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Review: *Rhizophora mucronata* as source of foods and medicines

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Abstract. *Setyawan AD, Ragavan P, Basyuni M, Sarno S. 2019. Review:* Rhizophora mucronata *as source of foods and medicines. Bonorowo Wetlands 9: 42-55. Rhizophora mucronata* Poir is a type of mangrove plant that is widely distributed in the Indo-Pacific (Indian and Pacific Oceans) region. This plant is mainly harvested for its wood for charcoal, firewood, and building materials. In addition, the bark and its propagule are used for natural dyes and leather tanning. However, its use in the food and health sector is still limited. This review intends to collect, compile, and summarize the use of *R. mucronata* as a source of food and medicinal ingredients. As a result, the starch obtained from *R. mucronata* propagule can be used as a carbohydrate source after removing the tannin content. In the health sector, various parts of this plant organ are traditionally used to remedy diarrhea, hepatitis, ulcers, etc. Further research shows that extraction with multiple solvents across multiple plant organs can be an antioxidant, anticancer, anti-inflammatory, anti-diabetic, antimicrobial (antiviral, antifungal, antibacterial). The main constituent of this plant is tannins, alkaloids, and flavonoids, which affect their biological/pharmacological activities. The part of the organ used and the extraction method significantly affects the chemical content produced, thus affecting its effect in treatment.

Keywords: Anticancer, antioxidant, food, medicine, *Rhizophora mucronata*

INTRODUCTION

Mangroves are halophytes plants that thrive in the transition zone between the terrestrial and marine environments (Giri et al., 2011). The word "mangrove" refers to a taxonomically varied collection of trees and shrubs that appear prominent among plant communities in tidal, salty marshes along sheltered tropical and subtropical coasts (Hamilton and Murphy 1988). Mangroves are multipurpose coastal plants; they protect coastal areas from damage environmentally (Hardoko et al. 2016; Kurniadi and Koeslulati 2020). Mangroves thrive in the dense tangle of roots, muck, and tidal water (Duke and Wain 1981). Following the December 2004 tsunami, mangroves became prominent as hotspots of coastal variety. The Indian Ocean region is home to around 55 species of mangroves from 22 genera (Kathiresan and Rajendran 2005). Mangrove swamps, tidal swamp woods, tidal swamp forests, and mangals are all terms used to describe the habitat of mangrove plants. Mangrove trees are found in 121 countries globally (Chandrasekaran et al., 2009).

Due to their unique physical environment, mangroves have evolved a suite of adaptations to cope with extreme environmental circumstances such as high salinity, strong winds, tidal changes, high temperature, and anaerobic tidal bogs. As a result, the mangrove environment is home to a diverse range of species that abundant bioactive compounds and enzymes. Whether it is the extensive supporting roots of *Rhizophora*, the breathing roots of *Avicennia*, the salt excreting leaves, or the viviparous water dispersed seedlings. Everything possesses an exceptional capacity to produce bioactive metabolites for obvious reasons of survival and propagation, thereby providing them with 'chemical signals' to respond to, thwart, or defend 'environmental clues' (Joel and Bhimba 2010).

Mangroves have historically been utilized for their lumber (in furniture, boats, and fishing equipment), fuelwood, charcoal, food, and medicine. Mangrove extracts and chemical components have been employed as insecticides and pesticides, tannins for the leather industry and dyeing, a salt, potassium carbonate, and sodium chloride alternative, tonic, wine, and a fruit beverage, a betel substitute, and a vegetable (Bandaranayake 1998; Alongi 2002). Food and medicine are derived from the roots, stems, leaves, blooms, and fruit of mangrove plants. Utilization was associated with the nutritional (proteins, lipids, carbs, vitamins, and minerals) and bioactive chemical content of mangrove plants (Bandaranayake 1998). Mangrove bark contains between 15% and 36% tannins, resulting in reddish-brown colors used in the tanning and coloring of leather (Duke and Allen 2006; Nazima et al. 2014). It is also used to print silk materials (Nakpathom et al., 2011).

Numerous mangrove plants have also been studied ethnopharmacologically. Mangroves produce various unique natural chemicals or secondary metabolites with substantial pharmacological effects utilized in ethnomedicine to treat multiple diseases (Bandaranayake 2002; Salini 2015). Mangroves have adapted to severe environments, resulting in a plethora of bioactive compounds that are toxicological, agricultural, and ecological (Kokpal et al., 1990). Mangroves adapt to harsh environments so that they contain many bioactive compounds that are toxicological, pharmacological, and ecological (Kokpal et al., 1990). Coastal communities have used extracts and raw materials from mangroves for natural medicinal purposes (Mahmiah et al., 2017). Mangroves have demonstrated their utility throughout history. Mangrove is a traditional Chinese medicine used to treat angina, diabetes, diarrhea, dysentery, hematuria, and hemorrhage (Duke and Wain 1981). It has antibacterial (Chandrasekaran et al. 2009), antiviral (Premanathan et al. 1999a), antifungal (Bose and Bose 2008), and antioxidant properties (Babu et al. 2007). Mangroves are biochemically unique in that they produce a diverse range of natural compounds that can be used to cure a variety of human ailments (Bandaranayake 1998).

For example, the Indian people employed mangroves to cure flatulence, epilepsy, smallpox, diabetes, asthma, rheumatism, stomach aches, fevers, malaria, cholera, hepatitis, cancer, ulcers, and wounds, as well as AIDS (Premanathan et al. 1999b; Prabhakaran et al. 2012; Revathi et al. 2014). Additionally, people in Bangladesh utilized mangrove trees as an antinociceptive, anti-inflammatory, and antipyretic (Shilpi et al. 2012), while people in Myanmar used this plant to treat inflammatory disorders and diarrhea (Rohini and Das 2010a; Shilpi et al. 2012). Additionally, the indigenous Thai people used mangrove bark extract to treat diarrhea, nausea, and vomiting and stop bleeding from newly opened wounds (Boonyapraphat and Chockchaicharaenphorn 1998; Laphookhieo et al. 2004).

Rhizophora leaves are traditionally used to treat diarrhea, while the fruit is consumed by those living near mangroves (Hardoko et al., 2015). Bandaranayake (1998) supports this by stating that traditional portions of plants of various types *Rhizophora* are used to treat a variety of ailments. *Rhizophora apiculata* is an antiemetic, antiseptic, diarrhea, hemostatic (bark), hepatitis (bark, flowers, fruit, leaves), typhoid (bark). *Rhizophora lamarckii* as a potential hepatitis drug (flowers, leaves). *Rhizophora mangle* is used to treat angina, boils, and fungal infections (bark), diarrhea, dysentery, elephantiasis, fever, malaria, and leprosy (bark, leaves), minor injuries (bark), plaster for fractured bones, (bark), tuberculosis (bark, leaves). *Rhizophora mucronata* is used to treat elephantiasis and as a febrifuge. It is also used to treat hematoma (bark), hepatitis (bark, flowers, fruit, leaves, and roots), and ulcers (bark). *Rhizophora racemosa* is the point at which the bleeding ceases (flowers, leaves). *Scaevola sericea* is an antiseptic and anti-inflammatory herb used medicinally to treat coughs, diabetes, eye infections, gastrointestinal diseases, headaches, stings, and bites (bark, leaves).

One type of *Rhizophora* that is widely distributed in the Indian and Pacific Oceans is *Rhizophora mucronata* Poir. *Rhizophora mucronata* is a medicinally significant mangrove plant (family Rhizophoraceae) that has been used in traditional medicine to treat diabetes, diarrhea, wounds, ulcers, and liver diseases (Hoppe-Speer et al. 2011; Arumugam et al. 2014; Manilal et al. 2015). The writing of this review is intended to collect, observe, and combine the use of *R. mucronata* as a source of food and medicinal ingredients.

DISTRIBUTION AND HABITAT

Rhizophora mucronata is a member of the Rhizophoraceae family (Schwarzbach and Ricklefs 2000) and is usually referred to as *bakau kurap* or looproot mangrove, red mangrove, or Asian mangrove (Grin 2006; Warui et al. 2020). *Rhizophora mucronata* is found in the coastlines of the tropical and subtropical region (Perry 1980; Rohini and Das 2009). It is located in the Indo-Pacific region on riverbanks and at the sea's edge (Gillikin and Verheyden 2005). It is native to tropical and subtropical coastal areas extending from the east coast of Africa to Asia and Australia and the islands of the eastern Pacific Ocean. Closely related to Atlantic-East Pacific red mangroves, whose natural ranges intersect only on a few southern Pacific islands (Duke 2006).

The plant is found in a variety of nations worldwide. *Rhizophora mucronata* is found in Africa (Egypt, Ethiopia, Kenya, Madagascar, Mauritius, Mozambique, Tanzania, Somalia, South Africa, and Sudan), Asia (Cambodia, India, Indonesia, Malaysia, Pakistan, Papua New Guinea, Philippines, Sri Lanka, Thailand, Taiwan, and Vietnam), and the South Pacific (Solomon Islands, Vanuatu) (Grin 2006). It is the only species of mangrove found in East Africa (Gillikin and Verheyden 2005). Its few small populations in Pakistan are located in the Miani estuary, Baluchistan, and the Indus delta (Atkinson et al. 1967; Saifullah 1982). Introduced to the Hawaiian Islands, it is widespread throughout Southeast Asia (Sulistiono et al. 2015) and is also found in East Africa, Australia, and the Indian Ocean (Gurib-Fakim and Brendler 2004).

Estuaries, tidal streams, and flat coastal environments are preferred habitats of *R. mucronata* because of the species' vulnerability to daily tidal flooding. As a result, it often forms an evergreen buffer zone around mangrove habitats, making it more resistant to floods than other mangrove species (Batool et al., 2014). It is frequently found growing along the banks of rivers and is commonly inundated by high tides (Sulistiono et al., 2015). *Rhizophora mucronata* inhabits a similar environment as *R. apiculata* but is more tolerant of sandier and harder substrates. It grows in clusters along the sides of creeks and tidal estuaries, rarely far from the tides. Growth is optimal in deeply submerged regions, on hard ground, and in areas rich in humus. This is one of the most significant and widespread mangrove species. Throughout the year, flowers bloom. Crabs frequently consume seedlings, limiting new growth. Seeds that have been dried in the shade for a few days before planting are less favorable for crab. This procedure is likely to result in the accumulation of tannins that provide protection. The presence is really prevalent (Giesen et al. 2006).

BOTANICAL DESCRIPTION

Rhizophora mucronata is an erect, 20-30 m tall mangrove tree with a diameter of up to 35-70 cm at the breast.

Bark. Barks are light grey, dark grey, light brown or dark to nearly black with horizontal fissures. Scaly bark with small slits that are square shape'.

Pole. It is cuneate, with an acute climax, with 16-22 cm in length and 8-11 cm in width.

Roots. It features stilt roots and aerial roots that originate from lower branches. Stilt roots buttress the species' trunk.

Leaves. It has dark green, thick leaves with a pronounced mucronate apex and an inferior surface covered in minute black dots. It has a green top and a yellowish-green bottom in a single formation. The layout is the opposite. Shape: a round elongated ellipse that stretches upward. Stipules range in length from 5.5 to 8.5 cm. 2.5-4 cm is the length of the petiole. Leaf-blades are broadly elliptic to oblong in shape, measuring 8.5-23 5-13 cm in length, leathery, with a cuneate base and blunt to sharp apex. The petiole is green in color and measures 2.5-5.5 cm in length; leaflets measure 5.5-8.5 cm in length.

Inflorescences. 2-3-forked with 2-5(-12)-flowered cymes; 2.5-5-cm peduncle.

Flowers. Flowers are sessile, creamy white, and grouped in a fork shape (compound limited type) with 2-3 flowers. Petals: 4, cream to white, lanceolate, 7-9 mm, fleshy, partially enclosing stamens, pilose edges (densely hairy margins). Stamens are eight in number, four at the base of the petals and four on the sepals, measuring 6-8 mm; anthers are sessile. Calyx lobes are four, ovulate 9-14 x 5-7 mm in length, deeply lobed, and cream to yellow. The ovary protrudes considerably beyond the disk; the free section is elongate-conic and is 2-3 mm in length; the style measures 0.5-1.5 mm in length.

Fruit. It produces green fruits in the shape of cigars. Fruit is dull, brownish-green, elongate-ovoid, 5-7 2.5-3.5 cm, tuberculate at the base, somewhat constricted at the apex. The hypocotyl is cylindrical, measuring between 30 and 65 cm in length and up to 2 cm in width. The fruit is viviparous, germinating before dropping to the ground. The fruit is formed like a Hypocotyl. The Hypocotyl is coated in lenticel and is green. Size: 60 cm in length and 2 cm in breadth (Gurib-Fakim and Brendler 2004; Setyawan and Ulumuddin 2012; Setyawan et al. 2014; Sulistiono et al. 2015).

TRADITIONAL USES

Rhizophora mucronata can be planted in fish ponds to defend levees and dikes and is also helpful for making fish traps (Giesen et al. 2006). The timber is used to make fuel, construct buildings, and construct fish traps, among other things (Mahmiah et al., 2017). It is dense to highly dense wood that is extremely hard and robust; it shrinks significantly and is relatively difficult to deal with due to its hardness. It is utilized in the production of firewood and charcoal (Giesen et al. 2006). The extraction of tannins is a significant usage of this plant (Rohini and Das 2010b). The tannin in the barks has been used for tanning and dyeing for centuries, most notably to reinforce fishing lines and rigging. The leaves are used to make a dye that is either black or chestnut (Burkill 1966). This mangrove species contain up to 70% tannins (Gurib-Fakim and Brendler 2004). Additionally, it has long been used to treat elephantiasis, hematoma, hepatitis, ulcers, and as a febrifuge (Bandaranayake 2002; Ravikumar et al. 2005), and its antiviral activity has been scientifically demonstrated (Padmakumar and Ayyakkannu 1997). It is occasionally used to treat hematuria (Giesen et al. 2006). Hypocotyl flour is also used as a food source during famines (Bunyapraphatsara et al., 2002).

The fruit of *R. mucronata* is used as food and drink, the young leaves are used as vegetables, the wood and bark are used as tanning and dyeing materials, and the boiled water (extract) of the wood can be used as a slimming, antidiarrheal, and antiemetic agent (Abidin et al. 2013).

SOURCE OF FOODS

Chemical characteristic of ripe fruit flour

A fruit is the edible component of mangrove plants. The fruit is dried and ground into flour for various food products (Hardoko et al., 2015). *Rhizophora mucronata*, according to Bunyapraphatsara et al. (2002), contains dietary fiber (29.25% ± 0.4%). According to Meyer et al. (2000), dietary fiber from whole grains protects against the development of diabetes. According to Jenkins et al. (2000), water-soluble dietary fiber is more protective against diabetes than insoluble dietary fiber. Chandalia et al. (2000) believe that adhering to the ADA's recommended intake of dietary fiber, particularly water-soluble fiber, can improve blood sugar management, hyperinsulinemia, and plasma lipid concentrations in people with type 2 diabetes.

Carbohydrates account for 90.67% of ripe *R. mucronata* fruit flour, containing 7.50% soluble dietary fiber and 38.60% insoluble dietary fiber. Qualitatively, ripe *R. mucronata* fruit flour contains flavonoids, steroids, saponins, and tannins. In diabetic rats, ripe *R. mucronata* fruit flour decreased blood glucose levels. Doses of 1,000 mg/day/head, 1,500 mg/day/head, and 2,000 mg/day/head are comparable to the action of glibenclamide (0.09 mg/day/200 g body weight) in diabetic rats (Hardoko et al. 2015).

Hardoko et al. (2015) reported that the chemical composition of ripe *R. mucronata* fruit flour was dominated by carbohydrates (90.67%) was low in protein and fat. Carbohydrates with a high fiber content constituted 38.60% insoluble dietary fiber and 7.50% soluble dietary fiber. Thus, ripe *R. mucronata* fruit flour was classified as having high dietary fiber content. The dietary fiber content of ripe *R. mucronata* fruit flour is higher (29%) than that of *R. mucronata* fruit. Meyer et al. (2000) reported that whole-grain dietary fiber is protective against diabetes. Consumption of soluble dietary fiber is more protective than consumption of insoluble dietary fiber (Jenkins et al., 2000). According to Chandalia et al. (2000), increasing dietary fiber intake, particularly soluble fiber, improves blood glucose management, lowers hyperinsulinemia, and decreases plasma lipid concentrations in patients with type 2 diabetes.

Toxicity test of fruit flour

Meyer et al. (1982) and Effendi et al. (2012) classified toxicity into five categories based on the LC_{50} value: (i) substances with LC_{50} values <1 ppm are considered very toxic, (ii) those with LC_{50} values of 100-1,000 ppm are considered moderately toxic, (iii) those with LC_{50} values of 1,000-10,000 ppm are considered low toxic, those with LC_{50} values of 10,000-100,000 ppm are considered nearly non-toxic. Referring to Hardoko et al. (2015), because the LC_{50} value of ripe *R. mucronata* fruit flour was 1,737.80 ppm, it was classified as having a low toxic rate. The low toxicity level is attributed to both HCN (2.97 ppm) and tannin (819 ppm). The safe level of HCN in the diet is 50 parts per million. Additionally, the safe daily intake of tannin is 560 mg/kg body weight. The HCN content, tannin content, and LC_{50} value can all be used to determine the food's level of safety. Yield is a ratio of ripe *R. mucronata* fruit flour to ripe *R. mucronata* fruit. The flour yield was 12.9%. The amount of water and other components lost during processing affects the yield fluctuation. Both the HCN and tannin concentrations of ripe *R. mucronata* fruit flour are within the safe consumption limit and have low toxic levels.

MEDICINAL USES

Herbal medicines have gained significant attention as a viable alternative to conventional medicine, and demand for these therapies has surged in recent years. Numerous mangrove plants have been used in folk medicine. Extracts from mangroves and mangrove-dependent species have recently been shown to be against human, animal, and plant pathogens. Still, only a few studies have been conducted to characterize the plant parts that are most effective for application and the metabolites responsible for their bioactivities (Lewis and Hanson 1991). Compared to terrestrial plants, mangrove plants contain an immense amount of secondary metabolites. As a result, the World Health Organization (WHO) recommended using plants to control diabetes mellitus and supported scientific investigation of their anti-hyperglycemic characteristics (Nabeel et al. 2010; Rahman et al. 2010; Gurudeeban et al. 2012).

Rhizophora genera are known to be beneficial in the treatment of a variety of diseases, including angina, hemorrhage, and hematuria. Interestingly, mature leaves and roots can be used to induce labor (Seepana et al. 2016), ulcers (Krishnamoorthy et al. 2011), diarrhea, fever, and burns (Sur et al. 2016), as well as stings of poisonous fish (Gurib-Fakim and Brendler 2004). Its bark and leaf extracts have been employed in traditional medicine as an astringent, antiseptic, and hemostatic agent with antibacterial, anti-ulcerogenic, and anti-inflammatory properties (Kaur et al., 2018).

Rhizophora mucronata possesses a plethora of therapeutic qualities (Perry 1980). Historically, the herb was used to treat diarrhea, constipation, nausea, hematuria, and diabetes (Bibi et al., 2019). *Rhizophora mucronata*'s bark, root, leaves, fruit, and flowers have been used in traditional medicine to treat diabetes, diarrhea, hepatitis, inflammation, sores, and ulcers, among other conditions (Duke 1992; Bandaranayake 1998; Ng and Sivasothi 2001). The leaf has been used in traditional medicine to treat diarrhea and dysmotility of the stomach (Bandaranayake 1998). The decoction of the root is used to treat diabetes and hypertension, while the infusion of the leaves is used to treat fever.

The Indonesians have long used the entire plant as a febrifuge and cure for elephantiasis, hematoma, hepatitis, and an ulcer (Rollet 1981; Nurdiani et al. 2012). The whole plant is used to cure elephantiasis, a disorder caused by tissue swelling induced by filarial worms (Rollet 1981; Nurdiani et al. 2012). Mangrove societies in East Java boil *R. mucronata* leaf to treat diarrhea. The bark of *R. mucronata* is frequently noted in ethnomedicine for its antidiarrheal qualities. However, there has been no noteworthy previously reported on the leaf's antidiarrheal activity. Diarrhea is defined by increased bowel movement frequency, moist stool, and stomach pain. Neurohormonal mechanisms, infections, starvation, chronic disease, and medications all can affect gastrointestinal physiology, resulting in alterations in the intestinal epithelium's fluid output or absorption. Anti-motility agents such as diphenoxylate and anticholinergic agents have been used to treat diarrheal illnesses, but they frequently cause side effects when administered for an extended period (Harrison 2005). Antidiarrheal qualities of medicinal plants have been linked to their tannin and flavonoid content (Rohini et al. 1999). *Rhizophora mucronata* leaf extracts are the most effective natural anti-diarrhea agent. They are natural substances utilized in traditional and modern therapies to improve human health with fewer adverse effects. Leaf extracts demonstrate the presence of new pharmacological compounds that could tackle the threat of human disease. Several studies have been published on this topic (Kuppusamy et al. 2015; Arumugam et al. 2016; Swamy et al. 2016).

The bark of *R. mucronata* has been used traditionally in Burma, India, and China to treat diarrhea, dysentery, fever, angina, diabetes, hematuria, and bleeding (Duke and Wain 1981; Kathiresan and Ramanathan 1997). Poultices of leaves are applied to armored fish injuries (Watt and Breyer-Brandwijk 1962). The Indochinese uses the roots to treat angina and hemorrhage. To help a woman give birth, Malays use old leaves and/or roots. The Burmese use the bark to treat bloody urine, the Chinese and Japanese use it to treat diarrhea and the Indochinese use it to treat angina (Perry 1980; Kusuma et al. 2011).

The indigenous people of Papua New Guinea used the stem to treat constipation, infertility, and menstrual issues (Liebezeit and Rau 2006). *Rhizophora mucronata* has historically been used to treat elephantiasis, hematoma, hepatitis, ulcers, and as a febrifuge (Bandaranayake 2002; Ravikumar et al. 2005). Its leaf is used in folk medicine to alleviate diarrhea and dysmotility of the stomach. The leaf extract of *R. mucronata* is used to treat diarrhea. The bark of *R. mucronata* is frequently noted in ethnomedicine for its antidiarrheal qualities (Harrison 2005).

The bark of *R. mucronata* or the entire plant has traditionally been used in Tamil Nadu, India, to treat angina, dysentery, hematuria, hepatitis, ulcers, diabetes, bleeding, vomiting, and nausea. In Mauritius, the indigenous people use the *R. mucronata* plant as a traditional medication to treat diabetes and hypertension and a natural cure for lowering the blood urea level. The root (5 cm in length) of *R. mucronata*, three entire *Bidens pilosa* plants, ten leaves of *Piper borbonense*, the bark (15 cm in length) of *Erythroxylum laurifolium*, fifteen leaves of *Aphloia jobi*, and ten leaves of *Antidesma madagascariense* are used to make a tea. The tea is consumed to maintain a healthy blood urea level (Gurib-Fakim and Brendler 2004).

The bark, root, leaves, fruits, and flowers of *R. mucronata* have been traditionally used as medicine in the coastal areas of South Asia to treat health problems such as diabetes (Bandaranayake 1998; Sur et al. 2004), diarrhea (Yunita et al. 2012), hepatitis (Ravikumar and Gnanadesigan 2012), inflammation (Rohini and Das 2009), and cognitive function (Suganthy and Devi 2016).

PHYTOCHEMICAL COMPOSITION

Rhizophora mucronata possessed alkaloids, condensed and hydrolyzable tannins, flavonoids, proteins, saponins, steroids, triterpenes, and flavonoids (Basak et al. 1996; Madhu and Madhu 1997). Diverse extraction methods in different parts can give different phytochemical content as well.

The leaves of *R. mucronata* are a natural source of tannins and flavonoids, although their chemical, biological, and pharmacological effects are unknown (Rahim et al., 2008). *R. mucronata* contains up to 70% tannins, which contribute to its therapeutic characteristics, including astringent, anti-diabetic, anti-rheumatoid, and hypotensive properties (Gurib-Fakim and Brendler 2004). Alkaloids, hydrolyzable tannins, polyphenols, flavonoids, triterpenes, inositols, polysaccharides, saponins, and anthocyanidins are some of the chemical constituents of *R. mucronata* (Kolkpol et al. 1990; Ghosh et al. 1995; Anjaneyulu and Rao 2001; Bandaranayake 2002). It possesses antibacterial and antiviral effects (Premanathan et al. 1999a). Although an ethanolic extract of *Rhizophora* has demonstrated anti-diabetic and antihyperglycemic action, the underlying mechanism remains unknown (Sur et al. 2004).

During phytochemical screening, tannin, saponin, flavonoid, and steroids were detected in ripe R. mucronata fruit flour. Ghosh et al. (1995) reported that *R. mucronata* possessed steroid, triterpenoid, alkaloid, flavonoid, tannin, catechin, quinone, and anthocyanidin. Basyuni (2008) reported that *R. mucronata* contains polyphenols at a concentration of 157.4±22.9 mg/g dry weight and free radical scavenging activity of 83.7±2.8 mg/mL (Agoramoorthy et al. 2008), Rhizophorins CE (1-3), Rhizophorin A, (6 R, 11 S, 13 S)-6,11,13-trihydroxy-2,3-seco-14-labden-2,8-olid-3-oic acid and Rhizophorin B, ent-3 β,20-epoxy-3,18-dihydroxy-15-beyerene and unknown activities (Ammanamanchi 2004) and triterpenoids: β-amyrin, lupeol, and taratàxol (Basyuni 2008).

Phytochemistry of the ethyl acetate fraction of *R. mucronata* bark produced compounds such as saponins, steroids, flavonoids, and anthraquinones. The results of the GC-MS analysis showed the presence of seven compounds identified in the ethyl acetate of the stem bark of *R. mucronata.* These compounds include one class of quinones, three classes of steroids, two groups of alkaloids, and one class of aromatics. The most abundant metabolite found in the ethyl acetate of the stem bark of *R. mucronata* is the alkaloid 1H-Purin-6-amine (2-fluorophenyl) methyl) (74.76%) (Mahmiah et al., 2017).

On the crude methanol *R. mucronata* leaf extract, phytochemical screening disclosed the presence of tannins, alkaloid, flavonoid, terpenoid, and saponin. Condensed tannins are present in the crude methanol extract of *R. mucronata* leaf. It included catechin 47.428 parts per million and epigallocatechin 3.150 parts per million. *Rhizophora mucronata* leaf crude methanol extract is used to treat gastrointestinal motility disorders such as diarrhea. It acts directly on smooth muscle cells to reduce ileal motility and acts as an antagonist cholinergic receptor. At a concentration of 0.30 %, a crude methanol extract of *R. mucronata* leaf had a substantial effect. This concentration eased 52% of methacholine-induced ileum contractions (Puspitasar et al., 2012).

The beneficial phytochemicals were more abundant in the methanol and ethanol extracts of *R. mucronata* than in the chloroform extract. Terpenoids and tannins are present in all three extracts. Still, a higher concentration of terpenoids was observed in the chloroform extract, which is consistent with the result of the previous study (Cowan 1999). All *R. mucronata* extracts contained various phytochemical components, including proteins, phenols, flavonoids, saponins, glycosides, terpenoids, and tannins. We previously discovered the presence of steroids in chloroform and methanol extracts and alkaloids in ethanol extracts (Cowan 1999). Phenolic chemicals are one of the most abundant and widely distributed classes of plant metabolites (Singh et al., 2007).

They have significant biological features, including anti-apoptotic, anti-aging, anti-carcinogen, anti-inflammation, anti-atherosclerosis, cardiovascular protection, endothelial function improvement, angiogenesis prevention, and cell proliferation (Han et al. 2007).

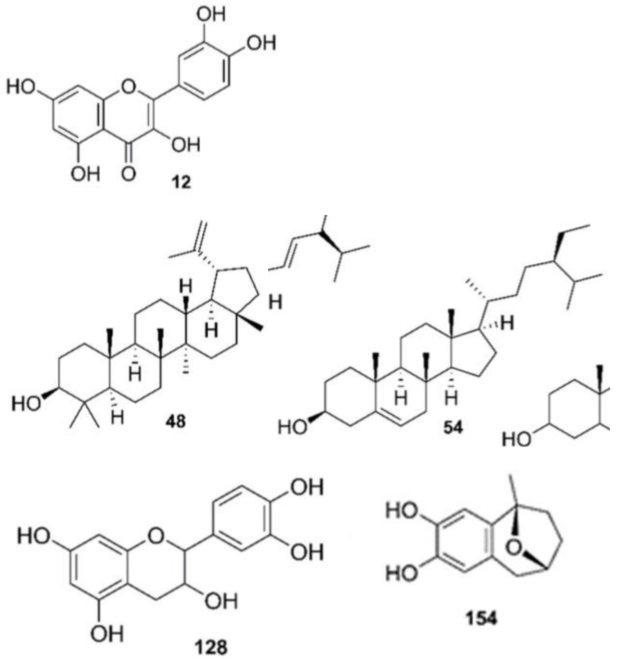

Figure 1. Chemical structures of compounds 1-20 isolated from *R. mucronata*

The methanolic leaf extract demonstrated significant anticholinesterase activity (AChE assay) with an IC_{50} value of 59.31±0.35 g/mL and important antioxidant activity (DPPH assay) with an IC_{50} value of 47.39±0.43 g/mL. These noteworthy findings may be related to the presence of a high concentration of flavonoids, particularly catechin (128) (Suganthy and Devi 2016). Due to the presence of phenolics, flavonoids, gallic acid (130), quercetin (12), and coumarin, *R. mucronata* is regarded as a good natural antidiabetic drug (Sur et al. 2016). Additionally, Rohini and Das (2010a) demonstrated that the bark extract of *R. mucronata* possesses excellent anti-inflammatory action due to the presence of the phytoconstituents lupeol (48), quercetin (12), β-sitosterol (54), and caffeic acid. According to Manilal et al. (2015), the primary ingredient extracted from the crude extract, ethanone (1-(2-hydroxy-5-methylphenyl), may play a critical role in the plant's antimicrobial action. The chemical structures of isolated mangrove chemicals are depicted in Figure 1.

PHARMACOLOGICAL PROPERTIES

Extracts from various mangrove plants and their partners exhibit antimicrobial activity against human and plant infections (Chandrasekara et al., 2009). Mangrove trees include a variety of phytochemicals with antimicrobial characteristics; they are a good source of saponins, alkaloids, and flavonoids (Bandaranayake 1998). Tannins, alkaloids, steroids, anthraquinone glycosides, and flavonoids are found in mangrove plants (Patra et al., 2009). Extracts of mangrove plants have been shown to have biological activity against a variety of human, animal, and plant pathogens, including the Human Immunodeficiency Virus (HIV) (Premanathan et al. 1999b), Semliki Forest virus (Premanathan et al. 1995), Newcastle disease virus (Premanathan et al. 1992), and cancer (Tosa et al. 1997). Chemical compounds and bioactive compounds found in mangrove plants are antimicrobial (Choudhury et al., 2005; Agoramoorthy et al., 2007; Sivaperumal et al. 2010; Abeysinghe 2012; Dhayanithi et al. 2012), anticancer (Prabhu and Guruvayoorappan 2011), antioxidants (Banerjee et al. 2008). Additionally, mangrove plants with bioactive compounds are used as food or functional food (Hardoko et al., 2015).

Rhizophora mucronata contains a diverse range of chemical constituents, including sugar, tannins, saponins, alkaloids, flavonoids, steroids, terpenoids, glycosides, and phenolics (Nurdiani et al. 2012; Revathi et al. 2014; Sreedhar and Christy 2015). According to the phytochemical screening test of *R. mucronata*, the alkaloid rhizophorine is a significant component of the plant's leaf (Bandaranayake 2002). In addition, the extract of *R. mucronata* bark had the strongest inhibitory action against α-glucosidase, with an IC_{50} of 0.08±1.82 μg/mL, suggesting that it may be a contender for anti-diabetic therapy (Lawag et al. 2012).

The various portions of *R. mucronata* cure various human illnesses, including angina, dysentery, and hematuria. The existing scientific literature indicates that evidence of the tree's numerous uses dates back to the 17^{th} century (Joel and Bhimba 2010). *Rhizophora mucronata* is a widespread mangrove plant that has been utilized as ethnomedicine from prehistoric times (Andikhari et al., 2016). *Rhizophora mucronata* has traditionally been used to treat bleeding, diarrhea, diabetes, angina, bleeding, and inflammation. It has been established that it has anti-HIV action (Kirtikar and Basu 1987; Bandarnayake 2002; Premanathanet al. 1999b).

The present data indicate that *R. mucronata* fresh leaf extract is not hazardous, as no significant alterations in hematological or biochemical parameters were found. Thus, *R. mucronata* fresh leaves extract is regarded as safe for long-term treatment of human illnesses at standard therapeutic concentrations (Babuselvam et al., 2012). Additionally, *R. mucronata* leaf extract has been traditionally used to treat diarrhea (Puspitasar et al., 2012) and as a blood sugar-lowering agent (Gaffar et al., 2011). The root extract of *R. mucronata* acts as an antioxidant and can repair liver damage caused by CCl_4 hepatotoxins in experimental rats (Ravikumar and Gnanadesigan 2012).

Rhizophora mucronata exhibits a diverse range of pharmacological activities, including antioxidant, anti-inflammatory, antibacterial, antimicrobial, antidiabetic, analgesic, anti-HIV, and anti-cholinesterase activity. Traditional usage of medicinal herbs is associated with no adverse effects, toxicity, and increased efficacy and safety. Significant biological activity investigated in medicinal plant extracts include antioxidant, anti-inflammatory, anti-diabetic, and antiviral properties (Andikhari et al., 2016; Chakraborty and Raola 2017; Aljaghthmi et al. 2018). This compound has antibacterial, antimalaria, antiviral, and antioxidant properties (Abidin et al., 2013; Purwaningsih et al. 2013; Yogananth et al. 2015). The bark of the plant is used as an astringent. Historically, it was used to treat diabetes, diarrhea, nausea, haematuria, hemorrhages, and angina (Khare 2007).

The following is the potential of *R. mucronata* as an antioxidant, anti-diabetic, antimicrobial, anticancer, anti-inflammatory, and analgesic.

ANTIOXIDANT

Numerous researches have been conducted to determine the antioxidant effects of medicinal plants that are high in phenolic compounds (Krings and Berger 2001). As mentioned in Ali et al. (2008), natural antioxidants are mainly derived from plants in the form of phenolic chemicals such as flavonoids, phenolic acids, and tocopherols. Plant phenolics are a large class of chemicals that act as primary antioxidants or scavengers of free radicals (Potterat 1997). Similarly, terpenoids and vitamins work as metabolic regulators and antioxidants (Soetan 2008). Plant polyphenols are antioxidants with redox characteristics that operate as reductants, hydrogen donors, and singlet oxygen quenchers (Middleton et al., 2000).

Rhizophora mucronata functions as an antioxidant because there are secondary metabolites, namely tannins, phenolics, chlorophyll, carotenoids, and alkaloids (Babuselvam et al., 2012; Abidin et al. 2013). Antioxidant activity of plant extracts was based on species, extraction method, season, and sampling area (Budhiyanti et al., 2012). Chakraborty and Raola (2017) determined the IC_{50} value for the crude chloroform leaf extract using the DPPH test to be 1.38±0.03 mg/mL, while Suganthy and Devi (2016) determined the IC_{50} value for the crude chloroform leaf extract using the DPPH assay to be 47.39±0.43 g/mL. Interestingly, Hardoko et al. (2014) discovered that the fruit's ripe flour includes 7.50 % soluble dietary fiber and 38.60 % insoluble dietary fiber. The methanol extract of *R. mucronata* bark was an antioxidant with an IC_{50} value of 438.8349 ppm (Mahmiah et al., 2016).

The most potent antioxidant is a methanol extract of *R. mucronata* leaves. This bodes well for utilizing *R. mucronata* as a source of potent antioxidants (Vigneswaran et al., 2018). The n-hexane leaf extract had an IC_{50} value of 151.13 ppm, while the ethyl acetate extract showed an IC_{50} value of 184.78 ppm, and the methanol extract showed an IC_{50} value of 113.41 ppm. This indicates that methanol extract has the strongest antioxidant activity than ethyl acetate and n-hexane extracts. This is because the total content of phenolics, chlorophyll a, chlorophyll b, and carotenoids are higher than the n-hexane extract and methanol extract (Kuppusamy et al., 2015). These compounds can reduce the activity of free radicals, react directly with free radicals, and turn them into new free radicals that are less reactive and less dangerous (Amic et al., 2003).

Methanol extracts of *R. mucronata* leaves had significantly higher antioxidant activity than other extracts (petroleum ether, benzene, ethyl acetate, and ethanol). The concentration of methanol extract of *R. mucronata* leaves required for 50% inhibition (IC_{50}) was 36.17 mg/ml. The extract effectively scavenges free radicals but to a smaller amount than normal ascorbic acid (IC_{50} = 31.04 mg/mL). The IC_{50} value of methanol extract of *R. mucronata* leaves was determined to be 36.47 mg/mL for superoxide radicals and 32.14 mg/ml for ascorbic acid, respectively (Vigneswaran et al. 2018). At low concentrations, the ethanol extract demonstrated excellent reducing power. However, its reducing power was smaller than that of the ethanol extract at greater doses (Vigneswaran et al., 2018).

The leaves of the *R. mucronata* mangrove plant contained more phenolic chemicals than the stem bark and root extracts (Banerjee et al., 2008). The leaves may contain natural antioxidants that may be beneficial in preventing or slowing the progression of aging and age-related oxidative stress-related degenerative illnesses (Palaniyandi et al. 2020). Numerous synthetic medications protect against oxidative stress, but they also have undesirable side effects (Suganya et al., 2017). The hydromethanolic extract of *R. mucronata* leaves included all key phytoconstituents, including alkaloids, phenolics, flavonoids, triterpenoids, steroids, glycosides, saponins, and tannins. It has long been established that phenolics and flavonoids play an important role in diabetes management (Bailey and Day 1989; Bravo 1998; Agoramoorthy et al. 2008). Gallic acid, quercetin, and coumarin found in the leaves of *R. mucronata* provide significant pharmacological evidence for the plant's antioxidant and radical scavenging activities (Bravo 1998; Rohini and Das 2011; Thakker et al. 2011).

ANTI-DIABETICS

Diverse plant parts of *R. mucronata* contain a diverse array of phytochemicals, including condensed tannins, polyphenols, lipids, inositol, gibberellins, alkaloids, tannins, and proteins (Anjaneyulu and Rao 2003; Ravindran et al. 2005; Nurdiani et al. 2012; Revathi et al. 2014; Chakraborty and Raola 2017). According to Patra et al. (2009) and Odom et al. (2013), a mixture of many fruits containing alkaloid, tannin, saponin, and flavonoid has hypoglycemic (anti-diabetic) efficacy against rat-induced alloxan. Aljaghthmi et al. (2018) show that the bioactive chemicals found in *R. mucronata* reduce blood sugar levels and stimulate insulin production. However, no additional investigations on ripe flour have been undertaken to verify or validate the findings of Hardoko et al. (2014). According to Alikunhi et al. (2012), the anti-diabetic activities of *R. mucronata* stem from the presence of an insulin-like protein in the leaves.

Alkaloids of *R. mucronata* operate as an effective anti-hyperglycaemic and anti-hyperlipidemic drug in insulin-dependent and non-insulin-dependent diabetic patients (Gurudeeban et al., 2016).

Thus, it is reasonable to hypothesize that DCM-F and glibenclamide may augment insulin release or mimic insulin-like action (Gurudeeban et al., 2016). T2DM rats treated with the dichloromethane fraction of *R. mucronata* have considerably lower total cholesterol and triglyceride levels while increasing high-density lipoprotein cholesterol. It elucidates the anti-diabetic and anti-hyperlipidemic functional context of *R. mucronata* (Gurudeeban et al., 2016). However, the complex pathology of non-insulin-dependent diabetes in humans remains unknown. Nicotinamide, a water-soluble vitamin, is beneficial in delaying the onset of type 1 diabetes in non-obese mice (Azooz et al., 2013). Nicotinamide treatment of pre-diabetics results in a person with diabetes with stable metabolic abnormalities and decreased pancreatic insulin (Szkudelska et al., 2014). On the other hand, the extract's hypoglycemic action in rats suggests that it inhibits intestinal glucose absorption and stimulates the glucagon-like peptide (GLP-1), a glucose-dependent insulin secretagogue (Goke 1993).

The ripe *R. mucronata* fruit flour has hypoglycaemic properties and may be functional diabetic food. The effectiveness of ripe *R. mucronata* fruit flour in lowering blood glucose levels is due to its high fiber content (46.10%) and bioactive anti-diabetic properties (Hardoko et al., 2015). Meyer et al. (2000) reported that whole-grain dietary fiber is protective against diabetes. Consumption of soluble dietary fiber is more protective than consumption of insoluble dietary fiber (Jenkins et al., 2000). According to Chandalia et al. (2000), consuming the required amount of dietary fiber, particularly soluble fiber, improves blood glucose management, decreases hyperinsulinemia, and decreases plasma lipid concentrations in patients with type 2 diabetes. According to Dianitami (2009), dietary fiber has physiological effects such as reducing transit time, slowing gastric emptying, prolonging satiety, restoring normal beneficial intestinal flora, increasing pancreatic secretion, increasing short-chain fatty acid production, serum lipid levels, and bile acid-binding. Fiber delays stomach emptying, preventing blood glucose levels from rising. Food is absorbed into the small intestine, and blood glucose levels gradually rise.

Rhizophora leaf powder is a strong anti-diabetic agent due to the presence of an insulin-like protein. Additionally, it was comparable to glibenclamide (Alikunhi et al., 2012). Further, by evaluating the average blood sugar level, the effect of mangrove fruit flour as an antidiabetic can be compared to that of the medicine glibenclamide (positive control). According to Davey (2005) and Katzung (2007), glibenclamide is a member of the sulfonylurea class of drugs that enhance pancreatic beta-cell insulin secretion.

According to Hardoko et al. (2015), the larger the wheat doses, the lower the rats' blood glucose levels. The LSD test revealed that oral administration of ripe *R. mucronata* fruit flour at doses of 1,000 mg/day/head, 1,500 mg/day/head, and 2,000 mg/day/head had no significant impact when compared to the positive control (glibenclamide 0.09 mg/day/200 g body weight) ($p<0.05$). Furthermore, ripe *R. mucronata* fruit flour 1000 mg/day/head significantly lowered blood glucose levels in rats treated with alloxan, similar to glibenclamide medication. By slowing the stomach emptying, dietary fiber lowers blood glucose levels and prevents increased blood glucose levels (Dianitami 2009). The extract of *R. mucronata* leaves and glibenclamide effectively maintained the bodyweight of Streptozotocin-induced diabetic rats, although the diabetic rats' bodyweight decreased (Pandey et al., 2014). The in vivo antidiabetic investigation demonstrated a decrease in blood glucose levels, indicating that the ripe flour of *R. mucronata* is an excellent functional diet for diabetic patients (Hardoko et al. (, 2015).

Numerous scientific publications support its potential use as an anti-diabetic medication; however, additional research is required (Ramanathan et al., 2008; Ray et al., 2014). Additionally, the chemical identification of *R. mucronata* has been determined, as well as the presence of secolabdane diterpenoid (rhizophorin A) (Anjaneyulu and Rao 2001), phomoxanthone (Shiono et al. 2013), lupeol, beta-sitosterol (Rohini and Das 2011), gallic acid, coumarin, quercetin (Sur et al. 2015) and tannins (Joel and Bhimba 2010).

ANTIMICROBIALS

Antibacterial

Rhizophora mucronata appears to possess a broad antibacterial spectrum of activity. Among the five solvents evaluated (ethanol, petroleum ether, acetone, methanol, and ethyl acetate), it was concluded that ethyl acetate was the best solvent for isolating bioactive secondary metabolites. *R. mucronata* foliar crude ethyl acetate extracts (50 µL) exhibited significant antibacterial activity with inhibition zones, particularly against *Escherichia coli*, *Staphylococcus aureus*, *Proteus vulgaris*, *Pseudomonas fluorescens*, and *Salmonella typhi* (Joel and Bhimba 2010). Maximum inhibitory action was observed using a methanolic leaf extract of Rhizophora mucronata against *S. aureus* (20 mm diameter) (Ravikumar et al., 2009). *Rhizophora mucronata* had a more significant inhibitory effect on bacterial and fungal infections (Ravikumar et al., 2009). The n-hexane and chloroform extracts of *R. mucronata* leaves were found to have a significant inhibitory effect on *Bacillus subtilis*, *S. aureus*, *Candida albicans*, *Aspergillus fumigatus*, *Aspergillus niger*, and a moderate inhibitory effect on *Pseudomonas aeruginosa* and *P. vulgaris*. The remaining extracts had moderate activity (Kusuma et al., 2011).

The leaves of *R. mucronata* displayed a high inhibitory effect on *B. subtilis*, *S. aureus*, *C. albicans*, *A. fumigatus*, and *A. niger*, and a moderate inhibitory effect on *P. aeruginosa* and *P. vulgaris*. Only the leaves contain various phytochemical substances, even though the tannin and saponin content is negligible. *Rhizophora mucronata* extracts exhibited antibacterial efficacy against *S. aureus* and *E. coli*. It's worth noting that nearly all components demonstrated broad-spectrum antibacterial action. It possesses antibacterial (Chandrasekaran et al. 2009), antiviral (Premanathan et al. 1999a), antifungal (Bose and Bose 2008), larvicidal (Thangam and Kathiresan 1989), and antioxidant properties (Babu et al. 2001).

Chou et al. (1977), Padmakumar (1988), and Akalanka et al. (2002) also observed that *R. mucronata* leaf and bark extracts included antimicrobial components active against a variety of human bacterial infections. The highest antibacterial activity is thought to be due to the presence of phenols such as tannins (Ravikumar and Kathiresan 1993), coumarin and their glycosides, anthraquinones and their glycosides, naphthoquinones, flavones and related flavonoids, and polysaccharides (Trease and Evans 1997); and sulfated compounds such as brugierol, isobrugierol, and 4-hydroxy-1,2m dithiolane (Kokpal and Chittawong 1987) in mangrove halophytes. Phenolic compounds are typically water-soluble, as they are frequently found in combination with sugar as glycosides and are usually found in the cell vacuole (Glossary of Indian medicinal Plants 1992). Flavonoids are hydroxylated phenolic compounds that plants produce in response to microbial infection and have been shown in vitro to be antibacterial agents against a wide variety of microorganisms (Wang et al., 2009).

Antifungal

Rhizophora mucronata mangrove leaf extracts revealed much-increased activity (20 mm) against *Streptococcus lactis*. The average zone of inhibition for bacterial pathogens indicates that Gram-positive bacteria are more vulnerable than Gram-negative bacteria. Compared to leaf extracts, *R. mucronata* bark extracts exhibited the highest inhibitory action (9 mm) against *Bacillus megaterium* (69.2 activity index) and *S. lactis*, respectively. The leaf extract of *R. mucronata* inhibits all bacterial isolates in a broad spectrum. *Rhizophora mucronata* had the most significant inhibitory activity (7 mm) against the fungus *Metarrhizum anisopliae* (Ravikumar et al., 2009). The ethanol bark extracts showed significant antiviral efficacy against Newcastle disease, vaccinia, encephalomyocarditis, and Forest viruses. Additionally, the ethanol flower extract demonstrated beneficial effects for human health (Premanathan et al. 1992).

Antiviral

Additionally, it has been scientifically demonstrated to possess antiviral properties (Padmakumar and Ayyakkannu 1997). The bark of *R. mucronata* contained an active material composed of acid polysaccharides that inhibits the HIV binding mechanism within cells (Premanathan et al. 1999b). Acid polysaccharides (sulfate polysaccharides) inhibit the binding process by utilizing the electrostatic interaction between the negative and positive charges (Battulga et al., 2019). *Rhizophora mucronata* bark was shown to be the most promising antiviral agent (Premanathan et al. 1992). The honey reported to be poisonous is extracted from the flowers (Khare 2007).

ANTICANCER

Lung cancer, blood cancer, prostate cancer, breast cancer, cervical cancer, and bone cancer are the most common types of cancer that cause death worldwide (Islam and Rahi 2018). *Rhizophora mucronata* is a plant that is frequently used in traditional medicine to treat a variety of conditions, including cancer. Different solvent extracts of *R. mucronata* leaves (e.g., methanol, ethanol, chloroform) revealed the presence of several bioactive components associated with antioxidant and free radical scavenging activities (Palaniyandi et al. 2020). Numerous components of *R. mucronata* are used to treat a variety of disorders. Mangroves are salt-tolerant plants native to the world's tropical and subtropical intertidal zones. Regardless of their monetary value, mangroves are employed in folk medicine. The plant possesses an acceptable amount of antioxidant and thrombolytic activity, as well as a modest level of cytotoxic activity (Sharmin et al., 2018). *Rhizophora mucronata* contains a high concentration of phytochemicals, including triterpenoids, lipids, alkaloids, and tannins (Sadeer et al., 2019). Additionally, it has the potential to influence cell cycle distribution and drastically reduce cyclin D1 expression (Zhou et al., 2017). The n-hexane: chloroform fraction from the methanolic extract of the bark of *R. mucronata* has successfully had cytotoxic activity on myeloma cancer cells (Harwoko and Utami 2010).

ANTI-INFLAMMATION

Rhizophora mucronata plants have the potential to be a significant source of modern medications for a variety of life-threatening illnesses. Keeping this in mind, we attempted to study the in vitro anti-inflammatory capabilities of several *R. mucronata* plant parts (Kaur et al., 2018). The anti-inflammatory efficacy of the extract was investigated and its potential to suppress protein denaturation. At various doses, it was efficient in suppressing heat-induced albumin denaturation. At stilt root extract, maximum inhibition was observed, and the IC_{50} value was determined to be 296.262 µg/mL. At a 500 µg/mL concentration of aspirin, a standard anti-inflammatory medicine, the maximal inhibition was 268.348%. These findings support the idea that their anti-inflammatory activity is partly mediated by membrane stability. This extract may perhaps stop neutrophils from releasing their lysosomal content at the site of inflammation. These neutrophil lysosomal contents include bactericidal enzymes and proteases, which, when released into the extracellular space, cause more tissue inflammation and injury (Chou 1997).

At concentrations ranging from 100 to 500 µg/mL, the extract protects human erythrocyte membranes from lysis caused by hypotonic solution. At a 500 µg/mL concentration, the extract prevented 327.91% of RBC hemolysis, compared to 285.01% caused by Aspirin at the same concentration. Because the membranes of human red blood cells are comparable to those of lysosomes, the inhibition of hypotonicity-induced HRBC membrane lysis was used to assess the anti-inflammatory effects of medicines. The maximal inhibitory concentrations obtained revealed that methanolic extracts of the root and leaves of *R. mucronata* could strongly and dose-dependently prevent HRBC hemolysis. The study's findings indicate that an extract of *R. mucronata* exhibited anti-inflammatory activity in vitro. However, the rigorous investigation should characterize extracts as having significantly greater activity, searching for an active candidate or chemical molecule primarily responsible for this activity (Kaur et al., 2018).

The methanolic extract of the *R. mucronata* mangrove plant (leaves, bark, and stilt root) exhibits good membrane stability, implying anti-inflammatory activity. Given that the methanolic extract of leaves, bark, and stilt root of *R. mucronata* possesses significant anti-inflammatory properties, further laboratory investigation and chemical isolation of these plant parts (leaves, bark, and stilt root) may confirm an effective drug molecule in pharmacologic terms, in both types of pharmaceutical arenas (Kaur et al. 2018).

ANALGESICS

Pain is a prevalent noxious phenomenon that contributes to one of the most pervasive healthcare problems and results in various complex physical and psychological disorders (Zareba 2009). Unfortunately, pain therapy with a variety of analgesics provides only symptomatic alleviation. Analgesics are a family of medications that can be broadly categorized into centrally acting analgesics and peripherally acting analgesics. While non-steroidal anti-inflammatory drugs (NSAIDs), steroids, and opiates are currently the most widely prescribed and most commonly used over-the-counter analgesics, they are associated with several adverse effects, including respiratory depression, addiction, and abuse potential in the case of central analgesics and gastric ulceration, gastrointestinal bleeding in the case of NSAIDs (Barua et al. 2011).

Additionally, non-reducing sugars, flavonoids, polyphenols, glycosides, terpenoids, Quercetin, and a significant amount of tannins were detected in the ethanolic extract of *R. mucronata* leaves. In a dose-dependent way, the ethanolic extract demonstrated a considerable analgesic effect in the acetic acid-induced writhing response in mice (Andikhari et al., 2016). Acetic acid injected intraperitoneally elicited visceral pain in the abdomen, triggering a localized inflammatory response that increased pain mediators such as prostaglandins, particularly PGE2, PGF2α, and lipoxygenase-mediated eicosanoids in the peritoneal fluid, resulting in abdominal constriction or writhing in mice (Derardt et al. 1980; Dhara et al. 2000). This model is well-established for assessing peripheral analgesic effectiveness; analgesic drugs act on visceral receptors, suppress pain mediators, and decrease the number of writhes. RME significantly reduced the writhing reaction; thus, it may be concluded that the leaf extract had peripheral analgesic efficacy (Andikhari et al., 2016).

The Eddy's hot plate and immersion of the mice’s tail in hot water are two approved procedures for determining the efficacy of centrally acting analgesics. Thermal stimuli elicit a non-inflammatory, central nociceptive response(D'Amour and Smith 1941; Sewell and Spencer 1976). In the hot plate model, the extract of *R. mucronata* leaves marginally enhanced the reaction time. Additionally, the test sample had a very low response when using the tail immersion procedure and administering the 200 mg/kg body weight dose (orally). As a result, the ethanolic extracts exhibit a lesser degree of central analgesic activity (Andikhari et al., 2016).

The ethanolic extract of *R. mucronata* bark was found to have a significant analgesic effect in doses of 250 mg/kg and 500 mg/kg bodyweight (Howlader et al., 2013). It is generally established that opioid or narcotic analgesics inhibit both peripheral and central pain, whereas non-steroidal anti-inflammatory medications (NSAIDs) inhibit mainly peripheral pain (Pal et al. 1999). The ethanolic extract of *R. mucronata* leaves decreased the acetic acid-induced writhing response in mice dosage dependently but was ineffective in the other two analgesic models. As a result, the extract demonstrated characteristics similar to NSAIDs (Andikhari et al., 2016).

It can be concluded that the ethanolic extract of *R. mucronata* (Sunderban mangrove) leaves possesses potential peripheral analgesic activity, which may be mediated peripherally. This could be because of its phytoconstituents, such as flavonoids, polyphenols, and tannins. Additional research is being conducted to confirm the analgesic efficacy and justify its therapeutic application. In the current investigation, an ethanolic extract of *R. mucronata* leaves was safe in mice at doses up to 2 mg/kg bodyweight (orally). The section at 200 mg/kg bodyweight (orally) inhibited the writhing reaction caused by acetic acid in mice. While the hot plate method extended the delay duration relative to the control by a small amount, the tail immersion test revealed no significant result. The present investigation established that the ethanolic extract of *R. mucronata* (Sunderban mangrove) leaves is high in tannin, flavonoids, and polyphenols and may exert peripheral and modest central analgesic effects (Andikhari et al. 2016).

CONCLUDING REMARKS

Rhizophora mucronata is traditionally used as a source of wood (timber) for building materials, boats and firewood and charcoal, tanning and dying, as well as to treat diseases such as diarrhea. Flour from ripe fruit can be a safe source of carbohydrates for people with diabetes, hepatitis, ulcers, etc. Recent studies have shown that various leaf and bark extracts of *R. mucronata* contain tannins, alkaloids, flavonoids, terpenoids, etc. Recent research has shown that this plant extract acts as an antioxidant, anti-diabetic, antimicrobial (anti-viral, anti-fungal, anti-bacterial), anti-cancer, anti-inflammatory, and analgesic. More research is needed to ground the drug's potential into actual drugs and the possibility of plant breeding to obtain high-quality cultivars of *R. mucronata* as a source of medicine and food.

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