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Mangrove-Derived Phytochemicals: Therapeutic Role in Depression and Hypertension Management

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Abstract: Mangrove is the name given to a group of trees and shrubs that live in salt soils and obtain oxygen through their lenticels in marshy, low-oxygen soils. Mangroves are an important source of a wide range of wood for construction, shelters, and fences, as well as non-wood forest products such as honey, sugar, alcohol, vinegar, and foliage for fodder and cattle. Various Mangrove species were also identified to treat different ailments, including skin diseases, bleeding, and snake bites, abscesses, orthopedic problems, rheumatism, kidney disorders, diabetes, ulcers, boils, asthma, hepatitis, fever, leprosy, smallpox, dysentery, epilepsy, and hypertension in ethnobotanical surveys in different countries. For instance, in the Comoros and Mauritius Islands, a decoction prepared from the root of the mangrove shrub *Bruguiera gymnorhiza* and five to seven leaves of *Piper borbonense*, boiled in two cups of water, is taken to treat hemorrhage and is also used for diabetes and hypertension. The mangrove plant species are a good source of potential bioactive compounds, such as flavonoids, polyphenols, terpenes, tannins, and alkaloids, which exhibit a variety of therapeutic properties. Although many mangrove species have been used by local inhabitants for an extended period to treat ailments, following folk traditions, the number of species studied extensively remains limited. Due to such rich phytochemical composition, pharmacological studies revealed their effects on various diseases. Among them, antidepressant and antihypertensive properties are also remarkable. Antidepressant effects are explained through mechanisms such as regulating neurotransmitters such as serotonin, dopamine, and norepinephrine, modulation of the HPA axis, and reduction of oxidative stress. Likewise, antihypertensive effects are associated with ACE inhibition, improved vascular endothelial function, and diuretic effects. The present study will investigate the impact of mangroves on hypertension and depression.

1. Introduction

Mangroves are salt-tolerant species living in tropical and subtropical climatic zones (Friess, 2016). Mangrove forests are of great significance in tidal processes, as they form part of an ecosystem. They make a substantial contribution to the reduction of the greenhouse effect by incorporating carbon dioxide into the photosynthesis cycle (Romañach et al., 2018). In accordance with the ecosystem they form, they are grouped as follows: 'true mangroves', 'mangrove-associated species' and 'companion or helper species'. "True mangroves" are species that can survive low-oxygen levels and salt (Sudhir, Arunprasath et al., 2022). Species living in mangrove ecosystems are referred to as "mangrove-associated species." Although they can grow in this special habitat, these organisms are not categorized as mangroves. (Basyuni et al., 2019). Species that do not have a direct taxonomic relationship with mangroves but work in symbiosis with them to support the health and vitality of these ecosystems are referred to as "companion or helper species." For instance, it has been demonstrated that *Phragmites australis* stabilises the soil with its strong root system, protecting mangrove root systems in the process (Chambers et al., 1999). It has been estimated that there are about 71 species of true mangroves (Sudhir et al., 2022). Due to their historical uses in traditional healing methods and folk medicine, mangroves are of great interest. Different species, in different mangrove habitats, the bitter juice made from the fruits is used to increase the abortive effect, the leaves are used to treat ulcers, the fruit oil is used to treat rheumatism, the seed powder is used as an antiseptic, the leaves are used as an antipyretic, moreover, the tree trunks are

used as a blood tonic (Mendrofa and Mulawarmanti, 2015). Mangroves' diverse high-value phytochemical content is responsible for their wide range of therapeutic benefits (Chowdhury et al., 2014).

2. Methodology

This study was carried out using a traditional literature review approach to comprehensively evaluate the traditional use of phytochemicals—bioactive compounds of plant origin—among the general public, their medical significance, and their therapeutic roles, particularly in the management of depression and hypertension. As part of the research, peer-reviewed articles, ethnobotanical studies, and clinical trials published between 2015 and 2026 and available in the Web of Science, Scopus, PubMed, and Google Scholar databases were searched using the keyword combinations "phytochemicals," "ethnobotany," "traditional medicine," "depression," "hypertension," and "bioactive compounds." From the retrieved literature, studies that linked folk medicine practices to clinical and pharmacological data, had strong methodology, and were up-to-date were selected and subjected to a qualitative synthesis process; thus, the mechanisms of action of phytochemicals in these two chronic health conditions and their contributions to future drug development processes were brought together on a structured basis.

3. Phytochemicals of Mangroves

3.1. Acanthaceae

Acanthus ilicifolius Lour. has been used for a variety of purposes, including as an aphrodisiac, diuretic, for asthma, diabetes, snakebite, and skin diseases

(Bandaranayake, 2002). *A. ilicifolius* has some compounds acanthicifoline, bisoxazolinone, and ilicifolioside C, and 2-benzoxazolinone, which particularly have an anti-leishmanial effect (Kapil, Sharma et al., 1994; Manikandan et al., 2014; Zohora, Hasan, Alam et al., 2023). Another compound, 4-hydroxy-2-benzoxazolone, has been isolated from leaves that exhibit hepatoprotective effects (Liu et al., 2013).

3.2. Combretaceae

Conocarpus erectus L. has spherical fruits, which have been utilized for anemia, diabetes, and antipyretic reagent in folk medicine (Morton, 1981). The plant/plant extract contains catechin, apigenin, and quercetin (Hameed et al., 2012). Later, additional compounds were isolated, including vescalagin, castalagin, and trimethoxy-ellagic glycoside (Abdel-Hameed et al., 2014; Ayoub, 2010). *C. erectus* methanol extracts showed a decrease in liver enzyme ALT (alanine aminotransferase) values, therefore, *C. erectus* might strongly have a hepatoprotective effect (Abdel-Hameed et al., 2013). The black mangrove *Lumnitzera racemosa* Willd. is used to treat conditions such as asthma and sore throats in traditional medicine (Acharyya et al., 2023). The juice of the *L. racemosa* is used to treat mouth wounds in China (Bandaranayake, 2002; Neamsuvan et al., 2012). According to phytochemical analyses, *L. racemosa* contains compounds such as lupeol, lupenone, friedeline, stigmasterol, myricetin, and punicalagin (Majumdar and Patra 1980; Basyuni et al. 2007).

3.3. Ebenaceae

Diospyros species grows on Papua Island is used for some medicinal properties,

including as a remedy for renal stones, infertility, oral hygiene, and haemostasis in folk medicine (Wanda et al. 2019; Vijayalakshmi and Ravindhran 2013). *D. ferrea* (Willd.) Dakh. leaves have shown an antidiabetic effect in an *in vivo* study (Prada et al., 2017). The species of the *Diospyros* has numerous phytochemical compounds such as β -sitosterol, phytol, citronellol, ursolic acid, gallic acid, isodiospyrin, betulin, stigmasterol, lupeol, and friedelin (Kuo et al., 1997; Prada et al., 2019).

3.4. Fabaceae

Cynometra iripa Kostel. is used in Ayurvedic medicine to treat inflammatory diseases. *C. iripa* leaves are used to treat wounds. (Sen and Bhakat, 2020). It has also shown antimicrobial effects against *Pseudomonas aeruginosa*. (Mrunalini N. Desai and Chavan, 2010). The species has numerous compounds, such as β -carotene, β -sitosterol, falcarinol, behenic acid, caproic acid, linoleic acid, and sculene (Desai and Chavan 2011; Desai and Chavan 2014). *Mora oleifera* (Triana ex Hemsl.) Ducke (Panama mangrove) contains numerous phytochemicals such as lupenone, lupeol, β -amyrin, palmitic acid, sitosterol, and stigmasterol (Cherigo et al., 2024; Palacios and Cantera, 2017). Traditionally, it is used for diabetes. Furthermore the extract of *M. oleifera* leaves has been scientifically studied for the *in vitro* α -glucosidase inhibition test showing an IC₅₀ value was calculated as 25.29 μ g/ml (Lopez et al., 2018).

3.5. Lythraceae

Sonneratia apetala Banks. grows in Bangladesh and India. The plant is used as a hemostatic, moreover, to treat ulcers and asthma traditionally (Bandaranayake,

2002). The studies on the plant extracts revealed a variety of compounds, such as catechin, rutin, myricetin, kaempferol, ferulic acid, and 2-methyltetracosane (Uddin et al. 2024). The methanol extract of the leaves has been investigated for its antidiabetic effects with the α -glucosidase enzyme showing the IC₅₀ value as 0.017 mg/ml (Patra, Das, and Thatoi, 2015). Furthermore, an *in vivo* study demonstrated that the hexane extract from the seeds demonstrated an antidiarrheal effect (Hossain et al., 2017).

3.6. Malvaceae

Heritiera littoralis Aiton grows in Madagascar (Tomlinson, 2016). The plant has been utilized to treat conditions like malaria, stomachaches, and diarrhoea in traditional medicine (Bandaranayake, 2002). Studies on the plant demonstrated some valuable phytochemical compounds such as β -sitosterol, epicatechin, betulinic acid, physcion, vallapianin, vanillic acid, and quercetin (Li et al. 2009). Additionally, the phytochemical investigations have revealed some isolated compounds such as Heritiera A and B, juglansin, quadronoside IV, and arjunglucoside II, which have terpenic structures (Liang et al., 2023). The antimycobacterial properties of 3-cinamoyltribuloside were investigated, and as a result, an MIC of 0.8 mg/mL was determined. (Christopher et al., 2014). Furthermore, Karim has found the plant extract highly effective against the gram-negative bacterium *Salmonella enterica* (Karim et al., 2020).

3.7. Meliaceae

The cedar mangrove *Xylocarpus granatum* J. Koenig is used to treat flu, diarrhoea, and malaria in folk medicine. (Shahid-Ud-

Daula and Basher, 2009). The investigation into the antidiarrheal properties of a methanolic extract from the bark revealed that the extract was most effective against diarrhea at a dosage of 250 mg/kg (Uddin et al. 2005). The phytochemical searches on the plant have reported several compounds, such as xylocarpin, xylocensin M, xylogranatin F-R, phragmalin, cipadesin A, and n-methylflindersine (Lakshmi and Gupta, 2008; Wu et al., 2008; Zhou et al., 2014).

3.8. Myrsinaceae

Aegiceras corniculatum (L.) Blanco grows in Singapore and China. It is used in several medical conditions, including diabetes, rheumatism, liver diseases, and asthma, in traditional medicine (Debnath et al., 2020). The plant has a wide range of phytochemicals, including rutin, oleanolic acid, palmitic acid, stigmasterol, acornine I, gallic acid, primulagenin A, rebeudioside C, arachidic acid, and lignoceric acid. (Wei et al., 2012; J. Zhang et al., 2021). The ethanol extract of the leaves effectively inhibited LOX (IC₅₀: 23.58 μ g/ml) in an *in vitro* study (Biswas et al., 2019). The hexane extract of *A. corniculatum* stems exhibited hepatoprotective activity (Roome et al., 2008). A preclinical study on *A. corniculatum* methanol leaf extract demonstrated an increased acetylcholinesterase activity with scopolamine-induced amnesia in mice (Bulbul et al., 2017). A dose of 25 mg/kg of leaf butanol extract is effective on mice with colon cancer (Luo et al., 2019). *Camptostemon philippinensis* (A.DC.) Mez. naturally grows in Indonesia and the Philippines. It is reported that the leaf extract exhibits anti-melanogenic activity (lightening effect) at concentrations of 175 μ g/mL and 200 μ g/mL (Mc Colleine et al., 2021).

3.9. Pellicieraceae

Pelliciera rhizophorae Triana & Planch., an endemic species, grows in Central America. Several compounds, such as β -amyrin, ursolic acid, oleanolic acid, betulinic acid, brugierol, kaempferol, quercetin, betulin, and lupeol, were determined in the plant. Furthermore, the antiparasitic activity of these isolated compounds was investigated, with a particular focus on triterpenic ursolic acid (IC_{50} : $2.4 \mu M \pm 0.1$) and oleanolic acid (IC_{50} : $5.3 \mu M \pm 0.2$). Both compounds demonstrated strong inhibitory activity against *Leishmania donovani* (López et al., 2015). Additionally, the extracts were tested for their α -glucosidase enzyme inhibition *in vitro*. The leaf extract was more effective in a low dosage showing IC_{50} values as 20.60 ± 0.7 compared to the stem extract showing IC_{50} value as 60.09 ± 3.12 (Cherigo and Martínez-Luis, 2019).

3.10. Plumbaginaceae

Aegialitis rotundifolia (S. Vidal) Becc. (small mangrove) had been utilized for their analgesic and anti-inflammatory effects in folk medicine (Ray, 2014). The plant has mostly phenolic compounds such as gallic acid, rutin, coumarin, quercetin; moreover, compounds like isochiapin B, emeguisin, and 5-vinylsalicylaldoxime are present in the plant extracts (Ghosh et al., 2017).

3.11. Pteridaceae

Acrostichum aureum Cav. has been used in various parts of the world historically. In India, the roots of the plant are used to treat diabetes and chest pain, additionally, the leaves are used as an antidote against to snake venom. (Badhsheeba and Vadivel, 2018). The rhizomes are used for wound healing in Vietnam and as an

antihelminthic agent in China (Page et al., 2021). *A. aureum* contains various secondary metabolites such as flavonoids, sterols, saponins, tannins, kaempferol, quercetin, tetracosane, stigmasterol, campesterol and gum (Khan et al. 2013; Kimura et al. 2017). Additionally, steroids and terpenic compounds like lupenone, squalene, stigmasterol, and phytol were reported in the plant extract (Basyuni et al. 2019).

3.12. Rhizophoraceae

The Rhizophoraceae family has numerous genus, such as *Bruguiera*, *Ceriops*, *Kandelia*, and *Rhizophora* (Bandaranayake, 2002). *Bruguiera cylindrica* (L.) Blume is considered as a medicinal plant among folk, who applied the plant for its blood tonic and wound healing effects (Krishnamoorthy et al., 2011). The plant has numerous phytochemical compounds such as butanoic acid, 2-furancarboxitrile, trifluoroguanidine, p-aminotoluene, 1,3-dioxolane, quinic acid, catechin, vanillin, epicatechin, ferulic acid, azelaic acid, brugierol, and syringic acid (Bibi Sadeer et al., 2020; Khadeeja et al., 2022). The ethanolic extract of the fruits demonstrated significant effects for tyrosinase enzyme inhibition (Bibi Sadeer et al., 2020).

Ceriops tagal (Perr.) C.B.Rob. is traditionally used for healing wounds and as a hemostatic agent (Wang, Li, and Wu, 2012). It contains compounds such as lupeol, betulin, betulinic acid, and cereotagalol (Pakhathirathien et al., 2005). In a study investigating the inhibition of α -glucosidase, as a promising agent for diabetes, the IC_{50} was calculated to be $0.85 \mu g/ml$ (Lawag et al., 2012).

The regional population frequently uses the plant *Kandelia candel* to treat diabetes (Ray, 2014). It has quite a few compounds, including epicatechin, oleanolic acid, corchoionoside C, mehirugins A, lupeol, stigmasterol, lanosterol, betulin, afzeleczhin, kandelside, and matricarin (Jasna and Khaleel, 2020; Thao et al., 2015; Zhang, Lin et al., 2010). The study found that at a concentration of 500 µg/ml, the extract produced 50.96% inhibition of α -amylase for diabetic conditions (Jasna and Khaleel, 2022).

The red mangrove *Rhizophora mangle* L. was utilized in folk medicine applications, including the treatment of diabetes, cardiovascular diseases, malaria, and tuberculosis, as well as the management of bone fractures (Bandaranayake, 2002; Cruz, et al., 2015). In a clinical study, an aqueous extract prepared from *R. mangle* bark was applied to patients with aphthous ulcers. It shows that the extract heals mucosal tissue and decreases erythema and pain, and no reported adverse effects (Armas, et al., 2005).

The effectiveness of *R. mangle* bark aqueous extract in healing open surgical wounds was investigated in a clinical study. There was a noticeable acceleration in the healing of the wound after application, furthermore, none of the patients observed a secondary infection. Furthermore, it was observed that the plant extract formed a red-coloured film on the wounds. This phenomenon has been linked to the presence of tannin group compounds within the plant (Fernandez et al., 2002).

The plant has been reported to contain phytochemical compounds: cinchonain Ia, cinchonain Ib, catechin, epicatechin,

lyoniside, and nudiposide (Andrade-Cetto et al., 2017).

4. Depression, Hypertension and Mangroves

Although depression and hypertension appear to be disparate ailments, they are, in fact, highly associated diseases. A study demonstrates that the likelihood of hypertension increases by approximately 42% in individuals with a history of depression (Meng et al., 2012). Furthermore, given the established relationship between psychosocial factors and both depression and hypertension, it can be concluded that depression and hypertension are diseases that affect each other (Bosworth et al., 2003). In this study, the potential of mangroves for the treatment of depression and hypertension will be evaluated. The relationship between hypertension, depression, and effective mangrove compounds is shown in Figure 1. Pictures of mangroves effective for depression and hypertension are shown in figure.

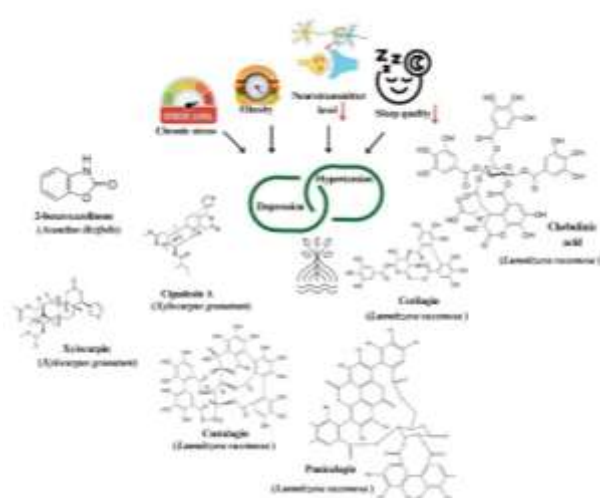


Figure 1. Hypertension-depression relationship and effective mangrove compounds

4.1. Mangroves in Hypertension

Hypertension is a health problem characterized by elevated blood pressure. It is estimated that this condition is responsible for approximately 9.4 million deaths per year (Forouzanfar et al., 2016). A comprehensive analysis of the pathophysiology of hypertension reveals a multifaceted nature. A multitude of mechanisms have been identified that are effective in regulating blood pressure, including the renin-angiotensin system, natriuretic peptides, and nitric oxide (NO) released from the endothelium (Oparil, et al., 2003). Antihypertensive pharmaceuticals also act through these mechanisms; in particular, angiotensin-converting enzyme (ACE) inhibitors lower blood pressure by blocking the production of angiotensin II, thereby affecting the renin-angiotensin system (Varagic et al., 2014). Synthetic drug use is often given priority; on the other hand, during clinical administration, these substances are known to cause a variety of adverse reactions, such as fatigue, numbness in the hands, dry mouth, coughing, and stomach problems (Tedla and Bautista, 2016). To prevent such conditions, there has been an increased focus on the search for antihypertensive drugs of natural origin. For instance, *Allium sativum* has been demonstrated to exhibit vasodilation properties by increasing nitric oxide release. Furthermore, clinical studies have demonstrated the antihypertensive properties of *Hibiscus sabdariffa* extract, whose efficacy is comparable to that of captopril (Herrera-Arellano et al., 2004). *Lumnitzera racemosa* was studied for its antihypertensive effects in vivo on rats. Phytochemicals were determined in the plant including corilagin, chebulinic acid, castalagin, and punicalagin (Lin, Hsu, and Cheng, 1993). Leaf extract of

Rhizophora mangle was studied *in vitro* on inhibition of the angiotensin-converting enzyme (ACE), consequently, IC₅₀ was determined as 1.75 µg/ml. A strong correlation was reported between the elevated flavonoid content and the higher ACE inhibitory action (Rodríguez-García et al., 2019).

4.2. Mangrove in Depression

Depression is a common psychopathological situation. This condition has some symptoms such as negative emotions, decreased interest in enjoyable activities, persistent sadness, and feelings of shame. A close examination of the pathophysiology reveals that monoaminergic systems are implicated in behavioral manifestations such as fatigue and low mood (Stahl, 1998). In particular, it has been observed that depressed patients tend to exhibit a decrease in serotonin levels (Stockmeier, 2003). Accordingly, the inhibition of the re-uptake of biological monoamines is a key objective in therapeutic interventions. Pharmacological agents characterized by these mechanisms have also been utilized in clinical practice. However, these pharmaceutical agents frequently induce adverse effects, including fatigue, weight gain, sedation, and nausea (Santarsieri and Schwartz, 2015). Consequently, there has been a rise in interest concerning antidepressants of natural origin. For instance, medicinal plants such as *Glycyrrhiza glabra*, *Hypericum perforatum*, *Valeriana officinalis*, and *Melissa officinalis* are frequently utilized for the treatment of mild depression in the Northern Hemisphere (Li et al., 2020; Sezer et al., 2020). *Rhizophora apiculata* was investigated extensively for antidepressant effect, by using the tail suspension test (TST) and the forced swim

test (FST). The administration of the aqueous extract at 200 mg/kg and 400 mg/kg and the ethanolic extract at 300 mg/kg and 600 mg/kg was found to have a significant antidepressant effect. This study examined the impact of the extracts on cognitive capacity, revealing a nootropic effect at elevated doses (**Mande et al., 2023**).

Xylocarpus granatum fruits contain xylocarpin, which has been determined to have antidepressant properties. According to an *in vivo* study, xylocarpin decreases stress and serum cortisol at a dose of 15 mg/kg. The compound has no determined adverse effects in mice (**Yin et al., 2015**). *X. granatum* seeds also contain cipadesin A that was found to have an antidepressant effect at a dose of 15 mg/kg, a decrease in stress level was observed. It was observed that Cipadesin A, similar to Xylocarpin, exerts a modulatory effect on serum cortisol levels and is devoid of substantial side effects (**Gao et al., 2016**).

The activity of the 2-benzoxazolinone compound, isolated from *Acanthus ilicifolius* leaves, was searched on serotonin and norepinephrine neurotransmitters *in silico*. As a result, molecular docking studies have been conducted, and this compound has been identified as a potential candidate for inclusion in antidepressant drug classes (**Manikandan et al., 2014**).

5. Conclusion

The unique characteristics of mangrove ecosystems are well-documented, as are the significant benefits they provide to both biodiversity and human health. Beyond these benefits, their phytochemicals have been shown to positively impact human health. However, the scientific community has thus far

undertaken an inadequate evaluation of these plants and plant extracts, particularly on depression and hypertension. The majority of available studies on these subjects have been limited to *in vitro* and *in vivo* research. Consequently, there is a need for further ethnobotanical investigation of mangrove forests to ascertain their potential for treating these diseases. Furthermore, large-scale screening might help obtain valuable results for those subjects. Recent advances in biotechnology, driven by technological progress, should also play a role in these studies. However, it is imperative to recognize that mangrove forests are not immune to the impacts of climate change, which could lead to their extinction if effective mitigation strategies are not swiftly implemented.

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Author Contribution

All authors have contributed equally.

Conflicts of Interest

There is no conflict of interest among the authors.

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