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Research Article

The Evaluation Of Pharmacological Activity Of Potential Mangrove Avicennia Officinalis & Heritiera Fomes: A Review Article

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ABSTRACT

Introduction: Mangroves are halophytic plants which distributed throughout the world's tropical and subtropical region specially in the Sundarban area. There are eight species of *Avicennia and* six species of *Heritiera* are identified for medicinal purposes. *Avicennia officinali and Heritiera fomes* are the two most prominent mangroves. There are both used in medicinal and commercial purposes. They give the therapeutic activity of antibacterial, anticancer, antihyperglycaemuic, antidirrheal, antioxidant and antiulcer properties.The goal of this article is to provide a thorough comprehensive data regarding *Avicennia officinalis* and *Heritiera fomes* including phytochemistry, pharmacological activities, traditional, ethnomedicinal uses and pharmacognostic features.
Methodology: Every information regarding traditional aspects and research study of *Avicennia officinalis* and *Heritiera fomes* were collected through a massive literature survey and Herbal books along with scientific resources.
Result & Discussion: *Avicennia officinalis* and *Heritiera fomes are* been used in medicinal agents to treat a variety of conditions, such as bacterial, fungal, and viral infections, ulcers, rheumatism, cancer and diarrheal disease. More than fifty bioactive compounds from each various plant parts have been identified and isolated as a result of laboratory research today. The phytochemicals reported as characteristic constituents of this plant are alkaloids, glycosides, flavanoids, steroids, terpenoids with polyisoprenoids, and tannins. Moreover, documents relevant to pharmacological assessment have demonstrated noteworthy properties like antibacterial, antiviral, antidiabetic, antioxidant, and carcinogenic properties, among many others.
Conclusion: This article provides a summary of the distribution and diversity of Avicennia *officinalis* and *Heritiera fomes* as well as a thorough analysis of the phyto-pharmacological research that has been done on this medicinal plant thus far. It also emphasizes the need for more research on the phyto-constituents that underline the validated traditional and folklore claims of the plant's extensive medicinal use.

Keywords: Mangrove, Halophytic, Anti-hyperglycemuic, Ethnomedicinal, pharmacological activities.

1. Introduction

Mangroves are a taxonomically diverse group of halophytic plants that are distributed throughout the world's tropical and subtropical regions [1,2] They are resilient to high salinity, extreme temperatures, and other unusual natural conditions. It is generally acknowledged that they improve biodiversity and stabilize coastal environments [3]

Sundarban is the world's largest continuous mangrove forest, some of which may have therapeutic benefits. Alkaloids, tannins, glycosides, phenolics, volatile oils, etc., obtained from medicinal plants contain a great potential for pharmacological activity and therapeutic effects [4]. As a result of their antioxidant qualities, they also display a broad range of biological activities, including analgesic, antimicrobial, antiproliferative, and anticancer effects [5]. This is because a number of Oxidative stresses is linked to a number of human diseases, including diabetes, rheumatism, cancer, heart disease, and neurodegenerative diseases [6,7] Evergreen mangrove species *Avicennia officinalis* L.& *Heritiera fomes* is primarily found in Bangladesh, India, Indonesia, Malaysia, Brunei, Myanmar, Vietnam, and southern Papua New Guinea; it has not been extensively introduced elsewhere. [8] The study's current objectives were to screen the phytochemicals in this plant and evaluate their pharmacological properties, including their analgesic, antioxidant, antibacterial, and toxicity properties.

Only one mangrove genus found worldwide which is Avicennia. Those eight species- *Avicennia officinalis, Avicennia balanophora Stapf & Moldenke, Avicennia bicolor Standl, Avicennia germinans, Avicennia integra N.C. Duke, Avicennia marina Vierh, Avicennia schaueriana Stapf and Avicennia tonduzii Moldenke* are group of the genus of *Avicennia*. This article emphasizes the significance of *Avicennia officinalis*, which is an important and well-known as Indian mangrove.

Another different species of mangrove is *Heritiera* which seen six species like *Heritiera fomes, Heritiera littoralis, Heritiera aiton, Heritiera elata, Heritiera sinplicifolia, Heritiera ornithocephala and Heritiera globosa*. All are from *Heritiera* genus. *Heritiera fomes* is a valuable mangrove. It's well known as Sundari. share certain morphological traits. It is available in sundarban area in west Bengal, Bangladesh and also found in Malaysia, Myanmar and Thailand especially costal region of Indo-Pacific area.

2. Avicennia officinalis & Heritiera fomes

2.1. Botanical Description: *Avicennia officinalis* is a fairly large tree with a height of 12–18 meters and a girth of 3.6–4.5 meters. It has smooth lenticels and light-colored, not fissured bark. Depending on the color of the bark, it is differentiated from other species (like black and mottled). *Avicennia officinalis* has extremely brittle, coarse-grained wood. [9] The leaf is coriaceous having salt crystals in the surface, especially in dry weather, The flower is the largest of all the species in its genus, measuring 1 cm in diameter. [10,11] It is ovoid, compressed, orange-yellow, and can be found in small globular heads or trichotomous corymbs. [9] The corolla sometimes has yellow throat, hence name bicolor. The fruit is shaped like an ovoid capsule that is 2.5–4 cm long and is filled with a single seed. A mature tree is 8–20 cm long. aerial stilt roots and pneumatophores that resemble pencils. Long horizontal thin roots beneath the soil give rise to many upright, air-filled roots that rise above it. [1,11,12]

Heritiera fomes is a medium-sized, evergreen tree that can reach a height of 25 meters. The leaves have tiny, one-centimeter petioles and are dark green in color. They are clustered in the direction of the branch tips. The species starts to produce pneumatophores at three years old. The pneumatophores are roughly 50 centimeters tall. The heartwood is dark to radish dark brown, while the sapwood grows pinkish. Wood is robust, heavy, and hard. The unisexual flowers are arranged in panicles. The pistilloid is a cylinder dumbbell made up of five fused stamens. The species typically blooms in April and March. Fruits start off as light green and turn brown as they ripen. They have fleshy endosperm and are single-seeded. Seeds range in length from 3 to 5.5 cm and width from 3.5 to 5 cm. The seeds are shed in June and July of calender. [13] Figure 1: *Avicennia officinalis & Heritiera fomes*

2.2. Taxonomic Ambiguity: The genus *Avicennia* is named after Avicenna or Abdallah Ibn Sina (980-1037 AD). A Persian physician. [14] This genus is classified under Tracheophyta, Spermatophytina, Magnoliopsida, and Lamiales. [15,16] The allocation of family to the genus *Avicennia* has long been a contentious issue. There are different opinions concerning the systematic rank of *Avicennia* as a monotypic family *Avicenniaceae,* as a subfamily *Avicennioideae*, or as a tribe *Avicenniae*.*T*he 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. [11,15,16]

A species of mangrove plant called *Heritiera fome*s is distributed throughout the world, with populations found in the western Pacific, Southeast Asia, and portions of the Indian subcontinent. Its taxonomy has changed and become more ambiguous over time. It was subsequently reclassified as *Heritiera fomes* based on molecular research and morphological factors, having previously been known as *Xylocarpus fomentarius*. Advances in scientific knowledge, such as genetic analysis, which can uncover relationships between previously unknown species, frequently lead to taxonomic revisions.[61]

Heritiera fomes and other species may exhibit taxonomic ambiguity for a variety of reasons, including: Morphological Variation: Differences in a species' physical traits can cause misunderstandings or incorrect classification. Genetic Analysis: Developments in DNA sequencing methods have made it possible to identify relationships between species that were not obvious from morphology alone.

Historical Classification: Taxonomic classifications may need to be revised when new data becomes available because they may be based on inaccurate or out-of-date information.[66]

Taxonomic disputes: Diverse researchers may have differing interpretations of the data or differ on the proper classification of particular species. With the help of taxonomic revisions, scientific endeavors such as ecological research and conservation can benefit from a more precise understanding of the evolutionary relationships between organisms.[13]

2.3. Ethnomedicinal Uses: The *Avicennia officinalis* are traditionally used throughout the world as medicine. The local community inhabiting the mangrove forest mainly uses *Avicennia officinalis* for the treatment of various diseases. The whole plant is generally used in treatment of tumor, rheumatoid arthritis, ulcers, and diabetes, [17,18] 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. [19,20] In Arabia, the root of *Avicennia officinalis* is used as an aphrodisiac and unripe seeds are used as 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. [9,21]

As a subclass of medical anthropology, which is the study of human disease and health care systems, ethnomedicine—sometimes synonymous with traditional medical cinema—focuses on individuals whose knowledge, experience, and practices have been orally passed down to future generations over centuries, in addition to pertinent written documents. Research on drugs and anthropology is conducted on the basis of scientific ethnomedical studies.[66]

In addition to offering wood and other resources like fish, crabs, and honey, Bangladesh's mangrove forest is economically valuable because it serves as a habitat to a diverse range of flora and fauna. There is a limited distribution of *Heritiera fome*s in Bangladesh's Suburbans.[61] In the southern regions of Bangladesh, this species of mangrove plant is well-known for the important traditional use(s) it has against a variety of diseases by the local traditional health practitioners (THPs). Rural residents use the leaves, roots, and stems of *Heritiera fome*s to treat hepatic, skin, and gastrointestinal conditions. [22.23] In rural areas, bark is used to treat goiter and diabetes.[24] Additionally, this plant is used locally as an herbal remedy for fever and pain. Individuals who relocate to these areas are unable to access contemporary healthcare.[62]

2.4. Other Economic Uses: The tannins found in *Avicennia. officinalis* bark is widely used in the leather and dye industries. The wood is used as building material and as fuel. It is also utilized in oil mills, rice pounder, door frames, low-cost beams, and boats. In Tamil Nadu, wood ash is used to wash clothes and also combined with paint to improve the paint's adhesion. Branches are prepared for doors and matting, and they are also fed to cattle as fodder. This plant's pneumatophores are utilized to make floats and bottle stoppers. Celebes use boiled seeds that have been soaked in water for a whole night as food during famines. In addition to being edible and consumed by fishermen in Java, the fruits are used as an insect repellent. Sometimes the bitter fruits and seeds are steamed or baked and then eaten. [14,21,25]

Hard wood is made from *Heritiera fome*s. Elastic, robust, and finely granulated. The sapwood is a lighter shade of reddish brown, while the heartwood is a deeper shade of reddish brown. Among its many applications is bridge construction. utility poles, tool handles, joinery, and the building of houses and boats. using as firewood and to make hardboard. [27] Plantations are the commercial sites for growing the tree [26]. *Heritiera fome*s has a bark that is abundant in procyanidins. It has been demonstrated that the ethanol extract possesses antioxidant qualities. It also demonstrates antimicrobial activity against the *Rhizophilic hocuria*. The aureus staphylococcus. Pseudomonas aeruginosa and Bacillus subtilis are non-toxic in the brine shrimp toxicity test. [28]

2.5. Potential Endophytes: A class of microorganisms known as endophytes is connected to the healthy plant tissues of a host plant. They mostly live in temperate and tropical rainforests, where their biological diversity is significant and abundant. [29,30] Endophytic fungi are a rich source of secondary metabolites, particularly from mangrove plants. These metabolites are important for a variety of pharmacological actions, most notably those related to bacterial infections and cancer. There are numerous reports on various *Avicennia officinalis* endophytes that have the potential to be active. These endophytes produce a wide range of compounds and could be good sources for novel natural products. [31]A variety of in vitro assay systems,

including 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 B-carotene-linoleate model system, demonstrate the antioxidant activity of the mangrove and its predominant endophytic fungus, Aspergillus flavus. This illustrates how the plant and endophyte cooperate to fend off a variety of biotic and abiotic challenges. [32]

A *Heritiera fome*s Roots, bark, and leaves had isolation frequencies of 50, 60, and 73% in that order. Compared to bark and roots, endophytic fungi were much more frequently isolated from leaves.

The endophytic fungal isolates exhibited significant variation in their colonization rates. The results indicated that Alternaria spp. had the highest colonization rate (25.6%), followed by Nigrospora spp., Penicillium spp., and Pestalotia spp., with colonization rates of 10.0%, 8.9%, and 7.8%, respectively. With values of 3.3%, 2.2%, 4/10 1 - 1.1%, and so on, the colonization rates for Epicoccum spp., Cladosporium spp., Bjerkandera spp., and Lasiodiplodia spp. were less than those of the aforementioned isolates. Based on their microscopic and macroscopic traits, Lates were classified into eleven types following the isolation of endophytes.

3. Pharmacological Activities of *Avicennia officinalis*

As *Avicennia officinalis* to posse's medicinal properties, it has been used as anti-oxidant from the ancient time.The medicinal potential of its extracts and the bioactives is discussed in detail to uncover therapeutic value of this species *Avicennia officinalis* exhibits a few of the pharmacological properties listed below-

3.1. Anti-Diabetic Activity: In a paper, it was observed that extracts from both the leaf and bark of *Avicennia officinalis* exhibit promising anti-diabetic properties. The study utilized a streptozotocin (STZ)-induced diabetic mice model, with five groups including Control, Normal, Standard, and two Test groups. Albino mice were chosen as experimental subjects, with STZ administered at a single dose of 200mg/kg to induce diabetes. The standard drug metformin was employed alongside petroleum ether and aqueous extracts from the bark or leaf of *Avicennia officinalis* as test substances.

The results indicated that *Avicennia officinalis* extracts possess the ability to inhibit or modulate key enzymes involved in diabetes, such as alpha-amylase and alpha-glucosidase. Specifically, the petroleum ether extract of *Avicennia officinalis* demonstrated significant inhibitory effects on these enzymes [13,74]. Further analysis revealed that both petroleum ether and aqueous extracts from the leaf were effective in inhibiting alpha-amylase and alpha-glucosidase enzymes at concentrations of 0.1, 0.5, and 1 mg/ml. Notably, the aqueous leaf extract exhibited superior inhibition of these enzymes compared to the petroleum ether extract.[33]

3.2. Anti-ulcer Activity: In a research study, *Avicennia officinalis* exhibited notable pharmacological properties, particularly in anti-ulcer activity. The investigation utilized standard models of acute pylorus ligation (APL) and indomethacin-induced acute gastric ulcer in albino rats to evaluate the ulcer-protective potential of the ethanolic extract derived from *Avicennia officinalis* leaves. The experiment comprised four groups: Control, Normal, Standard, and Test groups. Omeprazole (30 mg/kg) was administered orally as the standard medication, while indomethacin (30 mg/kg) was given orally to induce ulceration. The ethanolic extract of *Avicennia officinalis* leaves was orally administered at a dose of 500 mg/kg to the test group. The results revealed that the ethanolic extract significantly reduced the ulcerative lesion index in albino rats, comparable to the effects of omeprazole (30 mg/kg). This reduction indicated a substantial decrease in ulcer formation. Moreover, the study suggested that the leaf extract exerted potential anti-secretory and anti-ulcer effects by reducing both total and free acid levels in the gastric environment.

In another experiment, anti-ulcerogenic, 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. [34,35]

3.2. Anti-cancer and Cytotoxic Activity: Avicennia officinalis demonstrates pharmacological potential in anti-cancer and cytotoxic activities. In a brine shrimp lethality bio-assay against Artemia salina, a crude ethanolic extract of A. officinalis leaves exhibited cytotoxic effects, with an LC50 of 131.2 µg/ml [36]. Additionally, the leaf methanolic extract of Avicennia officinalis was investigated for its efficacy in managing cancer by inducing cancer in mice using Ehrlich ascitic carcinoma (EAC) cell lines.

The LD value of the extract administered to the mice was found to be higher than 4 g/kg. The study evaluated the effect of the extract on cancer cell growth and the survival of hosts by assessing cell count and the percentage increase in the lifespan of tumor hosts and drug-treated groups. Results indicated a notable increase in the mean survival time of EAC-transplanted mice, rising from 22.33 days in the EAC control group to 29.32 days (for 200 mg/kg) and 33.66 days (for 400 mg/kg) in the treated groups compared to the 5-fluorouracil (20 mg/kg) treated group. This increase was deemed significant. Furthermore, the extract was observed to correct hematological alterations induced by the EAC cell lines [37].

.3.3. Anti-inflammatory: *Avicennia officinalis* showcases significant pharmacological prowess in exerting anti-inflammatory effects. In studies conducted using rat models of inflammation induced by formalin, carrageenan, and Freund's adjuvant, the methanolic extract of *Avicennia officinalis* leaves at doses of 200 and 400 mg/kg demonstrated remarkable, dose-dependent anti-inflammatory properties. These effects were comparable to those of conventional medications such as diclofenac and indomethacin sodium. It was proposed that one of the triterpenoids present in the extract, betulinic acid, might be responsible for its anti-inflammatory effects by inhibiting prostaglandin activity. This mechanism of action suggests the extract's potential in modulating inflammatory pathways, thereby alleviating inflammation-associated symptoms [38].

3.4. Antidiarrheal Activity: In experiments where mice were induced with diarrhea using castor oil, the methanolic extract derived from *Avicennia officinalis* leaves demonstrated notable antidiarrheal activity. At an oral dosage of 500 mg/kg, the extract significantly prolonged the mean latent period and reduced the frequency of defecation when compared to the standard medication loperamide (50 mg/kg). The suggested mechanism of action involves the inhibition of autocoids and prostaglandins release, which subsequently hampers motility and secretion induced by castor oil. This antidiarrheal effect is attributed to the presence of saponins, steroids, and alkaloids in *Avicennia officinalis* [39,40].

3.5. Anti-nociceptive, Analgesic, and Antipyretic Activities: In the acetic acid-induced writhing test, mice treated with 500 mg/kg of dried leaf ethanol and methanol extracts displayed a 64.67% inhibition of writhing, a result comparable to the standard medication diclofenac sodium, which exhibited 85.95% inhibition at a dose of 25 mg/kg. The analgesic effect observed in mice may be attributed to the presence of pentacyclic triterpenes and polyphenolic compounds such as tannins and flavonoids in the leaf extracts [36,41,42]. Furthermore, using tail immersion and radiant heat methods, the analgesic activity of the methanolic extract from the aerial parts of *Avicennia officinalis* was investigated. At doses of 100 and 200 mg/kg, the extract demonstrated both central and peripheral mechanisms for pain inhibition. It was suggested that the extract modulates action potentials and hinders signal transmission from sensory mediators like delta and C fiber sensory neurons, thereby alleviating pain. Additionally, in the Brewer's yeast-induced fever model, oral administration of the same extract at a dose of 200 mg/kg exhibited an antipyretic effect akin to acetyl salicylic acid. This antipyretic effect may be attributed to the inhibition of prostaglandin synthesis through the blockade of cyclooxygenase enzyme activity [43].

3.6. Anti-HIV Activity: Significant in vitro antiviral effects were noted for petroleum ether and aqueous extracts derived from powdered *Avicennia officinalis* leaf in both the reverse-transcriptase inhibition assay and glycoprotein gp120 binding inhibition assay methods. The main mechanism of action involved binding to both the CD4 (T-cell) ligand and gp120, thus disrupting the gp120/CD4 interaction [44].

3.7. Antimicrobial Activity: Through the agar well-diffusion method, it has been demonstrated that extracts obtained from mature leaves and bark of *Avicennia officinalis*, utilizing hexane, chloroform, and methanol, exhibit antimicrobial activity against various plant and human pathogenic bacteria and fungi [36,45,46]. In a separate experimental study, the antimicrobial potential of several diterpenes isolated from *Avicennia officinalis* roots collected in Andhra Pradesh, India, was investigated. The findings revealed that Excoecarin A, ent-16-hydroxy-3-oxo-13-epi-manoyl oxide, and ent-15-hydroxy-labda-8(17),13E-dien-3-one exhibit moderate antifungal activities against *Rhizopus oryzae* and *Aspergillus niger*, while rhizophorin-B1 displays antibacterial activity against Bacillus subtilis [47].
Furthermore, in a bioactivity-guided fractionation study focusing on active antibacterial metabolites from *Avicennia officinalis* twigs collected from Malaysia, strong inhibitory effects were observed against Gram-positive bacteria such as Bacillus subtilis, Staphylococcus aureus, and S. epidermidis. The lowest inhibition concentration values ranged from 0.156 to 5.0 mg/ml. Notably, the plant extracts did not show any effect on Gram-negative bacteria including *Escherichia coli, Vibrio cholera, and Enterobacter cloacae*. It was suggested that the antibacterial activity could be attributed to two naphthofuranquinones, avicenol C and stenocarpoquinone B, which were isolated from the active fractions using chromatographic methods [48].

3.8. Antioxidant Activity: *Avicennia officinalis* fruit and leaf extracts exhibit notable antioxidant potential, as demonstrated by assays including 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid) (ABTS), chromium peroxide (CrO_2), and ferric reducing antioxidant power (FRAP) methods. Among the tested extracts, methanol and ethanol extracts displayed the highest activity, while aqueous and ethyl acetate extracts showed the lowest [11,49].

Furthermore, petroleum ether and aqueous leaf extracts showcased antioxidant capacity in assays targeting DPPH, superoxide, and hydrogen peroxide scavenging, with IC50 values ranging from 0.17 to 0.27 mg/ml. Additionally, ethanol extracts from both bark and leaf demonstrated a dose-dependent scavenging capacity against superoxide radicals, DPPH, and ABTS, with IC values ranging from 82 to 207.6 µg/ml [36,50,51].

3.9. CNS activity: In studies evaluating pentobarbital-induced hypnosis in mice, *Avicennia officinalis* leaf extracts at doses of 250 and 500 mg/kg were found to enhance the duration of sleep and decrease sleep onset latency, indicating central nervous system (CNS) depressant activity. Additionally, a reduction in exploratory behavior responses in tests such as hole cross, head dip, and open field tests further confirmed a potential tranquilizing effect [40,52].

Further investigation confirmed the CNS depressant activity of the leaf's ethyl acetate extract through neuropharmacological tests assessing muscle coordination and movement in mice. Oral dosages of 250, 500, and 1000 mg/kg of the extract led to decreased locomotor activity in forced swim and Rota rod tests in a dose-dependent manner. Moreover, all three extract dosages enhanced diazepam-induced drowsiness, reinforcing the sedative effect [53].

In vitro assays evaluated the cholinesterase inhibitory activity of the leaf methanolic extract at concentrations below 2 mg/ml. Using Ellman's colorimetric method, the extract's ability to inhibit 50% of total and butyryl cholinesterase was measured, yielding results similar to those of the standard medication donepezil. These findings suggest that A. officinalis could hold promise in the development of safe and effective medications for neurodegenerative disorders like Alzheimer's disease [54].

3.10. Other Potential Biomedical Uses

Phytoremediation capacity: *Avicennia officinalis* exhibits a strong ability to retain metals through the use of phyto-extraction and phyto-stabilization techniques. Different trends of heavy metal (lead, arsenic, mercury, and cadmium) and trace metal (cobalt, chromium, copper, iron, manganese, nickel, and zinc) accumulation by the pneumatophore, leaves, and bark are identified in a variety of experimental investigations. The highest concentration of metals is demonstrated to accumulate in the pneumatophore tissues, highlighting the enormous potential for eliminating pollutants from a wide range of abiotic milieu (soil, water, and sediments) without negatively impacting the ecosystem. [55,56,57]

Biosynthesis of Silver Nanoparticles: According to studies, mangrove plants like *Avicennia officinalis* and *A. marin*a produce biologically active silver nanoparticles very effectively, which the pharmaceutical industry may use to prevent a number of terrible diseases. The extract from the leaves of *Avicennia officinalis* contains terpenoids and polyphenolic compounds, which have been shown to have the potential to act as reducing agents during the synthesis of silver nanoparticles. This biological method would be the most cost-effective way to produce silver nanoparticles on a large scale, and it would be the greatest substitute for the traditional chemical and physical methods. [58,59]

4. Pharmacological Activities of *Heritiera fomes*

A review of the literature revealed that *Heritiera fomes* is used to treat a variety of illnesses; the gastrointestinal disorders have been linked to the use of the leaves and seeds of the plant. (constipation, acidity, indigestion, diarrhea, dysentery, and stomachache) [60,61,62]. Well-known treatments for diabetes and skin conditions (dermatitis, eczema, builds, abscess, acne, sores, and rash) include the bark and stem bark [24, 60,62]. It is observed that locals use twigs to relieve coughs and clean their teeth [63]

Significant groups of phytochemical constituents found in *Heritiera fomes* have been shown to have a variety of pharmacological activities in other plants. Significant biological activities of plant saponins are reported to include spermicida[1] [64], molluscicidal [65], antimicrobial, anti-inflammatory, and cytotoxic [66] effects. It is known that flavonoids have been shown to exhibit antioxidant activity against a broad range of oxidizable compounds [67]. Flavonoids are known to scavenge different types of radicals, including hydroxyl, peroxyl, and superoxide radicals. This ability allows flavonoids to block different steps in the arachidonate cascade by blocking lipoxygenase and cyclooxygenase-2 [68]. Plant species may be able to prevent disease because of the presence of polyphenols. In fact, one of the main components of the defense mechanism produced by medicinal plants is polyphenols [69].

According to reports, they have antimicrobial, anticancer, and free radical scavenger properties [70,71]. Additionally, polyphenolic substances have the capacity to prevent human platelet aggregation [72]. Plants that contain tannins and proanthocyanidins exhibit a range of biological activities, including antibacterial, antiherpetic, cytotoxic, antineoplastic, and anthelmintic properties. These compounds also offer protection against herbivores and invasive parasites [73,74]. Flavonoid polymers called proanthocyanidins are thought to have anti-diarrheal properties [75,76]. Several studies have demonstrated the effectiveness of specific flavonoids, such as proanthocyanidins, catechins, and proanthocyanidin-rich extracts, as antidiarrheal agents [77,78]. They are potent antioxidants that can prevent dysentery brought on by Shigella dysenteriae toxin [79] and Entamoeba histolytica lectin.[80]

4.1. Anti-diabetic Effects: According to the experimental study, mice treated with 250 and 500 mg/kg body weight of *Heritiera fomes* bark extracts showed positive effects. In Swiss albino mice, the extracts (at a dose of 250 mg/kg body weight) decreased the level of serum glucose to 49.2% after 60 minutes. glucose loading, glibenclamide (at a dose of 10 mg/kg body weight) decreased serum glucose by 43.5% in a standard dose. After 120 minutes of glucose loading, the *Heritiera fomes* bark extracts decreased serum glucose levels by 35.6 and

44.7%, respectively, at doses of 250 and 500 mg/kg body weight. In contrast, glibenclamide decreased serum glucose levels by 30.1% when given at a dose of 10 mg/kg body weight [81].
To treat alloxan-induced diabetic rats, an ethanolic extract of *Ceriops decandra* leaves was given orally daily for 30 days at a dose of 120 mg/kg. The effects on liver glycogen, hemoglobin, acetylated hemoglobin, and blood glucose were comparable to those of glibenclamide, a common antidiabetic medication [82]. Additionally, extract of leaf powder from the mangrove species Rhizophora mucronata, Rhizophora apiculata, and Rhizophora annamalayana has been shown to have an antidiabetic effect in alloxan-induced diabetic rats [83]. After being administered to diabetic rats induced with alloxan, a leaf suspension of the black mangrove species *Aegiceras corniculatum* was also reported to have antidiabetic effects.

4.2. Antimicrobial Activity: Leaf of *Heritiera fomes* (at doses of 500 µg/disc and 250 µg/disc) showed strong antimicrobial activity. Activity against gram-positive and gram-negative pathogens tested, with the zones of inhibition spanning 3.92 to 7,63 mm and 7.86 to 13.45 mm, respectively [84]. Significant antibacterial activities against *P. aeruginosa, S. aureus, K. rhizophila,* and *B. subtilis* were reported by the bark extracts of *Heritiera fomes* [85]. Pneumatophores from *Xylocarpus mohiccensis* and *Heritiera fomes* were compared in vitro for antibacterial activity, and the results showed that in most cases, the zones of inhibition were greater than 10 mm. Pneumatophores derived from *Heritiera fomes* showed a strong zone of inhibition when tested against *Enterobacter arrogenes*. The inhibition zones' diameters ranged from 19 to 21 mm. By using the broth dilution method, the *Heritiera fomes* extract's minimum inhibitory concentration (MIC) against Shigella boydu and Shigella sonnei was determined to be 400 and 500 µg/ml, respectively [86]. The Activities of Antioxidants and Their Correlated Effects. It has been demonstrated that several mangrove species plants contain antioxidant phytoconstituents or have *antioxidative* effects. *Heritiera fomes* leaf extract was tested for antioxidant activity on both a quantitative and qualitative level. The DPPH assay (hydrogen donation assay) was used to complete the quantitative assay technique, and the qualitative assay was conducted using DPPH spray after thin layer chromatography, the leaves extract showed a significant amount of antioxidant activity, with an IC (50 percent inhibitory concentration) value of 26.30 µg/ml. [84] With an effective concentration (EC) value of 19.4 µg/ml and a 50% inhibitory concentration (C) value of 22 µg/ml, respectively, *Heritiera fomes* bark extracts demonstrated strong antioxidant activity. [85] With an effective concentration (EC) value of 19.4 µg/ml and a 50% inhibitory concentration (C) value of 22 µg/ml, respectively, bark extracts of *Heritiera fomes* demonstrated strong antioxidant activity. [85]
Pneumatophores from *Xylocarpus mohaccensis* and *Heritiera fomes* were compared in vitro for antibacterial activity, and the results showed that in most cases, there were no inhibitions of 10 mm. Pneumatophores derived from *Heritiera fomes* showed a strong zone of inhibition when tested against Enterobacter aerogenes. The inhibition zones had a diameter of between 19 and 21 mm. By using the broth dilution method, the minimum inhibitory concentration (MIC) of *Heritiera fomes* extract against *Shigella boydii* and *Shigella sonnei* was determined to be 400 and 500 µg/ml, respectively.

4.3. Antioxidant Activity and various Related Effects: The Activities of Antioxidants and Their Correlated Effects. It has been demonstrated that several mangrove species plants contain antioxidant phytoconstituents or have antioxidative effects. *Heritiers fomes* leaf extract was tested for antioxidant activity on both a quantitative and qualitative level. The qualitative assay was conducted using thin layer chromatography technique, which was followed by DPPH spray, and the quantitative assay technique was carried out using the DPPH assay (hydrogen donation assay). The extract from leaves demonstrated noteworthy antioxidant activity, with an IC (50 percent inhibitory concentration) of 26.30 µg/ml. [84] With an effective concentration (EC) value of 19.4 µg/ml and a 50% inhibitory concentration (IC) value of 22 g/ml, bark extracts from *Heritiers fomes* exhibited strong antioxidant activity. [85]
A study conducted on rats using diclofenac-induced gastric ulcers has demonstrated the protective effect of an aqueous extract of Rhizophora mangle bark. Since administration of the extract resulted in significant increases in glutathione peroxidase and superoxide dismutase activity as well as inhibition of lipid peroxidation, the protective effect was attributed to the extract's antioxidant activity. In a rodent model of gastric ulcers caused by acetic acid, this plant's bark extract has also been shown to have anti-ulcer properties. [87] Bruguierins A–C, three dammarane triterpenes with antioxidant properties, have been isolated from Bruguiera gym- norrhiza. Moreover, bruguierin A selectively inhibited cyclooxygenase-2 activity and blocked nuclear factor-KB activation induced by phorbol ester. [88] It has been demonstrated that the butanolic fraction of Rhizophora mangle bark extract protects rats' stomachs from damage brought on by absolute ethanol and ischemia-reperfusion. The antioxidative properties of the polyphenols in the fraction have been linked to the protective action. [89]
It has been demonstrated that the sulfated polysaccharides in *Rhizophora apiculata* bark extract protect against naphthalene-induced mitochondrial dysfunction by scavenging free radicals.[90] From the aerial parts of *Avicennia marina*, iridoid glucosides and flavones with a,a-diphenyl-β-picrylhydrazyl (DPPH) radical scavenging activities have been isolated. [91] From the stems and twigs of *Rhizophora stylosa*, a novel acetylated flavanol, 3,7-0-diacetyl (-)-epicatechin, and other flavanol derivatives have been reported. The substances exhibited the ability to scavenge DPPH radicals. [92] From the stems of this plant, flavan-3-ol glycosides and flavan-3-ols with DPPH scavenging activity have also been reported. [93] It has been reported that the

methanolic extract of *Rhizophora mucronata* leaves has a very high total phenolic content and antioxidant activity. [94]

4.4. Anti-inflammatory and antinociceptive properties: The number of inhibitions of acetic acid-induced writhings in mice was significantly decreased by oral administration o*f Heritiera fomes* bark extracts (at doses of 100, 250, and 500 mg/kg) by K.5, 26.4, and 43.4%, respectively, whereas aspirin (250 mg/kg), used as a reference drug, showed 20.9% writhing inhibition.[24] *Heritiera fomes* leaf extracts at doses of 250 and 500 mg/kg body weight significantly ($P < 0.001$) inhibited writhing (34.83% and 59.20%, respectively), while the reference drug, diclofenac sodium (25 mg/kg), inhibited writhing (70.65%). Leaf extracts (500 mg/kg) in the hot plate test method showed the greatest nociceptive inhibition and required a longer reaction time than morphine sulfate (standard drug) at a dose of 5 mg/kg. [23] There have been reports of luteol from *Sonneratia apetala*, a species of mangrove. [95] This compound has been described as having antinociceptive properties. [96] It has been reported that betulinic acid is reparted from *Ceriops tagul* [97] and *Sonneratia apetala*. [95] It has been reported that this *Tetracera potatoria* compound has anti-inflammatory, analgesic, and antipyrexic properties [98] Bruguierin A., which is isolated from *Bruguiera gymnorrhiza*, has been shown to inhibit cyclooxygenase-2 (COX-2) activity, which can have analgesic and anti-inflammatory effects by inhibiting prostaglandin biosynthesis. [88] It has also been demonstrated that Rhizophora mangle's aqueous extract and polyphenolic fractions inhibit the activity of COX-2 [99] *Excnecaria agallocha* sterns and twigs contained diterpenoids that had anti-inflammatory properties that could suppress lipopolysaccharide (LPS)-induced expression of nuclear factor-KB and AP-1 targeted genes in mouse macrophages Raw 264.7 cells, including tumor necrosis factor-a (TNF-a) and interleukin 6 (IL-6). [100] It has been demonstrated that the methanol extract of *Cerbera manghas* contains kaempferol, which contributes to its anti-inflammatory properties. [101]

4.5. Anticancer Activity: *Heritiera fomes* leaf extract was subjected to a phytochemical analysis, which revealed the presence of reducing sugars, alkaloids, flavonoids, tannins, steroids, gums, and flavonoids. [23] Furthermore, it has been reported that proanthocyanidins, which are bioactive compounds found in a variety of medicinal plants such as *Heritiera fomes*, have antiviral, antibacterial, antioxidant, and anticarcinogenic properties. [102,103,104] *Heritiera fomes* leaf and stem extract showed 40% inhibition of B16 mouse melanoma (an in vitro system) as anticancer properties. and the in vivo system of Ehrlich Ascites Carcinoma (EAC) in Swiss albino mice. [22]

The anti-inflammatory and antitumor properties of Rhizophora apiculata methanolic extract have been assessed against B16F10 melanoma cells in BALB/c mice. When mice were given the extract, the growth of solid tumors was inhibited. In the tumor-bearing animals, extract treatment dramatically lowered the levels of glutamyl transpeptidase (GGT), nitric oxide (NO), and GSH in tumor cells. The extract's analysis showed the presence of pyrazole, ketone derivatives, and 4-pyrrolidinyl. [105]

It has been reported that several other mangrove species may have anticancer properties. It has been shown that 3-chlorodeoxylactone, a naphthoquinone derived from *Avicennia germi*- nans, has antitumor activity. [106] It has been reported that limonoids extracted from Xylocarpus granatum seeds are cytotoxic to the tumor cell lines P-388 and A-549. [107] One isolated limonoid from the same plant that was shown is called gedunin. inhibition of the colon cancer cell line CaCo-2's growth in vitro. [108] Xylomexicanin A, a different limonoid that was extracted from the same plant, showed antiproliferative activity against KT cells, which are human breast cancer cells. [109] It has been demonstrated that hamsters' buccal pouch carcinogenesis caused by dimethyl benz alanthracene (DMBA) is prevented by *Ceriops decandra* black tea extract. [110] AGS, MDA-MB-231 and MCF-7 cells, as well as AGS, MDA-MB-231, HT-29, and NIH 3T3 cells, were reportedly subjected to moderately cytotoxic activity by patriscabratine and tetracosane, which were extracted from the Bangladesh mangrove fern *Acrostichum aureum*. Within 24 hours of treatment, AGS cells showed an apoptotic response to the sesquiterpene (2R, 35)-sulfated pterosin C, which was isolated from the same fern. [111] It has been reported that B16F-10 melanoma-induced lung metastasis in C57BL/6 mice was inhibited by methanolic extract of *Rhizophora apiculata*. [112] When considered collectively, the different reports suggest that mangrove species plants could be excellent providers of possible anticancer medications.

4.6. Thrombolitic Activity Using the technique outlined by *Tabassum et. al.* [120], the experimented extracts' in vitro thrombolytic potentiality was assessed. Ten healthy human volunteers (n = 10) without a history of hematological disorders or anticoagulant therapy were given venous blood samples (4 ml). The drawn blood sample was then divided into multiple sterile, preweighed, microcentrifuged tubes (1 ml/tube). Written informed consent was obtained from every willing donor of blood. Each preweighted, sterile Eppendorf tube received one milliliter of blood, which was then incubated for 45 minutes at 37°C. The formation of clots eliminated the serum entirely. To determine the clot weight, each tube containing a clot was further weighted (clot weight = weight of clot containing tube - weight of tube alone). Next, 100 µl of various crude extracts were added, one by one, to each of these tubes. In this case, the positive and negative controls were streptokinase and distilled water, respectively. Subsequently, 100 µL of streptokinase and 100 µL of distilled water were separately added to the Eppendorf tubes designated as the control. Following a 90-minute incubation period

at 37°C, clot lysis was monitored in each tube. The released fluid was disposed of after incubation, and tubes were weighed once more to determine the weight difference following clot disruption.[120]

4.7. Antiarthritic Activity: To assess Antiarthritic Activity done by the model of denaturation of serum albumin. At first 0.45ml bovine serum albumin (5% aq. Solution) and 0.05ml of different experimenal extract of *H. fomes* were tested for their antiarthritic properties in five different concentrations (100–500 µg/ml) were mixed together. Then, all the sample were incubated at 37 C for 30 minutesand further heated at 57 C for 3 minutes to induce denaturation of protein. Later 2.5ml phosphate buffer (pH 6.3) was added to each tube after cooling them to room temperature and absorbance of turbidity was measured 660nm. Diclofenac sodium was used as standard at te same concentration. The root extract in chloroform showed the highest percentage inhibition of protein denaturation (63.28±5.96% at 500 µg/ml), while the root extract in ethanolic medium showed the lowest inhibition (36.12±5.77% at 500 µg/ml).[121]

4.8. Anthelmintic Activity: The anthelmintic activity of *H. fomes* extracts was assayed. It is used as earthworms (*Pheretima posthuma*). It is used in freshly prepared standard and test solutios. Test samples of the experimented extracts were prepared at the concentrations of 20-75 mg/ml in Tween 20 (1%) solution diluted with normal saline. Nearly equal sized earthworms were divided into seven groups (consisting of six worms in each) and were released into 30 ml of experimental formulation. The first group recived Tween 20 along with normal saline and was taken as control; group two was treated with reference drug albendazole at a concenteration of 20mg/ml, 25mg/ml, and 75mg/ml). Time of paralysis and tme of death of the experimented worms were noted, the ethanolic bark extract at a concentration of 75 mg/ml caused paralysis in less time and killed earthworms in a little more time. [122,123]

4.9. Anti- obesity activity of *H. fomes:* The high-fat cafeteria diet (HFCD) has been shown to raise blood sugar, triglycerides, LDL cholesterol, VLDL cholesterol, body weight, fat pad, and organ weight. In comparison to the normal control level, it also lowers HDL cholesterol. However, when MEHF treatment was administered, there was a notable decrease in body weight gain, as well as an increase in dose-dependent HDL cholesterol and a decrease in LDL and VLDL cholesterol, glucose, serum triglyceride levels, kidney weight, spleen weight, and organ weight of the liver (Mirza et al., 2017). The anti-obesity potential of *H. fomes* has been found in this work. The TG and TC levels in cafeteria diet fed animals noticeably increased during de novo cholesterol production and intestinal absorption. Additionally, increased oxidative stress makes treatment for various illnesses through conventional means. reactive oxygen species (ROS), which can assemble oxidation by reacting with lipoproteins states, thereby reducing the body's cellular uptake of lipids. This occurs as a result of the reduced cholesterol retention from the slim down or as a result of the antioxidants present. The increased cellular lipid uptake may have been facilitated by the plant sedate. Furthermore, a significant Devaluation of serum total cholesterol in the groups treated with plant drugs may be related to a decrease in the liver enzyme's activities 3-methyl-3-hydroxy glutaryl coenzyme an (HMG-CoA) reductase, a threshold enzyme in the pathway for the biosynthesis of fat (Mirza et al., 2017). The activities of antioxidants that are enzymatic (GPx, SOD, and CAT) were undoubtedly elevated in the liver while receiving MEHF treatment, and this raised antioxidant capacity might have been determined by the plant drug's natural antioxidants. (Mirza and others, 2017). [124]

5. Future Prospects for Medicinal Discoveries:

This review found that *H. fomes* has substantial chemical constituents and pharmacological potential. Rural residents who live next to the Sundarbans use this plant to treat a variety of human ailments. This indigenous knowledge must be gathered, properly documented, and preserved for use in future studies. Notwithstanding its intriguing biological and pharmacological potential, this plant has been the subject of relatively few reports. Further investigation is necessary regarding the phytochemical components of this plant. Future researchers will find it easier to find new therapeutic agents thanks to this review, as the plant has promising biological and pharmacological potential.

Mangroves have an extensive variety of bio active compounds and are biochemically unique due to their distinct ecology and extreme tropical environmental conditions. They are the main source of newly discovered compounds with a wide range of physiological effects. Isolated compounds from mangrove species may serve as lead compounds in the drug-discovery process. These plants are still unknown despite their vast ethnomedical and folkloric applications.

Secondary metabolites such as alkaloids, phenolics, steroids, and terpenoids are found in mangrove plants and have been found to have pharmacological, ecological, and toxicological significance. For example, two mangrove species, *Avicennia marina* and *Avicennia officinalis*, have been found to contain phytoconstituents (alkaloids, flavonoids, terpenoids, phenolics, and saponins) with antimicrobial properties. [113] *Heritiera fomes* were shown to contain reducing sugars, saponins, flavonoids, phenols, polyphenols, and tannins through an in vitro investigation. Certain compounds, such as polyphenols, phenols, and flavonoids, have the ability to scavenge free radicals and function as antioxidants. [114,115] Nitrogen and oxygen species (ROS), which are highly reactive free radicals, have the ability to oxidatively damage DNA, proteins, and lipids, leading to a variety of diseases. [116] Cells are shielded from oxidative damage by antioxidants. High levels of antioxidant activity are found in proanthocyanidins, their metabolites, and hydroxylated phenolic acids. [117] Proanthocyanidin-rich

products and proanthocyanidins have been found to have significant RNS/ROS scavenging activity.[102] The plant (*Heritiera fomes*) has a high procyanidin content, which allows it to function as a 15-LO inhibitor as well as a radical scavenger. Procyanidin B2 derivatives have been reported to exhibit anti-tumor and anti-human promyelocytic leukemia (HL-60) cell lines. [118] According to reports, a combination of procyanidins caused cytotoxic activity in human squamous cell carcinoma. [119] It is evident from the discussion above that the plant might be a valuable source of phytomedicines with anticancer properties.

5. Discussion & Conclusion

The world's most productive ecosystems are thought to be mangroves. In addition to the anticipated effects on global warming, sea level rise, coastal erosion, and other natural and man-made disturbances, reintroducing mangrove vegetation is imperative because of the plant's enormous therapeutic potential, as per conventional wisdom and scientific research. The review provides a thorough discussion of the botanical identification, distribution, possible secondary metabolite composition, and bioactivities of *Avicennia officinalis*. It is a medicinal plant, which is traditionally used as astringent, diuretic, anti-ulcer, treatment for snake nibbles the ancient time etc. Examines on this plant are expanding step by step due to its strong pharmacological employments. The various phytochemical investigations resulted in the separation of several potent mixtures, which is the cause of its unique pharmacological experiments. The purpose of this audit was to compile the exploration work that has been undertaken at better locations thus far by various researchers in order to provide a standard for future. Numerous in vitro investigations have demonstrated the plant's noteworthy antioxidant, antinociceptive, antimicrobial, antidiabetic, and anticancer properties. It is imperative to separate the bioactive substances causing these effects. Systematic methods like bioassay-guided fractionation can be taken into consideration in this regard. The current work should open up new avenues for drug discovery and act as a foundation and crucial tool for upcoming chemical screening and biological assays.

The plant possesses significant antioxidant, antinociceptive, antimicrobial, and antidiabetic properties, according to several in vitro studies.as well as anticancer properties. Isolation is imperative. The bioactive substances in question are what cause these effects. In this context, methodical techniques like bioassay-guided fractionation are an option. The current investigation ought to provide as a foundation and a crucial instrument for upcoming biological assays and chemical screening, and they ought to provide fresh perspectives on drug discovery.

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