive size and a surface that is characterized by irregular angularity and corrugation, which confers upon them a high surface area about their mass. This feature renders the seeds well-suited for transportation over long distances via water.

1.4 Pests and Insects Infestation on *S. apetala*

Most of the species that consume *S. apetala* were documented as being minor pests. However, certain species have the potential to emerge as pests, leading to the possibility of an epidemic in nurseries and plantations. The categorization of damages can be classified into six distinct categories based on their nature, which are (i) the sap suckers, comprising a pair of *Homoptera* species, are observed to extract sap from plants, (ii) the defoliators consist of a total of two *Coleoptera* species and ten *Lepidoptera* species, (iii) The bark-eaters comprise a group of organisms that consist of two distinct species of *Lepioptera*, (iv) the live tree borer comprises a single species of *Lepidoptera*, (v) the wood borer is comprised of a single species of *Coleoptera*, and (vi) the fruit borer is also comprised of a single species of *Coleoptera*. The taxonomic entities are delineated in the following manner. The *Lepidoptera* species, include *Trabala vishnou* Lefebvr, *Streblote siva* Lefebvre, *Orgyia osseata* Walker, *Spirama retorta* Linn., Dasychira spp., Maurilia spp., *Thalassodes* spp., *Antherea frithi* Moore, *Zeuzera conferta* Walker, *I. tetraonis* More, *Indarela quadrinotata* Walker; *Homoptera* species includes *Orthezia* spp., *Psylla* spp.; *Coleoptera* species including

Tanymecus marginalis Gyllenhal, *Platypus maritimus* Schedl, *Altica coeruea*, and *Alcidodes* sps., are known to consume the entire leaves of the plant[18].

1.5 Taxonomical Classification

Kingdom: Plantae
Subkingdom: Viridiplantae
Infrakingdom: Streptophyta
Phylum (Division): Tracheophyta
Subphylum (subdivision): Spermatophytina
Class: Magnoliopsida
Superorder: Rosanae
Order: Myrtales
Family: Lythraceae
Genus: *Sonneretia*
Species: *Sonneretia apetala*

2. Source of Information

The investigations were conducted by utilizing a variety of electronic databases and search engines, including Google Scholar, Science Direct, Medline, PubMed, and Scopus. The purpose of this review is to compile the available literature on the pharmacological properties of *S. apetala*. The search was conducted without any temporal limitations, with the most recent one being executed in December, 2022. A search was conducted using various combinations of the terms *Sonneratia apetala*, biological activity, nano-formulations, phytoconstituents, a natural compound, etc., to retrieve articles about the specified topics.

3. Traditional Uses

Leaves of the plant are being conventionally employed for the treatment of hepatitis[28,29] sprains, dysentery, eye ailments, bruises, and open sores in children's ears[30]. Its bark as well as fruits also being used in febrifuge, asthma, bleeding, swelling, ulcers, sprains, piles and haemorrhages[29], gastrointestinal disorders[31], and heart troubles[30]. Fruits possess anti-bacterial, antioxidant, and anti-fungal activity[32,33], whether its juice is utilized as a tonic or for the management of diarrhoea. The bark extract exhibits a moderate level of anti-inflammatory activity[34]. Anthocyanin, present in seeds and pericarp, has been found to restrict the progression of various ailments such as diabetes, cancers, and neurodegenerative- and cardiovascular-diseases[35]. Apart from the previously mentioned utilizations, this plant's leaves are being consumed as a source of food for the deer populace inhabiting the Sundarbans region. Fruits are also ingested by humans, deer, primates, and aquatic organisms within their respective ecosystems. It could be eaten as vegetables and pickles. Flowers are a good source of honey[36].

Sonneratia apetala wood is commonly utilized in industrial applications such as furniture and boat construction, as well as in the production of panels, boards, and boxes[37]. Furthermore, it is utilized as a primary component in the match industry to manufacture matchsticks[38]. According to Lakshman *et al.*, the pneumatophores serve a dual purpose of being utilized in cork manufacturing as well as for ornamental objectives.

4. Isolation and Characterization of Phytochemicals

The different phytochemical studies of *S. apetala* have disclosed that it contains different phytochemical constituents. The methanolic extracts obtained from *S. apetala* demonstrated the existence of steroids, terpenoids, alkaloids, tannins, flavonoids, polysaccharides, and saponins. The preliminary isolation of a Gibberellin (Compound 1) was conducted by Ganguly *et al.*, in 1970. The analysis of the leaf extracts of *S. apetala* indicated the existence of anthrone and coumarin compounds. Nevertheless, the presence of anthraquinones was also detected in the leaf extract obtained using methanol and acetone solvents[11]. In addition to coumarins, this species has also been found to contain flavonoids, essential oils, and triterpenes[12,13,39].

The pericarp and seeds comprise a variety of macronutrients, including proteins, carbohydrates, lipids, and ash, as well as notable polyphenolic compounds like quercetin (Compound 2) and caffeic acid (Compound 3). The plant also comprises (-)-catechin (Compound 4), epicatechin (Compound 5), ellagic acid (Compound 6), and gallic acid (Compound 7)[40].

The identification of twenty-three compounds was made possible through analysis of the GS-MS Chromatogram of the n-hexane fraction of *S. apetala* seeds. The identified phytoconstituents include ascorbyl palmitate (Compound 8), cycloodecacyclotetradecene

14,15-didehydro-1,4,5,8,9,10,11,12,13,16,17,18,19,20-tetradecahydron (Compound 9), margaric acid (Compound 10), 8,11-octadecadienoic acid methyl ester (Compound 11), stearic acid and its methyl ester (Compound 12), linoleic acid methyl ester (Compound 13), oleic acid methyl ester (Compound 14), oleic acid (Compound 15), arachidic acid (Compound 16), linoleic acid (Compound 17), stearic acid (Compound 18), tetracosanoic acid (Compound 19), cholesteryl bromide (Compound 20), stigmast-5-en-3-ol, oleate (Compound 21), stigmast-5,22-dien-3 ol, acetate (Compound 22), and *β*-sitosterol acetate (Compound 23), betulinic acid (Compound 24), lupeol (Compound 25), lupeone (Compound 26), stigmast-5-ene-3-beta (Compound 27), ethyl propanoate (Compound 28), *β*-amyrin hexadecanoate (Compound 29), 5β-cholestane-3α,7α-diol (Compound 30), physcion (Compound 31), n-hexanal (Compound 32), 2,4-decadienal (Compound 33), n-propyl acetate (Compound 34), palmitic acid (Compound 35) and methyl palmitate (Compound 36), symgaresinol. Ethyl propanoate, n-propyl acetate, n-hexanal, 2,4-decadienal, oleic acid, and 2-methyldecahydronaphthalene are the compounds shown in seed extraction[41]. Polyphenols are present in both bark and seeds. Tannins are also present in seeds. The aerial components of the plant are composed of various chemical compounds such as terpenoids, alkaloids, steroids, flavonoids, saponins, tannins, and polysaccharides. The leaf and bark of the plant in question are known to contain a variety of chemical compounds, including alkaloids, glycosides such as anthraquinone and cardiac, tannins, saponins, steroids, gums and steroids, flavonoids, carbohydrates, terpenoids, protein and amino acids, vitamins such as thiamine and riboflavin, and certain mineral[39,42,43].

4.1 Tannins (Polyphenols)

Polyphenolic compounds derived from plants are commonly referred to as tannins. There exist two distinct categories of tannins, namely hydrolysable tannins, and condensed tannins. Hydrolysable tannins are composed of polyesters of gallic acid and various individual sugars, while condensed tannins are comprised of polymers of flavonoid phenols. In their study, Tan, and Thuy utilized the Folin-Ciocalteu reagent to determine the total polyphenol content of various bark extract fractions (crude extract fraction, ethyl acetate fraction, and methanol-HCl) derived from *S. apetala*[44]. The researchers discovered that the crude extract exhibited the greatest concentration of overall polyphenol, measuring at 10973.2±2453.5 µg GAE/ml. Various polyphenols from the *S. apetala* pericarp and seeds have been describe[10,12,39,40].

4.2 Fatty acid

Four compounds within the n-hexane fraction of *S. apetala* seeds account for 85% of the total fraction, with a total of 23 compounds present. The constituents are stearic acid, ascorbyl palmitate, palmitic acid, and linoleic acid, which make up 11%, 21%, 23%, and 30% of the composition, respectively. Linoleic acid is classified as a polyunsaturated omega-fatty acid with the chemical name *cis*-9-, *cis*-12-octadecadienoic acid. On the other hand, oleic acid, which constitutes 2% of fatty acids, is a monounsaturated omega-9 fatty acid identified as *cis*-9-octadecenoic acid. Various fatty acid derivatives from the *S. apetala* seeds have been described[45].

4.3 Triterpenes

Triterpenes are a class of organic compounds that are classified as isoprenoids and are characterized by their possession of 30 carbon atoms on average. Various triterpenes from the *S. apetala* plant have been described[45].

4.4 Other Compounds

The various parts of the *S. apetala* plant also contain some flavonoids, alkaloids, saponins, and glycoside (free anthraquinones)[46,47].

The details of the chemical components of *S. apetala* with their processing and characterization are portrayed in Table 1 given below (Figure 2).

Abbreviation: NMR, nuclear magnetic resonance; HPLC, high-performance liquid chromatography; GS-MS, gas chromatography-mass chromatography; FT-IR, FT-IR-Fourier Transform-Infra Red Spectrum Analysis.

5. Pharmacological Study

5.1 Antimicrobial Activity

Jamini *et al.*, evaluate the anti-bacterial activity of *Sonneretia apetala* leaves by susceptibility test and reports

Table 1. *Sonneretia apetala* chemical constituents extracted from various plant sections

Phytochemical name	Characterization techniques	Plant parts	Extracts used	Reference
Gibberellin (**Compound 1**)	HPLC, NMR	Leaf	Methanol Extract, n-butanol	[40]
Quercetin (**Compound 2**)	GS-MS	pericarp and seeds	Methanol Extract.	[48]
Caffeic acid (**Compound 3**)				
(-) Catechin (**Compound 4**) Condensed tannin				
Epicatechin (**Compound 5**)				
Ellagic acid (**Compound 6**)				
Gallic acid (**Compound 7**)				
Ascorbyl palmitate (**Compound 8**)	GS-MS	seeds	n-hexane, methanol diethyl ether, chloroform, ethyl acetate	[49]
Cyclodecacyclotetradecene, 14, 15-dihydro-1,4,5,8,9,10, 11,12,13,16,17,18,19,20 tetradecahydron (**Compound 9**)				
Margaric acid (**Compound 10**)				
8,11-otadecadienoic acid, methyl ester (**Compound 11**)				
Steric acid, methyl ester (**Compound 12**)				
Linoleic acid, methyl ester (**Compound 13**)				
Oleic acid, methyl ester (**Compound 14**)				
Oleic acid (**Compound 15**)				
Arachidic acid (**Compound 16**)				
Linoleic acid (**Compound 17**)				
Stearic acid (**Compound 18**)				
Tetracosanoic acid (**Compound 19**)				
Cholesteryl bromide (**Compound 20**)				
Stigmast-5-en-3-ol, oleate (**Compound 21**)				
Stigmast-5,22-diene-3-ol, acetate (**Compound 22**)				
β-sitosterol acetate (**Compound 23**)				
Betulinic acid (**Compound 24**)	HPLC, FT-IR	Methanol extract	Entire plant	[42,43]
Lupeol (**Compound 25**)				
Lupeone (**Compound 26**)				
Stigmast-5-ene-3*β* (**Compound 27**)				
Ethyl propanoate (**Compound 28**)				
β-amyrin hexadecanoate (**Compound 29**)				
5*β*-cholestane-3α-,7α-diol (**Compound 30**)				
Physcion (**Compound 31**)				
n-hexanal (**Compound 32**)				
2,4-decadienal (**Compound 33**)				
n-propyl acetate (**Compound 34**)				
Palmitic acid (**Compound 35**)				
Methyl palmitate (**Compound 36**)				

Abbreviation: NMR, nuclear magnetic resonance; HPLC, high-performance liquid chromatography; GS-MS, gas chromatography-mass chromatography; FT-IR, FT-IR-Fourier Transform-Infra Red Spectrum Analysis.

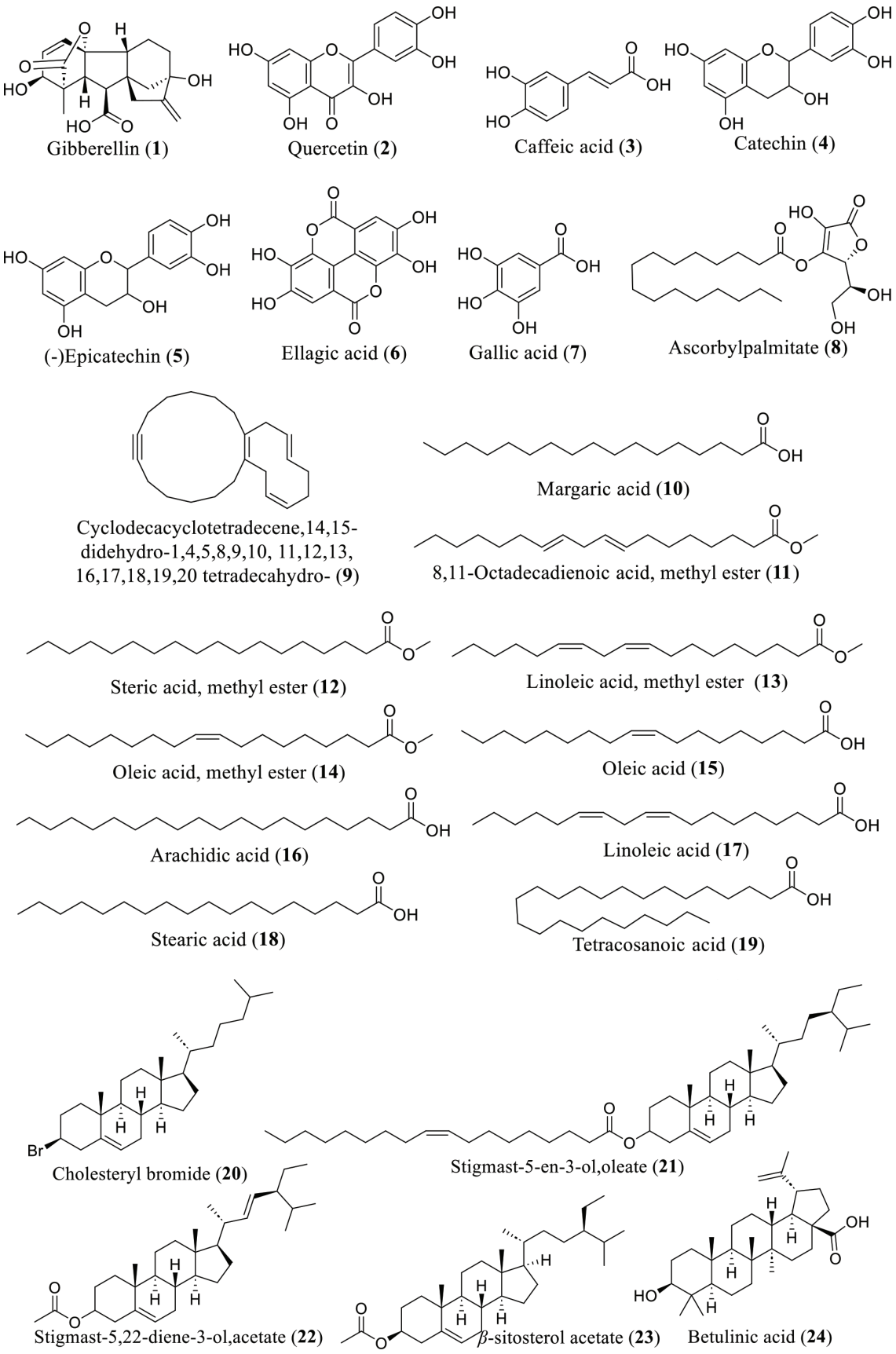

Figure 2. Phytoconstituents of *Sonneratia apetala.*

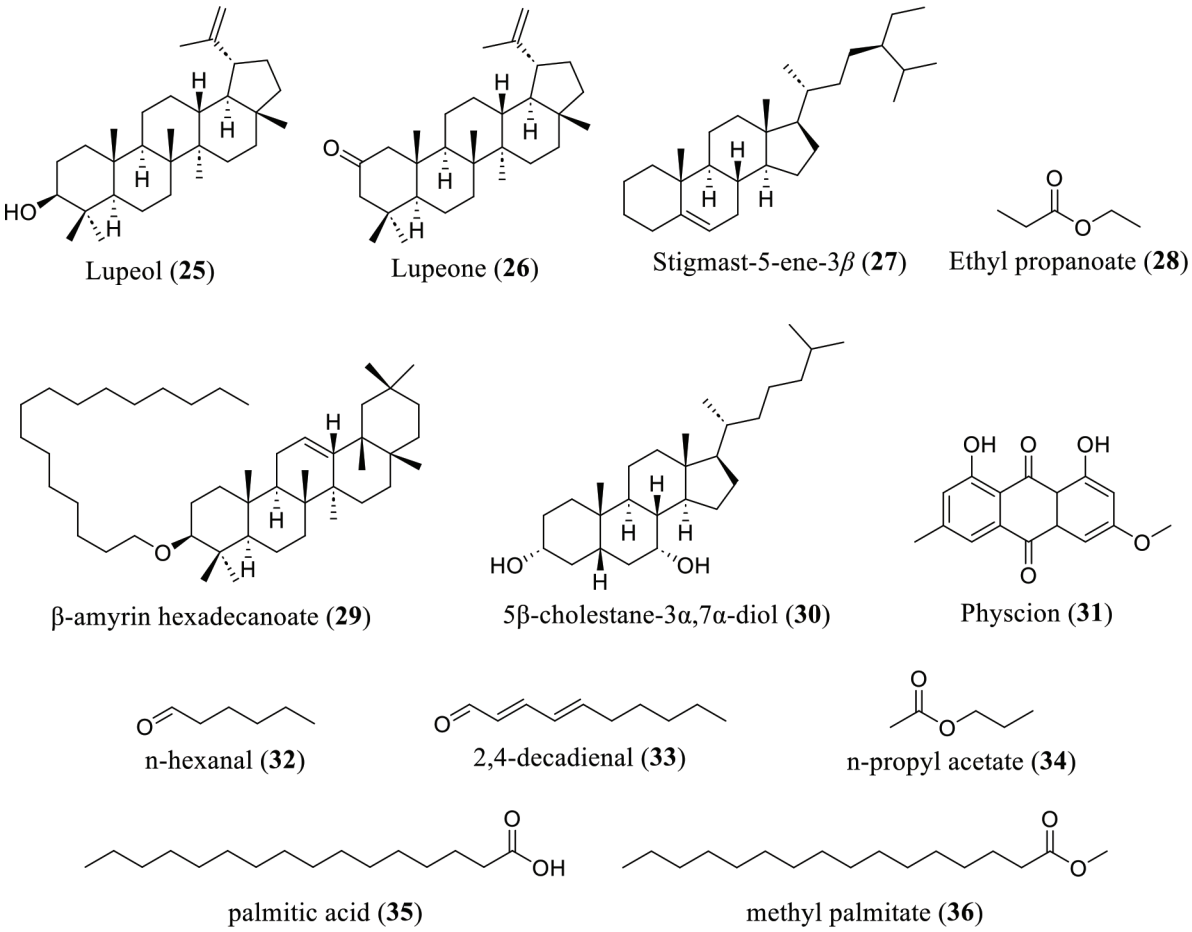

Figure 2. *Continued.*

that acetone extract of the *Sonneretia apetala* leaves exhibited antibacterial activity against *Staphylococcus aureus, Escherichia coli, Bacillus subtilis, Salmonella typhi*, and *Pseudomonas aeruginosa,* where zone of inhibition was obtained between 16 and 21 mm. Their findings reported that acetone extract exhibited inhibition against all the bacterial species except *Klebsiella aerogens* which was found to be resistant against the extract[50].

The antibacterial properties of *S. apetala* seeds were investigated by Hossain *et al*., using susceptibility testing. The authors reported that the methanolic extract of *S. apetala* seeds demonstrated antibacterial activity against a range of bacterial strains, including *E. coli*, *Pseudomonas* spp., *Proteus* spp., *S. paratyphi* A, *Shigella dysenteriae*, *S. typhi*, *S. flexneri*, *Enterococcus faecalis*, *V. cholerae*, *S. epidermidis*, and *S. aureus*. Additionally, the pericarp extracts were found to inhibit the growth of Proteus spp., *S. typhi*, *S. paratyphi* A, *S. dysenteriae*, *S. aureus*, and *V. cholerae*. Both extracts employ the tube dilution method to ascertain the minimum inhibitory concentration, which ranges from 100 to 250 µg/mL and 350 to > 500 µg/mL, respectively[36].

According to Tan *et al.,* the anti-bacterial activity against *E. coli* was observed in the methanol extract of leaves, fruits, bark, and pneumatophore of *S. apetala* obtained through Soxhlet extraction[44]. Hossain *et al*., have performed that diethyl ether, n-hexane, ethyl acetate, chloroform, and methanol extract of seeds exhibited antibacterial activity against *S. paratyphi* A, *S. Typhi*, *E. coli, V. cholerae,* and *S. dysenteriae*, where zone of inhibition between 7.0 ± 0.7 to 16.3 ± 2.0 mm[51].

Nagababu and Rao have recently published a report indicating that the anti-bacterial properties of silver nanoparticles (AgNPs) developed with the water-based leaves extract of *S. apetala* were found to be significant against *Micrococcus luteus*, *S. aureus*, *Enterococcus faecalis*, *Arthrobacter protophormiae*, *B. subtilis*, *B. megaterium*, *Lactobacillus acidophilus*, *Rhodococcus*

rhodochrous, *Streptococcus mutans*, *Alcaligens faecalis*, *Proteus vulgaris*, *Salmonella enterica*, *Proteus mirabilias*, *Enterobacter aerogenes*, and *P. aeruginosa*. The findings about the anti-bacterial efficacy of AgNPs unambiguously demonstrate the potential of nanoparticles as agents for combating bacterial infections[46].

5.2 Antioxidant Activity

The antioxidant properties of extracts obtained from the seeds and pericarps of *S. apetala* were assessed by Hossain *et al.*, through the utilization of various methods, including 1-1-diphenyl 2-picrylhydroxyl (DPPH), reducing power, and nitric oxide radical scavenging activity. The activities exhibited a positive correlation with an increase in concentration levels. The seed and pericarp of *S. apetala* have been found to exhibit antioxidant properties due to their ability to donate hydrogen. The IC_{50} values about the scavenging of DPPH radicals for the seed and pericarp were determined to be 4.3 and 59.8 µg/ml, respectively[36]. Patra *et al.*, suggested that ethanol leaf extract of *S. apetala* shows more antioxidant capacity as compared to other extracts and bark samples with EC_{50} values up to 3436.42±1.45 µg/ml[43]. Tan and Thuy *et al.*, investigated the antioxidant properties of the bark of *S. apetala* using the DPPH free radical scavenging assay. For the extraction, methanol, ethyl acetate and methanol hydrochloric acid are used[44]. In a separate study, Hossain *et al.*, utilized a range of *in vitro* assays, including DPPH, reducing power, nitric oxide radical scavenging activity, and ferric reducing capacity, to assess the antioxidant and free radical scavenging properties of diethyl ether, n-hexane, chloroform, methanol, and ethyl acetate extracts of both the seeds and pericarp of *S. apetala*[52].

The antioxidant capacity of synthesized nanoparticles was assessed by Thatoi *et al.*, through the measurement of their ability to scavenge DPPH free radicals. The findings indicate that the silver (Ag-NPs) and zinc oxide (ZnO-NPs) nanoparticles exhibited efficacy against the DPPH radical, with IC_{50} values ranging from 53.64-169.71 µg/ml. Furthermore, both AgNPs and ZnO-NPs demonstrated moderate antioxidant activity[53].

5.3 Anthelmintic Effect

According to Shefa and colleagues, the ethanolic extract derived from the fruit of the plant exhibited a noteworthy cytotoxic impact on *Haemonchus contortus*. The results of the experiment indicate that paralysis was observed at 441.5, 276, 255, and 209 seconds for concentrations of 25, 50, 100, and 200 mg/ml, respectively. Additionally, the time of death was recorded as 615, 438, 354, and 222 seconds for the same concentrations, respectively[54].

5.4 Anti-Diarrhoeal Activity

Diarrhoea is a nationwide issue, particularly among kids. Many medicinal plants show ant diarrhoeal properties for the presence of alkaloids as well as saponins, tannins, flavonoids, etc. The components are also detected in *S. apetala*, which are accountable for the antidiarrheal properties. According to the report, the ethanolic extract of the fruit of the plant exhibited a prolongation of the latent period and a reduction in the overall number of stools in a castor oil-induced diarrheal model in mice. The active constituent of castor oil is ricinoleic acid, which has been shown to promote peristaltic activity and induce diarrhoea by reducing the absorption of sodium and potassium ions[54].

Another analysis revealed that diethyl ether, n-hexane, chloroform, methanol, and ethyl acetate extracts of seeds displayed an anti-diarrheal effect against the diarrhoeal model induced by castor oil[51].

5.5 Analgesic Activity

Shefa *et al.*, suggested that ethanolic fruit extract showed analgesic effects in acetic acid-induced writhing models in Swiss albino mice. The experiment involved the oral administration of test samples at doses of 250 and 500 mg/kg distilled water, a standard drug at a dose of 25mg/kg of diclofenac Na, and a control vehicle consisting of Tween 80 in water at a dose of 10ml/kg. The administration was carried out 30 minutes before the intraperitoneal administration of 0.7% acetic acid. Following a 15-minute interval, the mice were observed exhibiting writhing behaviour for a duration of 5 minutes[54].

Hossain *et al.*, conducted a study to examine the effects of various seed extracts on acetic acid-induced writhing in mice. The extracts, including diethyl ether, n-hexane, chloroform, methanol, and ethyl acetate were administered orally at a dose of 500mg/kg. The results showed a significant reduction in the occurrence of acetic acid-induced abdominal constrictions in the mice[51].

5.6 Antidiabetic Effect

Hossain *et al.*, studied the hypoglycaemic effect of methanolic seed and pericarp extract of *S. apetala* with that of streptozotocin (STZ) in type–II diabetes rats. Following a period of thirty minutes of appropriate treatment, all the animals utilized in the experiment were sacrificed and their anti-diabetic properties were analyzed. The study's findings indicated that the administration of methanolic seed and pericarp extract resulted in a significant reduction of blood glucose levels in the treated rats[36].

Thatoi *et al.*, conducted a study to assess the α-amylase inhibition activity of synthesized nanoparticles and found that they exhibited moderate activity. Additionally, the study confirmed that AgNPs demonstrated superior potential for anti-diabetic purposes[53].

5.7 Hepatoprotective Effect

In a study conducted by Liu *et al.*, it was observed that the administration of fruit extract from a particular plant at doses of 100, 200, and 400 mg/kg (p.m., daily for 1 week) resulted in a significant increase in the survival rate of mice with acetaminophen-induced liver damage. The extract also demonstrated a reduction in hepatic histopathological damage in rats and a decrease in the concentration of alanine aminotransferase and aspartate aminotransferase in the serum[55].

5.8 Cytotoxicity/Anticancer Effects

Shefa *et al.*, investigated that the plant's fruit extract had a significant cytotoxic impact on brine shrimps[54]. In another study, Patra *et al.*, evaluated that Swiss albino mice's Ehrlich Ascites Carcinoma (EAC) cell was discovered to be inhibited (34% inhibition) by the plant's methanol leaf extract[53]. Moreover Hossain *et al.*, reported that seed extracts in n-hexane, diethyl ether, chloroform, ethyl acetate, and methanol showed cytotoxic effects on the artemia salina (brine shrimps) (LC_{50}s: 46 to 68 µg/ml)[51].

5.9 Gastroprotective Activity

Sur *et al.*, investigated that the plant's leaf extract can protect gastric mucosal injury caused by alcohol ingestion[56].

5.10 Hypouricemic Activity

Chen *et al.*, evaluated that the seed oil of these plants had a significant effect on hyperuricemic and renal injury in mice[57]. Jiang *et al.*, suggested that gallic acid which is a bioactive compound from the plant's leaves and branch shows a hypouricemic effect[58].

All the pharmacological properties are summarized in Table 2.

6. Toxicological Study

6.1 Evaluation of Acute Toxicity in Mice

The study on acute toxicity test (LD_{50} determination) was conducted by the guidelines of the Organisation for Economic Co-operation and Development (OECD)-423[59]. A cohort of Swiss albino mice, with a body weight ranging from 20 to 25 grams, was subjected to random allocation into four distinct groups, each consisting of five animals. The animals underwent an overnight fasting period before the oral administration of the drug via feeding needle at varying dosages. The administered dosages correspond to 200, 400 1000, and 2000 mg per kg[60].

6.2 Evaluation of Sub-Acute/Chronic Toxicity in Mice

Following the OECD guideline for a 28-day repeated toxicity study, a sub-acute or chronic toxicity test was conducted. After obtaining the LD_{50} result, it was observed that no mortality occurred within the first seven days. Subsequently, a dosage of 400 mg/kg was administered to conduct a sub-acute toxicity investigation. By guideline 407 (2008) set forth by the OECD[61], repeated dose toxicity studies were conducted on both male and female groups of rats for the fruit over 28 days. The control group was administered with distilled water. The daily intake of food and water was quantified by measuring the quantity of food and water provided and the residual amount after a 24-hour period[60].

6.3 Nano Formulaions of *Sonneratia apetala*

Nanoparticle synthesis using plant extract is the most demanding synthesis for researchers. it is more advantageous than other biological processes.

Table 2. Pharmacological properties of *Sonneratia apetala*

Activity	Plant part used	Extract type	Dose	*In vitro* or *In vivo* Models	Observations	References
Antimicrobial activity	Leaves	Acetone	0.5, 1, 5, 10 mg/ml	Agar cup method	The leaves of *S. apetala* exhibit potent anti-bacterial properties against both gram (-) ve and gram (+) ve bacterial strains	50
	Leaves, fruits, bark, pneumatophore	Methanol – HCl fraction	100 µL of extract. In the positive control, a volume of 100 µL of 0.04% chloramphenicol was utilized, while in the negative control, a volume of 100 µL of distilled water was employed in place of the crude extract	Agar well diffusion method	Highest antibacterial activity against *E. coli*	44
	Seeds and pericarp	Methanol	10 mg/ml	Disc diffusion method	In the case of seed, ↓ MIC for *S. dysenteriae* and Proteus spp. pericarp extract showed no inhibition of *E. faecalis*, *E. coli*, *S. flexneri*, *Pseudomonas* spp., and *S. epidermis*	36
	Seeds	diethyl ether, n-hexane, chloroform, methanol, ethyl acetate	500 (µg/disc)	Disc diffusion method	Among the fractions, the methanol fraction of the seed strongly inhibited all the *E. coli* strains used, *S. Typhi*, *S. Paratyphi* A, *S. dysenteriae*, and *S. aureus* at 500 µg per disc.	51
	Leaves	Silver nanoparticle synthesized aq. Leaf extract	100 µg/ml in DMSO	Agar well diffusion method	The observed antibacterial activity of AgNPs suggests a potential application of nanoparticles as effective antibacterial agents	46
Antioxidant activity	Seeds and pericarp	Methanol extract	10 mg/ml	DPPH, NO free radical assay	The seed and pericarp of *S. apetala* have been found to exhibit antioxidant properties through their ability to donate hydrogen	36
	Leaves	Acetone, ethanol, methanol and crude extract	25 g/100ml	DPPH free radical, NO free radical, ABTS free radical scavenging activity, Reducing power capacity, ion chelating activity	The ethanol leaf extract exhibited a higher antioxidant capacity (271.52 ± 3.85 mg per gm dry weight) in comparison to the remaining extracts and bark specimen	43

(Continued)

Table 2. To be Continued...

Activity	Plant part used	Extract type	Dose	*In vitro* or *In vivo* Models	Observations	References
	Bark	Crude extract Ethyl acetate fraction Methanol-HCl fraction	One millilitre of the reaction mixture was combined with 0.05 mL of the samples. In the context of the experiment, 0.95 ml of ethanol was added to the samples. To establish control, a solution comprising 0.95 millilitres of 0.3 millimolar concentration of DPPH in ethanol was blended with 0.05 millilitres of the test samples	DPPH free radical scavenging assay	The crude extract exhibited the most significant activity with an IC_{50} value of 3.4 µg/ml, which is equivalent to 0.86 times the activity of ascorbic acid	44
	Pericarp and Seeds	diethyl ether, n-hexane, chloroform, methanol, ethyl acetate	10mg/ml	DPPH free radical, NO free radical scavenging activity, Reducing power capacity, Ferrous (Fe^{2+}) ion chelating activity	The seed's diethyl ether, methanol, and ethyl acetate fractions exhibited substantial DPPH radical scavenging activity, with all fractions exhibiting activity exceeding 80%. Conversely, the hexane fraction of the seed did not demonstrate any such activity	52
	Young fresh bark and leaves	Synthesized nanoparticles with aqueous extract	25g/100ml	DPPH free radical scavenging assay	The remarkable DPPH radical scavenging capacity exhibited by Ag-NPs and ZnO-NPs can be ascribed to their capacity to furnish electrons or hydrogen ions, thereby counteracting the unstable DPPH free radicals present in the reaction medium	54
Anthelmintic effect	Fruits	Ethanol	**Test group-**25,50,100 and 200mg/ml **Standard (albendazole)-**15 mg/mL and 10 mg/mL of 10 mL in PBS **Control group -** 0.1% tween-80 in PBS**.**	*Haemonchuscontortus* (Nematode**)**	The binding of Albendazole to ***β***-tubulin results in the inhibition of parasitic microtubule polymerization. As *S. apetala* showed anthelmintic action in contrast to albendazole, may be due to their same mode of action.	54

Table 2. To be Continued...

Activity	Plant part used	Extract type	Dose	*In vitro* or *In vivo* Models	Observations	References
Antidiarrheal activity	Fruits	Ethanol	**Test groups** - crude extracts at the doses of 250 and 500 mg per kg distilled water orally. **Negative Control group-** The test substance was administered orally to the subjects at a dose of 10 ml per kg distilled water using a vehicle consisting of 1% Tween-80 in water. **Positive control group** – Loperamide at 3mg/kg orally.	young Swiss-albino mice	The medicinal plants in question were discovered to possess anti-dysenteric and anti-diarrheal properties, which were attributed to the presence of tannins, alkaloids, saponins, sterols, flavonoids, reducing sugars and triterpenes	54
	Seeds	diethyl ether, n-hexane, methanol and chloroform	**Test groups-** 250 and 500 mg/kg body weight. **Negative control group-** distilled water containing 0.1 % Tween-80. **Positive control group-** loperamide hydrochloride (3 mg/kg distilled water)	young Swiss-albino mice	The methanol fraction of seeds showed the highest inhibition (68%). Hence, the fractions' efficacy in mitigating diarrhoea can be ascribed to the presence of tannins, flavonoids, polyphenols, and/or antioxidants.	51
Analgesic activity	Fruits	Ethanol	**Test groups-** 250 and 500 mg/kg body weight **Standard (Diclofenac Na)-** 25mg/kg body weight **Vehicle-** 1% Tween-80 in water at a dose of 10 ml/kg body weight**.**	acetic acid-induced writhing model in young Swiss-albino mice	The extract exhibited writhing inhibition at the doses of 250 mg/kg and 500 mg/kg, with respective inhibition of 46.54% and 69.62%. In comparison, the standard drug Diclofenac Na demonstrated an inhibition of 82.31% at a dose of 25 mg/kg b.w.	54
Antidiabetic effect	Seeds and pericarps	Methanol	**Test groups** at a dose of 1.25 g/10 mL water/kg b.w orally. pericarp at a dose of 1.25 gm per 10 mL water/kg distilled water orally. **Standard** (glibenclamide) at a dosage of 5 mg per kg distilled water orally) **Vehicle-deionized** water at a dosage of 10 ml/kg distilled water	The experimental subjects were male Long-Evans rats of adult age, with a weight range of 170-200 g.	↓Serum glucose level	36

(Continued)

Table 2. To be Continued...

Activity	Plant part used	Extract type	Dose	*In vitro* or *In vivo* Models	Observations	References
	Young fresh bark and leaves	Synthesized nanoparticles with aqueous extract	**Test groups -** 100 µl different concentrations of the NPs + α-amylase (200 µl) enzyme + 2 mM phosphate buffer (100 µl) + 1% starch solution (100 ml) (after 20 min incubation) **For the control**- a substitution was made wherein 200 µl of the enzyme was used with the buffer	*α*-amylase inhibitory activity	AgNPs exhibited superior potential in inhibiting α-amylase activity, which is associated with diabetes	[53]
Hepatoprotective effect	Fruits	Aqueous	low dose of *S. apetala* fruit extract (SAFE) group- (220 mg/kg acetaminophen (APAP) + 100 mg/kg SAFE), middle dose of SAFE group- (220 mg/kg APAP + 200 mg/kg SAFE), and high dose of SAFE group- (220 mg/kg APAP + 400 mg/kg SAFE) (orally daily for 1 week)	8 weeks ago male Kunming mice	↓Survival rate using APAP-induced liver damage mouse model ↓Hepatic histopathological damaged rats, aspartate aminotransferase and alanine aminotransferase	[55]
	Fruits	Methanol and Ethyl-acetate	400, 200, 100, 50, 25, 12.5, 6.25, 3.123, 1.563, 0.781 µg/ml	Brine shrimp nauplii	fruit extract of *S. apetala* exhibited lethality, thus indicating the presence of biological activity in the extract. The LC_{50} and LC_{90} values of the test sample were determined to be 61 µg/ml and 616 µg/ml, respectively, using a software	[54]
Cytotoxicity/ anticancer effects	Leaves	Methanol	at a dose (*i.p.*) of 0.2 mmol and kg or 100 µL/10 g body weight. Standard - Mitomycin C was administered at a dosage of 1 mg and 10 mg per kg of distilled water, respectively.	Ehrlich Ascites carcinoma (EAC) cells Swiss Albino mice (10 weeks old; 18–20 g).	The methanol extract of the leaf of *S. apetala* exhibited an *in vivo* anticancer effect, demonstrating a 34.0% inhibition rate against EAC	[43]

Table 2. To be Continued...

Activity	Plant part used	Extract type	Dose	*In vitro* or *In vivo* Models	Observations	References
	Seeds	diethyl ether, n-hexane, Chloroform, methanol and ethyl acetate	**Test group** – Not specified. **Positive control group** - vincristine Sulphate **Negative control group** - 1% DMSO in distilled water	Brine shrimp nauplii	The lethality of brine shrimp nauplii exhibited a dose-dependent relationship with all fractions of *S. apetala* seeds, with LC_{50} values significantly below 250 µg/mL	51
Gastroprotective activity	leaves	Hydromethanol	**Test Group-** 125 mg/kg, 250 mg/kg Leave Extract **Positive control group –** Omeprazole 20 mg/kg **Negative control group** -5 ml/kg distilled water.	Wistar male albino rats (adult)	Pre-treatment of *S. apetala* exhibits a significant and dose-dependent reduction in the elevation of lipid peroxides. Additionally, it enhances the concentration of glutathione and catalase Ars in the gastric mucosa about the control induced by alcohol	56
Hypouricemic activity	Seed oil	Butane	50, 100 and 200 mg kg−1	Male KM mice	*Sonneretia* seed oil exhibited protective effects against potassium oxonate/hypoxanthine-induced hyperuricemia and the associated renal injury in mice	57
Hypouricemic and nephroprotective activity	leaves and branches	Ethyl acetate	200 mg kg−1	Male Kunming mice	GA treatment in potassium ozonate/hypoxanthine-induced mice exhibited remarkable dual hypouricemic and nephroprotective effects.	58

Nanoparticle synthesis by *Sonneratia apetala* is mainly targeted to cure various types of diseases like antifungal, antioxidant, anti-angiogenic, anti-inflammatory, antiulcer, and anticancer effects. Green synthesis is an eco-friendly, bio-degradable, biocompatible, and green method use of synthesizing nanoparticles for various applications in the medical field[62]. Plant-based silver nanoparticles (AgNPs) Gold nanoparticles (AuNPs) Zinc oxide nanoparticles (ZnO NPs), and Copper (Cu) have been used to prepare plant-based nanoparticles with various pharmaceutical industrial applications. silver nanoparticles (AgNPs), Zinc oxide nanoparticles (ZnONPs), and Copper NPs low-cost, safe, and simple synthesis is to reduce toxicity. Metal Nanoparticles as magical bullets with a mixture of biomolecules such as natural polysaccharides, vitamins, amino acids, proteins, phenolics, saponins, alkaloids, and terpenes used in various biomedical fields[63]. *Sonneratia apetala* Plant-based metal nanoparticles and their pharmacology activity are antiproliferative, antiparasitic, pro-apoptotic, anti-inflammatory activities, pro- or anti-oxidative depending on the context, etc[64] (Table 3).

7. Patents Information

The patents granted on S. *apetala* are shown in Table 4.

8. Future Scope of Research

Further research on metal nanoparticles utilising the leaves of *S. apetala* is conducted to assess their antioxidant, antibacterial, and phytochemical activity. The leaves are used topically and consumed to cure a variety of ailments, such as dysentery, hepatitis, sprains, open sores, bruises, and eye issues. The fruit of *S. apetala*, in conjunction with its leaf and flower, is utilized as a medicinal agent in China for the treatment of internal maladies, as well as sprains and coughs. *S. apetala* is a botanical specimen that is rich in nutrients, minerals, vitamins, and biologically active phytochemicals. Compared to conventional techniques such as mass selection, inbreeding, and hybridization, which are contingent upon environmental factors and the existing gene pool for plant growth and development, callus culture offers expedited means for genetic cell transformation through soma clonal variation, induced

Table 3. Evaluation of the pharmacological activity of *Sonneratia apetala* nanoformulations

Formulation	Size	Targeted Site	Evaluation Specifications	Pharmacological Activity	Reference
Sonneratia apetala leaves with some amount of aqueous silver nitrate ($AgNO_3$) solution were subjected to heating at a temperature of 60°C, and subsequently monitored for the emergence of a brown-yellow solution, indicative of the synthesis of AgNPs	425 to 475 nm	Free radical scavenging and antibacterial activities	the screening of phytochemicals, the evaluation of antibacterial and antioxidant activities, as well as the green synthesis and characterization of silver nanoparticles. In addition, the antibacterial activity of the synthesized nanoparticles was also investigated.	*In vitro* DPPH free radical scavenging activity	46
AgNPs have been produced using *Sonneratia apetala* fruit extract and $AgNO_3$ solution. The synthesized AgNPs were then evaluated for their catalytic activity in the degradation of organic dyes	400-480 nm	The electron transfer mechanism of a catalyst shows potential in the degradation of methyl red and methyl orange	Effect of physiological condition on AgNPs formation, FTIR analysis, XRD analysis, Atomic Force Microscope analysis, Catalytic degradation of methyl orange and methyl red	Catalytic degradation of methyl red and methyl orange	65

Table 3. To be Continued...

Formulation	Size	Targeted Site	Evaluation Specifications	Pharmacological Activity	Reference
synthesizing Ag-NPs and ZnO-NPs through photo-conditioning, utilizing aqueous extracts derived from *S. apetala* mangrove plants. The synthesized NPs were then evaluated for their potential bio-medical possibilities	HF- AgNPs and SA-AgNPs 375 nm and 383 nm respectively HF-ZnO-NPs and SA ZnO-NPs 350 nm and 354 nm	the evaluation of antioxidant activity through the DPPH free radical scavenging assay. The potential of NPs to inhibit α-amylase and exhibit anti-inflammatory activity in the context of diabetes management is a subject of interest	UV-VIS spectroscopy FT-IR analysis DLS analysis XRD analysis	anti-diabetic, antioxidant, anti-bacterial and anti-inflammatory activities	[53]

Table 4. Patents on *Sonneratia apetala*

Title	Publication	Description
Method for breeding *Sonneratia apetala* sprout	CN1806491A	The technique described in the invention involves repeatedly training the seed bud in salt and fresh water, protecting the seed bud from the cold, and immersing the mulberry in water with a 5 per cent salinity and freshwater alternately. The peel is also removed, the seed is sterilised, the field is chosen, and the seedbed is sterilised. This approach can improve bud survival rates, reduce breeding time, and boost seed germination.
Cultivation method for *Sonneratia apetala* Buch-Ham seedlings	CN103782789A	In forestation beginning stage of *Sonneratia apetala* Buch-Ham, the survival rate is poor, and the preservation rate is low. Stem cutting and secondary root cutting are carried out on container-grown seedlings of specific specifications in the later stage of *Sonneratia apetala* Buch-Ham seedling cultivation, and the cultivation method has the advantages that the *Sonneratia apetala* Buch-Ham seedlings are developed in the root system, plants are robust, and the thickness of stems is increased. The technology-cultivated seedlings may raise the original survival rate of forestations to 95% from 85% and increase the original preservation rate of annual growth *Sonneratia apetala* Buch-Ham to 90% from 81%.

mutagenesis, and genetic engineering. These methods not only surpass conventional breeding in terms of efficiency but also have the potential to generate novel genes and genotypes[66].

9. Conclusion

Sonneratia apetala is a mangrove plant that is edible and is known to contain a variety of essential micro-nutrients and significant secondary metabolites. Historically, this substance has been utilized for its anti-inflammatory properties, as well as its efficacy as a vermifuge and hepatoprotective agent. Additionally, it has been employed in the management of cough, gastrointestinal disorders, haemorrhage, intestinal parasites, dysentery, bruises, sprain, cataracts, hepatitis, sores in the ear, and cardiac diseases. According to scientific reports, *S. apetala* along with its nanoformulations exhibit a wide range of biological effects such as anti-inflammatory, antioxidant, anthelmintic, anti-microbial, cytotoxic/

anticancer, anti-diarrheal, analgesic, anti-diabetic, and anti-hyperlipidaemic activities. Further research is required to conduct a thorough toxicological evaluation of the extract, to ascertain its safety for human consumption.

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