

[HTTPS://DOI.ORG/10.48047/AFJBS.6.SI4.2024.6060-6077](https://doi.org/10.48047/afjbs.6.si4.2024.6060-6077)



## African Journal of Biological Sciences



# A Review On Potential Bioactive Compounds For Therapeutic Alternatives From Mangrove Species

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Volume 6, Issue Si4, Aug 2024

Received: 10, Jan 2024

Accepted: 03, Aug 2024

Published: 10, Aug 2024

doi: [10.48047/AFJBS.6.Si4.2024.6060-6077](https://doi.org/10.48047/afjbs.6.si4.2024.6060-6077)

### Abstract

Emerging drug resistance among pathogens is a growing threat to mankind. The rise of MDR strains of bacteria has generated a great challenge to treat infections caused by bacteria with the available antibiotics. For ages, the vast floral species of the mangrove ecosystem have been used for medicinal importance as they represent a valuable source of novel drug compounds although the chemistry and bioactivity of flora remain partly uninvestigated. Recently plant-derived therapeutic agents have gained an immense importance in the field of medical sciences for treating several health disorders and chronic diseases. An extensive literature is available on phytochemical profiling of mangroves but in this review an attempt was made to focus on latest findings of different mangrove species which have been reported for high phytochemical constituents with other biological activity.

**Keywords**— Drug resistance, Bioactive potentialities, Mangrove extracts, GC-MS analysis

## I. INTRODUCTION

The discovery of antibiotics has created a turning point in medical interventions to treat pathogenic infections, but unfortunately, each discovery was consistently followed by the emergence of drug resistance. Today, research is active in finding alternative therapy for combating multidrug-resistant pathogens. To support and to guide the efforts, the WHO has published a list of the most dangerous bacteria that are resistant to current treatments and requires the development of new antibiotics for combating the resistance. Among them are various Gram-positive bacteria that are responsible for serious healthcare and community-associated infections. Methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus faecium*, and drug-resistant *Streptococcus pneumoniae* are of particular concern. The resistance of bacteria is an evolving phenomenon due to genetic mutations and/or acquired genomes. Thus, antimicrobial resistance demands continuous efforts to create strategies to combat this problem and optimize the over usage of antibiotics. The World Health Organization (WHO) published a global priority pathogens list and categorized them as critical, high, and medium antibiotic-resistant bacteria that need to be addressed urgently through research and development of new alternative drug treatments.

Serious effects like gastrointestinal abscesses, blockages and haemorrhages have been observed with the usage of non-steroidal and synthetic anti-inflammatory drugs (NSAIDs). On the contrary, Indian medicine has many traditional herbal extracts of plants like *Andrographis paniculata* which are being safely used for treating hepatitis. Likewise chronic environmental stress and genetic disorders induced lethal diseases like Parkinson's, cardiovascular, Alzheimer's, cancer, etc are due to hyper-accumulation of free radicals.

Mangroves have always been captured the attention of scientists and still confounds the research community. They are categorised as salt tolerant ecosystem that is found mainly in tropical and subtropical intertidal regions of the world (Bandaranayake, 2002). Due to the unique habitat of mangroves, their ability to grow in the intertidal zone develops different physio-chemical processes to survive and reproduce. Hence they develop a very special ecosystem of microbial flora that trigger the production of novel compounds with variant biological activity that can be used as therapeutic drugs in the future. (Saleh Amer et al., 2020).

Traditional use of mangrove plants in ethno-medicine is continuing till today and extracts from mangrove species have proved to have strong inhibitory activity against the plant, animal, and human pathogens (Saranraj and Sujitha, 2015). Mangrove plants are extensively studied for antimicrobial components for pharmaceutical importance. Traditionally, *R. racemosa* bark is used to treat boils and fungal infections. An infusion of its leaf and bark is used to treat diarrhoea, dysentery, fever, malaria and leprosy (C.N. Duke, J.A. Allen et al., 2006)

New age drug discovery is based on natural product mainly plant products as they are cheaper alternative and mostly effective. Essential phytochemicals present in medicinal plants as secondary metabolites serve as precursors for synthesis of useful therapeutic drug compounds. They include alkaloids, flavonoids, tannins and phenolic compounds and derive the medicinal value to the plant species. These metabolites have been identified from different mangroves and mangrove associates belong to categories like alkaloids, flavonoids, carbohydrates, carotenoids, aliphatic alcohols, amino acids, hydrocarbons, fatty acids, phenolic compounds, tannins, saponins, terpenes, and related compounds (Bandaranayake, 2002). According to Wu et al. 2008, 349 metabolites have been isolated from mangrove species out of which 200 metabolites are exclusively reported from true mangroves. For supporting life processes, biomolecules such as amino acids, carbohydrates, and proteins, that are the product of primary metabolism, are essential for live growth, and products of secondary metabolism like alkaloids, flavonoids, phenolics, steroids, terpenoids, etc., have pharmacological, toxicological and ecological importance (Bandaranayake, 2002). Therefore, DPPH and FRAP assay are very reliable methods to measure anti-oxidative capacity of natural organic molecules.

An extensive literature reported on mangroves for their bioactivities like Latex of *Excoecaria agallocha* has a biocidal effect on marine organisms and phytoplanktons (Reddy et al. 1991; Bandaranayake, 2002). Different plant extracts from Rhizophoraceae mangroves have been shown to be effective against different human pathogens [Sravya et al.,]. A polysaccharide constituent obtained from the leaf of *Rhizophora apiculata* has shown toxicity against HIV-1/HIV-2 or SIV viral strains causing AIDS under controlled conditions [Mariappan Premanathan et al.,].

Over 200 bioactive metabolites have been isolated from true mangroves which contain antibacterial and antifungal properties (Bose and Bose, 2008; Wu et al. 2008 and Chandrasekaran et al. 2009). They contain huge number of phytochemicals that are beneficial for human body acts as natural antioxidants by protecting from free radical damage. Antioxidants control and reduce the damage by inhibiting the oxidation caused by reactive oxygen species (ROS). ROS plays an important role in human physiological processes (D'Autr'eaux and Toledano, 2007). Proper extraction methods play a major role in qualitative and quantitative plant based bioactive compound research. Several research studies and traditional knowledge among the coastal population reveals an effective anti-inflammatory, antiviral, antimicrobial, anticancer, anti-diabetes, antifungal and insecticidal properties of mangrove plants (Habib et al., 2018; Sachithanandam et al., 2021). Study on *A. officinalis* determined that ethyl acetate extract of *A. officinalis* has numerous natural molecules that could be useful for pharmaceutical applications like anticancer, antioxidant, antimicrobial, anti-inflammatory.

#### **Bioactive potentiality of mangroves:**

Being ecologically and biochemically unique, mangroves produce a wide array of natural compounds. Khafagi et al. 2003 studied the presence of tannins, flavonoids, sterols, glycosides, and natural acids in the ethanol concentrate of the shoot framework of *Avicennia marina*. The methanolic concentrate of *Avicennia marina* indicated the optimum presence of pentanoic acid, decanoic acid, diethylhydroxylamine,  $\alpha$ -amyrin as active compounds in *Ceriops decandra*. Plant tissues of bark, root and leaves of three different mangrove species were screened qualitatively and quantitatively for total phytochemical analysis. Presence of highly polar bioactive compounds (alkaloids, saponins, tannins, flavonoids and reducing sugar) were reported in them. *Avicennia africana* showed the highest concentrations of alkaloid and saponin. Leaves showed the highest concentration of alkaloids whereas barks showed the highest concentration of saponins. *Rhizophora racemosa* had the highest mean concentrations of flavonoids and tannins, leaves had the highest concentration of flavonoids whereas the stem contained the highest concentration of tannins. The GC-MS results of active column fraction of *A. officinalis* revealed that the active principals were a mixture of hydroxyl-4 methoxy benzoic acid, di ethyl phthalate, oleic acid. (Valentin Bhimba B et al. 2010) In their study, crude extracts failed to exhibit desired response, where as the fractions had broad spectrum activity against few test organism. Study on *Landolphia owerrience* has revealed that phytochemical compounds like glycoside, saponin, tannins, flavonoids, terpenoids, alkaloids have antimicrobial activity *Nypa fruticans* showed the highest mean concentration of reducing sugars (Edu et al. 2015)

#### **Antimicrobial activity:**

Throughout the world, comprehensive research studies on mangroves reported for their antimicrobial properties as they possess a strong bactericidal property against numerous microorganisms. As these plants are rich in secondary metabolites, they have been found in vitro to have antimicrobial properties. The antibacterial potential of the methanolic extract of *Excoecaria agallocha* was reported by Chandrasekaran et al. (2009). Abeyasinghe et al. (2006) reported the promising antibacterial activity of *Avicennia marina*. Alamgir et al. (2007) studies on methanolic extract of *Xylocarpus granatum* suggested the antimicrobial activity is due to presence of triterpenes. Moderate antibacterial activity by *Suada maritima* is due to presence of phenolic compounds like tannins (Patra et al. 2011b). Presence of glycosides, saponins, tannins, flavonoids, alkaloids, terpenoids may influence the antibacterial activity of *Avicennia officinalis* (Bhimba et al.

2010). Presence of flavonoids as an active constituent in *Lumnitzera racemosa* extract can be attributed for its antibacterial activity (D'Souza et al. 2010). Studies of Kumar et al. (2011) reported best antifungal activity in Chloroform and methanolic extracts of *Avicennia marina*, *Excoecaria agallocha*, *Lumnitzera racemosa*, *Derris trifoliata*, *Bruguiera gymnorrhiza*, *Ceriops decandra* and *Acanthus ilicifolius* against the *Aspergillus niger*, *Rhizopus oryzae*, *Candida albicans* and *Saccharomyces cerevisiae*. A study reported by H.Jahnmanchi & Raju et al.(2017) the purified ethyl acetate fraction using the microwave extraction method of *Aegiceras corniculatum* have shown a very potent inhibition of *Mycobacterium tuberculosis* in the microgram range with negligible cytotoxicity against mammalian cells.

In a similar study, Das et al., (2018), revealed that *A. officinalis* bark and leaves ethanolic extract exhibited antimicrobial activity against *B. subtilis*, *E. coli* and *P. aeruginosa*. Das (2020) also reported promising antibacterial activity due to the presence of terpenoids, phenolics and alkaloids. Thus, pharmacological screening of natural products can be a source of innumerable bioactive therapeutic agents. The antibacterial activity of crude extract of *A. officinalis* leaves showed strong activity against five different test microorganisms *S. mutans*, *K. pneumkiae*, *P. aeruginosa*, *B. subtilis* and *E. aerogenes*. (P. Lalitha, A. Parthiban 2021)

The antimicrobial effectiveness of plant extracts also depends upon parts of the plant used and the solvent utilized for extraction Okla et al. (2021). The investigation of Muhammad Sohaib, Fahad N.I. et al 2022) in a comparative study on antimicrobial, antioxidant, and cytotoxic activities of *A. marina*, *P. australis*, and *M. oleifera* based ethanolic plant extracts has depicted that ethanol as a solvent for the extraction of phyto-constituents can play an important role in *Moringa oleifera* antimicrobial and antioxidant properties. *Moringa oleifera* based ethanolic extract was found maximum cytotoxic potential against HepG2 cell lines as indicating that phenolic ingredients playing a major role in cytotoxic activities because Etanol extract contains maximum phenolic contents comparatively. The leaf extracts of *R. apiculata* have exhibited significant antibacterial activity against *P.aeruginosa*, *A.hydrophila*, *S. aureus* and *B. subtilis* The highest zone of inhibition was exhibited by the aqueous extract against all the strains, disclosed that the phytocompounds in the aqueous are highly potent to act against the bacterial strains. (Sravya M.V.N., Sampath Kumar 2023).

Several research groups screened different species of mangrove plants *Lumnitzera littoral*, *Avicennia*, *Rhizophora apiculat*, *Bruguiera gymnorrhiza*, *Heritiera littoralis*, *Suaeda nudiflora*, *Lumnitzera racemosa*, *Ipomoea tuba*, *Avicennia alba*, *Rhizophora mucronata*, *Sonneratia alba* and *Exoecaria agallocha*, *Avicennia Alba Blume*, *Acanthus ilicifolius* [73 to 80] for their antioxidant and antimicrobial properties in order to identify potent new molecules with therapeutic value against many Gram positive and Gram negative multi drug resistance human pathogens

#### **Antioxidant Property:**

Free radicals and oxidative injuries are a consequence of various diseases in humans. Several free radicals like hydroxyl (HO·), per-hydroxyl (HO<sub>2</sub>·), superoxide (O<sub>2</sub>·-), nitric oxide (NO·) are produced in plants and human body as a result of on-going physiological processes. Environmental stresses like high-light intensity, extreme temperatures, drought condition, floods acts as trigerring factor for the production of ROS in plants inducing oxidative stress (Thatoi et al. 2014; Jithesh et al. 2006). Krishnamoorthy et al. (2011) studied the antioxidant capacities of two

Indian mangrove species *Bruguiera cylindrica* and *Ceriops decandra*. Patra et al. 2009, studies disclosed that *Excoecaria agallocha* possesses tremendous antioxidant properties that are tested for DPPH radical scavenging, reducing power and H<sub>2</sub>O<sub>2</sub> radical scavenging property. Previous Studies also revealed the Bark extract of *Rhizophora apiculata* have free radical scavenging activity.

Investigations of Banerjee et al. (2008) on leaf, stem, bark and root extracts of six mangroves species and four mangrove associates, have found high phenolic content (GAE), strong reducing ability and anti-radical activity. Another study on Stem and bark extracts of *Ceriops decandra* showed the best possible result. In an another study by Malik et al. (2017) showed that *Bruguiera sexangular* extract with polar solvents showed high flavonoid and highest phenolic contents. Also found that the methanol extract of *Lumnitzera racemosa* exhibit most active radical scavenger activity.

The studies of G. Eswaraiyah et al. 2020, reported the maximum scavenger activity, 95.62% was found in the leaf exact of *Lumnitzera racemosa* at concentration of 200 mg/ml and the minimum scavenging activity, and 37.78% was found in the leaf extract of *Suaeda nudiflora* at concentration of 50 mg/ml by DPPH radical scavenging activity

The study of Sachithanandam et al., (2020) extensively studied methanolic crude extract of *Rhizospora mucornata*. Based on UV-visible spectroscopy, FTIR, NMR and HRMS analysis they reported the presence of bioactive compound termed as Quinizarin. This study identified Quinizarin has potential antimicrobial, antioxidant, and cytotoxic activity. Antioxidant activity study on ethyl acetate crude extract of *A. officinalis* leaves by DPPH method (P. Lalitha, A. Parthiban, V. Sachithanandam 2021) confirmed high antioxidant activity associated with low concentrations ( $23.6 \pm 0.43 \mu\text{g/ml}$ ). These results correspond to the amount of bioactive compound present in crude extracts of the *A. officinalis* leaves.

A study on *A. marina* leaves showed that ethyl acetate extract has a good antioxidant activity along with substantial potential for preventing and disrupting the biofilm formation, which worsens microbial infection. Furthermore, GS-MS analysis detected the wide range of biological activities, especially acting as antimicrobial, antibiofilm and antioxidant agents with minimal adverse side effects. (Hassan et al, 2022)

A study on *R. racemosa* stem bark demonstrating excellent ability to effectively scavenge free radicals, chelate metal ions and donate hydrogen. The extracts showed promising activity against the tested dermatophytes, with ethyl acetate and ethanol extracts being the most effective. It suggests that it can serve as leads for alternative and renewable source of phyto - based antioxidants with antifungal potential for the treatment of dermatophytic infections in humans (Basil N. Ita, Samuel 2022)

In Silico molecular Docking studies of *Acanthus ilicifolius* leaf extract against four Multidrug-resistant bacteria was evaluated for identifying lead molecules to inhibit cell division. These findings showed that the *Acanthus ilicifolius* leaf extract have a greater affinity for the FtsZ (6YMI) protein, which is responsible for bacterial cell division, and the DPPH free radical scavenging activity of leaf extract was reported to have moderately strong antioxidant activity. Thus it could be employed to fight antibiotic-resistant bacteria [Amrun Naher et al., 2022]. The combination of polysaccharide and selenium has many advantageous properties which may be applied in various

fields of nanobiotechnology due to higher stability, biocompatibility, and biodegradability. In a study on Selenium Nano Particles of *Rhizophora mucronata leaves polysaccharides* (RMLP–SeNPs) showed an excellent scavenging capacity on DPPH, ABTS, and reducing power when compared to other forms of selenium. Moreover, selenium nano particles showed good antimicrobial and antibiofilm activity against tested strains of *Aeromonas hydrophila*, *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. Results suggested that these findings may also provide an opportunity to use SeNPs in food industries, biomedical, cosmetics, and pharmaceutical applications, especially to develop novel antioxidant and antimicrobial compounds (Natwar Jha et al. 2022).

#### **Anticancer property:**

As reported by WHO 2020, Cancer accounts for the death of 10 million people worldwide. It is brought about by dynamic abnormalities in the expression of tumour suppressor proteins, growth factors and transcription factors which leads to malignant growth of the cell called Cancer. The need to search for complementary and alternative medicines is the need of the hour because of the side effects related with the traditional cancer chemotherapies and the supposed advantages of more natural treatment alternatives. Anti-inflammatory and anticancer properties of several medicinal plants have been studied extensively. Cytotoxic activities of *Xylocarpus granatum* against various cell lines found to be the presence of Xylogranatins A–D compounds. (Yin et al. 2006; and Das et al. 2015). Several studies on mangrove plant extracts have been revealed the anticancer properties. in an in vitro cytotoxic assay studies of Tian et al. (2009), has found that 3',4',5,7- Tetrahydroxy flavone isolated from *Sonneratia caseolaris* have potential inhibition activity against cell proliferation of SMMC–7721 human hepatoma cells. The methanol extract of the leaves *Sonneratia apetala* against EAC cell line showed positive response giving 34% inhibition against EAC cells in swiss albino mice model (Patra et al. 2015). Studies on methanolic extract of *Rhizophora apiculata* have found good anti-inflammatory and anti-tumor activity against B16F10 melanoma cells in mice model of Prabhu and Guruvayoorappan (2012a). Sari et al. (2018), revealed the anti-cancer potentials of *Nypa fruticans* is due to polyisoprenoids.

Earlier studies by Huang et al. (2016) suggested that Ethanol extracts of *Avicennia marina* are rich in phenolic and flavonoid content and can be used to induce apoptosis in human breast and liver cancer cells. The Cytotoxicity studies against pancreatic cell lines by Patil et al. (2011) confirmed that the stem extracts of *Excoecaria agallocha* has promising cytotoxicity. Batsa and Periyasami (2013) extensively studied the anticancer activity of *Excoecaria agallocha* leaf extracts in cell line model. A detailed study and thorough clinical trials on extracts of *Excoecaria agallocha*, *Bruguiera sexangular*, and *Avicennia africana* have been carried out by Kathiresan 2000; Subhan et al. 2008a, b; Kathiresan et al. 2006; Patra et al. 2011b and it is been observed that they are potential anti-viral, anti-cancer, anti-HIV, and anti-tumor agents.

In a comparative study on *Avicennia marina*, *Phragmites australis*, *Moringa oleifera* the cytotoxic effects of ethanolic plant extracts in HepG2 cell lines were investigated and confirmed that all the tested extracts have cytotoxicity up to some extent. Among them *Moringa oleifera* contains maximum phenolic contents as compared to extracts of *Avicennia marina* and *Phragmites australis*, which might be the major contributor to its anticancer activities. (Muhammad Sohaib, Fahad et al. 2022). GC–MS Studies of Eswaraiyah et al., 2020 disclosed that the *Avicennia marina* has anti-cancer properties against various cancer cells. Momtazi-borojeni studies reported the crude

extract of *Avicennia marina* exhibited with excellent anti-cancer properties at 250 µg /ml. Later studies by Shan Tian, Kandasamy Saravanan et al., revealed that *Avecinnia marina* mediated Ag NPs was excellent anti-cancer agent against A549 lung cancer cells. The result was proved that the Ag NPs was concentration dependent inhibitor agent and 54% of inhibition was observed at 50 µg/mL and it was comparatively low than previous reports.

### Anti-inflammatory

The evaluative anti-inflammatory study of *R. apiculata* extract on carrageenan-induced paw edema in BALB/c mice evinced anti-inflammatory properties. the extract (at 10 mg/kg BW, for 10 consecutive days) exhibited reduction in paw size at 4 h post-carageenan injection (0.39 [± 0.04] mm) relative to that seen in control (no extract) mice (0.47 [± 0.03] mm) group animals on the same hour. The total white blood cell count and hemoglobin levels were also remarkably increased in extract-treated hosts. Analysis of this methanolic extract revealed the presence of a high content of 4-pyrrolidinyl, pyrazole, and ketone derivatives. These studies suggest that *R. apiculata* extract could be used as a (natural) anti-inflammatory and anti-tumor agent. (V. Vinod Prabhu and C. Guruvayoorappan, 2012)

The results of anti-inflammatory and α-glucosidase inhibitory activities of *Brugueria parviflora* leaves showed that the crude extract significantly increased the percentage inhibitory activity against α-glucosidase and decreased NO production in LPS-stimulated RAW 264.7 cells in a dose-dependent manner. The purified fractions were further evaluated for the anti-inflammatory and α-glucosidase inhibitory effects. The results indicated that flavonoid quercetin showed the most potent inhibitory effect against α-glucosidase activity with an IC<sub>50</sub> value of 3:4±0:5 µg/mL and the LPS-induced NO production of 11.8 µM at the concentration of 100 µg/mL. These findings suggest that flavonoids from *B. parviflora* leaves may be useful as anti-inflammatory agent. (Tung Thanh Bui, Khanh Phuong, 2022) *In vitro* anti-inflammatory activity of four different extracts of *A. corniculatum* was revealed through protein denaturation assay. Diclofenac sodium was used as a standard reference Among all the 4 extracts, methanol extract showed significant anti-inflammatory activity with 85.32 ± 1.63 percentage inhibition of protein degradation which was comparable with standard. The aqueous extract also showed potential anti-inflammatory activity (71.9167 ± 1.12970) when compared to other remaining extracts. (Kulkarni BD et.al., 2019)

An *in vitro* anti-inflammation activity of *Rhizophora mucronata* Lam. from Pichavaram Mangrove Forest, Tamil Nadu, India showed whole plant can be the potent source. Protein denaturation (bovine albumin) findings showed that the *R. mucronata* leaf, bark and stilt root extract could serve as an important anti-inflammatory agent, as maximum inhibition (296.26%) was observed from root extract followed by bark (259.48%) and leaf (237.62%). Moreover, among the three extracts, the maximum inhibition 284.17% was observed from bark extract followed by root (265.05%) and leaf (232.61%). These results provide evidence from membrane stabilization as an additional mechanism of their anti-inflammatory effect. (KAUR, S.; SYED ALI et al.2018)

In the evaluation of anti-inflammatory activity of hydro alcoholic extract of *L. racemosa* leaves (EHA-Lr) revealed that the 200 mg/kg dose was most effective in reducing leukocyte migration in the paw edema model in mice and showed superior inhibition compared to indomethacin and in the LPS-induced acute lung inflammation model the 50 mg/kg dose was most effective in reducing plantar volume and was able to prevent acute lung inflammation with low toxicity (Jhonatta

Alexandre Brito *Dias et al.*2022). One new neolignan compound, racelactone A (1), together with seven known compounds were isolated from the methanolic extract of the leaves and twigs of *Lumnitzera racemosa*. Mass and NMR spectroscopic data interpretation determined compounds 1 (racelactone A), 4 (methyl gallate), and 5 (myricitrin) showed significant anti-inflammatory effects with IC50 values of  $4.95 \pm 0.89$ ,  $1.95 \pm 0.40$ , and  $2.57 \pm 0.23$   $\mu\text{M}$ , respectively with anti-inflammatory assays on superoxide anion generation and elastase release in fMLF/CB-induced human neutrophils. (Yu, Szu-Yin, Shih-Wei Wang et al.2018)

#### **Bio active compound and drug discovery:**

Traditional techniques such as TLC and column chromatography using silica gel as stationary phase have been opted by several researchers for the separation of bioactive constituents from plant extracts. Apart from this some of the highly sensitive techniques used were HPLC-MS, GC-MS, LC-MS. Proper identification and structure elucidation of the extracted compounds have been performed mostly using UV, FTIR, NMR, and MS by several research studies. A detailed review of literature (Sayantani Mitra, Nabanita Naskar et al., 2021) lists different phytochemicals that have been qualitatively identified from mangrove species. Qualitative phytochemical screening studies of mangroves identified various classes of alkaloids, terpenoids, flavonoids, fatty acids, sugars, carbohydrates, tannins, lipids, phenolic compounds, proteins, etc., Different bioactive compound classes have been majorly reported from *Avicennia sp.*, *Bruguiera sp.*, *Acanthus sp.*, *Rhizophora sp.*, *Ceriops sp.*, *Sonneratia sp.*, and *Xylocarpus sp.* Further studies (isolation, extraction) using these species may provide new leads in the field of natural product research.

#### **GC-MS/ LC-MS analysis:**

Earlier reports by researchers documented by GC-MS analysis of crude extract of *A. officinalis* leaves revealed the presence of different bioactive compounds such as organic aliphatic and aromatic acids, phenols, esters, alcohol, steroids and terpenoids. The GC-MS chromatogram of ethyle acetate extract of the *A. Officinalis* leaves components corresponding to the eight peaks were determined as Trans-cinnamic acid (27.7%), 2,4-Di-tert-butylphenol (3.33%), Phenol, 3-(2-phenylethyl) (3.31%), n-hexadecanoic acid (18.79%), Dibutyl phthalate (100%), Phytol (2.47), b \_ Sitosterol (5.9%), Androst-7-ene-6 and 17- dione, 2,3,14-trihydroxy (6.69%). The Structures of identified bioactive compounds were illucidated. Among these Dibutyl phthalate (aromatic organic ester) had the highest percentage composition (100%) and the chemical compound phenol, 3-(2-phenylethyl) (3.31%) the lowest percentage composition. Their study determined that ethyl acetate extract of *A. Officinalis* composed of numerous natural molecules which could be attributed to pharmaceutical applications like anticancer, antioxidant, antimicrobial, anti-inflammatory. (Lalitha Parthiban). The GC-MS analysis of *A.officinalis* active column fraction (F13) identified the active principals as hydroxyl - 4 methoxybenzoic acid, diethyl phthalate and Oleic acid. (Bhimba et al. 2010). GC-MS along with FTIR analysis of the methanolic extracts *Bruguiera gymnorhiza* and *Excoecaria agallocha* revealed the presence of various phytoconstituents namely alkaloids, terpenoids, phenols and quinones that may contribute to the antimicrobial activity against *Staphylococcus aureus* and *Klebsiella pneumonia*, and antioxidant potential and have great promise in treating various diseases (Khadeeja S, Ragunathan R, Johny J, Muthusamy K (2022)

The GC-MS profile of crude methanolic extract of *A. marina* on the basis of spectral data analytical studies revealed the presence of a mixture of volatile compounds. In a study, (Aseer Manilal et al., 2016) a total of nine prominent peaks were observed with retention times Benzaldehyde,3-methyle



(6.811), 2-Methoxy-4-vinylphenol (9.211), Cyclobuta (1,2:3,4) dicyclooctene,hexadec (11.669), Benzeneethanol,4-hydroxy (12.173), 4-(2,6,6-Trimethylcyclohexa-1,3-dienyl)b (13.709), Lycorenan-7-one,9,10dimethoxy-1-methyl (14.531), 1,2-Dicarboxy-3-(4,chlorophenyl)2,3(1H) (23.249), Phenol,2-(1,1-dimethylethyl)-4-(1-methyl (23.350), Methyl p-(2-phenyl-1-benzimidazolyl)benz (26.490). Among them the major constituents identified were benzeneethanol,4-hydroxy- (RT = 12.173), followed by benzaldehyde,3-methyle- (RT = 6.811). Their findings attributed the antibiotic potency displayed by the *Avicenia marina* could be associated with the high percentage of benzene ethanol, 4-hydroxy and benzaldehyde,3-methyle.

Another study on *Avicennia marina* GC-MS analysis, 5 bioactive compounds was identified from the partially purified leaf extract of mangrove plant. The identification was performed based on the peak areas, molecular weight and molecular formula. The n-hexadecanoic acid was recorded maximum at the retention time of 30.94 with 10.7026 % of peak value followed by 2-cyclohexen-1-one, 4-hydroxy-3,5,5-trimethyl-4- (3-oxo-1-butenyl) (8.6%), phytol (8.4 %), hexadecanoic acid, ethyl ester (6.2 %) and 3,7,11,15-tetramethyl-2-hexadecen- 1-ol (4.9 %) at the retention time of 27.89, 33.27, 31.23 and 28.27 respectively (Fig-3). These five compounds were found active molecules responsible for the inhibition of multi-drug resistant *Staphylococcus aureus* agents. (Dayanidhi, Ajith kumar 2012)

Study on the extracts of mangrove plants: *Acanthus ilicifolius*, *Excoecaria agallocha*, *Rhizophora apiculata* and *Rhizophora mucronata* had been reported for the presence of a wide range of bioactive compounds. A total of 135 chemical constituents were identified and compared with their retention time in the NIST library 2011. The chemical constituent's characterization analysis reported as essential oils, higher alkanes, acid, alcohol and esters. The major peaks obtained indicated the presence of 8-pentadecane, 1, 2, 5-trimethylpyrrole, Di-(2-ethylhexyl) phthalate, diethyl phthalate, epoxyhexobarbital and cyclooctacosane (Satyavani et al 2015). The NMR and mass spectrometric analysis Raola and Chakraborty (2017) reported that the extracts of *Rhizophora mucronata* showed the presence of terpenoids, Olean-12- en-3-yl acetate which has the antimicrobial, antidiabetic, antiinflammatory, antidepressant and anticancer activities.

Vundru Anil Kumar, Kandru Ammani et al. (2013) investigated and identified bioactive phytochemical constituents of the methanol, chloroform and ethanol extracts of leaves of *C. decandra* by GC-MS analysis (Table 1). The methanol extract of *C. decandra* is found to contain fatty acids, esters, steroids, triterpenes, alcohols, the chloroform extract is found to contain esters, alkanes, alkenes, steroids, diterpenes, triterpenes, and the ethanolic extract is found to contain esters, alkanes, alkenes, steroids, alkaloids and alcohols. Among three organic solvent extracts, it is observed that chloroform extracts were comparatively more effective against the third and fourth instar larvae at very low concentrations. This investigation illustrates the potency of organic solvent extracts of leaves of *C. decandra* in controlling the wide spread of fungal diseases and larvae and thus contributes as an affordable way to control phyto pathogenic fungi, *S. Litura* and *A. aegypti*. This is explained by the different solvents properties, such as polarity which enables them to extract different type of compound(s) that results in different larvicidal properties.

The qualitative investigation of phytochemical analysis carried out on the leaves from the methanol extracts of *Acanthus ilicifolius* revealed the presence of medicinally important constituents such as alkaloids, saponins, phenolics, flavonoids, steroids, cardiac glycosides, tannins and terpenoids,

which may account for antioxidant effects of these plants tested. Similarly, *H. curassavicum* methanol extracts showed the presence of all phytochemicals except cardiac glyco-sides (Chinnathambi et al.2021). A detailed study on *A. marina* leaves ethyl acetate extract (MEE) was analyzed by GC-MS, and a total of 22 (88.5%) constituents were identified and quantified in the extract (Table 1). The chemical composition of mangrove ethyl acetate extract mostly constituted of alcohol (33.97%), fatty acids and their derivatives (18.13%). The major components in MEE were found to be 2H-Pyran-3-ol, tetrahydro-2,2,6-trimethyl-6-(4-methyl-3-cyclohexen-1-yl) (31.13%), b-Sitosterol (11.58%), 1,2-Benzenedicarboxylic acid (5.26%), and Bergamotol (4.43%) (Hassan et al., 2022)

#### GC-MS analysis:

Gas chromatography-Mass spectroscopy of *Lumnitzera racemosa* methanol leaf extract revealed the peaks that indicated the occurrence of different compounds. The mass spectral finger print of compounds identified using the data library, the compound names are listed in (Table 1). This study revealed the presence of different bioactive compounds mainly: furfurals and fatty acids. In vitro anticancer activity on MCF 7 and HeLa cancer cells using MTT assay of bioactive compounds present in *L. racemosa* revealed significant cytotoxic activity against MCF 7 with IC50 value, 46.098 mg/mL and HeLa cells with IC50 value of 59.497 mg/mL, indicating leaf extracts has high anticancer activity on MCF 7 cells in comparison with HeLa cell lines (G. Eswaraiah, K. Abraham Peele et al., 2020).

Species	Compounds	References
<i>A. Officinalis</i> leaves	Trans-cinnamic acid (27.7%), 2,4-Di-tert-butylphenol (3.33%), Phenol, 3-(2-phenylethyl) (3.31%), n-hexadecanoic acid (18.79%), Dibutyl phthalate (100%) Phytol (2.47), b _ Sitosterol (5.9%), Androst-7-ene-6 and 17- dione, 2,3,14-trihydroxy (6.69%)	Lalitha Parthiban et al.
<i>A. Officinalis</i>	hydroxyl - 4 methoxybenzoic acid diethyl phthalate Oleic acid	Bhimba et al. 2010
<i>A. marina</i>	Benzaldehyde,3-methyle (6.811), 2-Methoxy-4-vinylphenol (9.211), Cyclobuta (1,2:3,4)dicyclooctene,hexadec (11.669), Benzeneethanol,4-hydroxy (12.173), 4-(2,6,6-Trimethylcyclohexa-1,3-dienyl)b (13.709), Lycorenan-7-one,9,10dimethoxy-1-methyl (14.531), 1,2-Dicarboxy-3-(4,chlorophenyl)2,3(1H) (23.249), Phenol,2-(1,1-dimethylethyl)-4-(1-methyl) (23.350), Methyl p-(2-phenyl-1-benzimidazolyl)benz (26.490)	Aseer Manilal et al. 2016
<i>A. marina</i>	2-cyclohexen-1-one, 4-hydroxy-3,5,5-trimethyl-4-(3-oxo-1-butenyl) (8.6%), phytol (8.4 %), hexadecanoic acid, ethyl ester (6.2 %) 3,7,11,15-tetramethyl-2-hexadecen- 1-ol (4.9 %)	Dayanidhi, Ajith kumar et al. 2012
<i>C. decandra</i> leaves Methanol extract	1,3-Diolein (triterpene) RT 21.557 Lupeol (triterpene) RT28.708 Stigmast-5-en-3-ol, oleate (steroid) RT 26.011 Glycidol stearate (esters) RT 20.067 Methyl linolenate (ester) RT 21.518 Clionasterol (triterpene) RT 27.760	Vundru Anil Kumar, Kandru Ammani et al. (2013)
Chloroform extract	Phthalic acid dioctyl ester (ester) RT22.030 squalene (triterpene) RT24.022 Stigmast-5-en-3-ol, (3.beta.) (steroid)RT27.783	

	<p><math>\alpha</math>-amyrin (triterpene) RT28.250            Lupeol (triterpene) RT28.855            1H-Purin-6-amine, [(2-fluorophenyl)methyl] (purines or alkaloids) RT21.151            A-Neooleana-3(5),12-diene (alkene) RT24.941            9,19-Cycloergost-24(28)-en-3-ol, 4,14-dimethyl-,acetate,(3. <math>\beta</math>,4. <math>\alpha</math>.,5. <math>\alpha</math>.) (steroid) RT25.942            Stigmast-5-en-3-ol, (3.beta.) (steroid) RT26.016            9,19-Cycloergost-24(28)-en-3-ol, 4,14-dimethyl-, acetate (steroid) RT26.405            Cycloartenol (alcohol) RT26.450            Methyl commate B RT28.710            Fumaric acid, tetradec-3-enyl tridecyl ester (ester) RT28.979</p>	
<i>A. marina</i> leaves (Ethyl acetate extract)	<p>Hassan, Ibrahim, Hala et al.            4.06 12,15-Octadecadiynoic acid, methyl ester 0.63 %            7.00 Cyclohexanol,1-methyl-4-(1-methylethenyl)-, acetate 3.12%            8.87 Undecane 2.36 %            12.82 2-Cyclohexen-1-one, 2-methyl-5-(1-methylethen yl) 1.13%            19.76 Bergamotol, Z-à-trans 4.43 %            21.76 Diethyl phthalate 2.58 %            23.15 2-Furanmethanol, tetrahydro-à,à,5-trimethyl-5-(4-meth yl-3-cyclohexen-1-yl)            23.79 5,8,11,14-Eicosatetraenoic acid, methyl ester, (all-Z)- 2.90 %            25.182H-Pyran-3-ol,tetrahydro-2,2,6-trimethyl-6-(4-methyl-3-cyclohexen-1-yl)-,[3S-            [3à,6à(R*)]]- 31.13%            27.27 E-8-Methyl-9-tetradecen-1-ol acetate 0.91 %            27.74 1,2-Benzenedicarboxylic acid, bis(2-methylpropyl) ester 5.26 %            28.01 (E)-Tonghaosu 1.45 %            28.94 Pentadecanoic acid, 14-methyl-, methyl ester 1.03 %            29.71 Hexadecanoic acid 2.59 %            32.15 Ethyl (9z,12z)-9,12-octadecadienoate 1.09%            32.28 9-Octadecenoic acid (z)- 2.05 %            32.51 Phytol 2.33 %            33.04 12-Methyl-e,e-2,13-octadecadien-1-ol 1.93 %            39.81 1,2-Benzenedicarboxylic acid 4.36 %            42.53 Campesterol 1.90 %            43.24 Stigmasterol 3.89 %            44.08 á-Sitosterol</p>	
<i>Lumnitzera racemosa</i> leaf (Methanol extract)	<p>5.568 Furfural            9.041 2-Furan Carboxaldehyde, 5-methyl            14.227 2-FuranCarboxaldehyde-5-(hydroxyl methyl)            19.496 Benzyle chloride            22.407 Hexa decanoic acid - methyl ester</p>	G. Eswaraiah et al. 2020
<i>Avicennia alba</i> leaf (Methanol extract)	<p>14.202 Catechol borane            15.344 2-Methoxy -4- vinyl phenol            17.465 Cyclohepta Siloxane, Tetra deca methyl 9.317%            18.042 Neophytadiene (7,11,15 Trimethyle -3- methylene -1- hexadecene 16.989%            18.234 Hexadecanoic acid 29.499%            19.496 Docosanoic acid (Behenic acid) 4.079%            21.249 3,7,11,15 Tetra methyl -2-hexadecene-1-ol 1.481%            21.343 3- (3-Fluoro anilino)- 1- (3-nitrophenyl) -1- Propanone 7.954%            22.406 Hexa decanoic acid - methyl ester 2.386%            24.265 Phytol 2.337%            27.404 Alpha amyryn 8.219%            27.645 Docosanoic acid, Methyl ester 2.277%</p>	G. Eswaraiah et al. 2020
<i>Bruguiera gymnorrhiza</i> (Methanol extract)	<p>23.4844 Butanoic acid            23.9434 Succinic acid, pent-4-enyl propyl ester            24.0194 2-Pentenoic acid, 4-oxo-, methyl ester            24.3651 Thiazolidine, 3-methyl-            7.6253 6,7,8-Trimethoxy-3,4-dimethyl-1-methylsulfanyl-3,4-dihydroisoquinoline            23.8980 L-Leucine, methyl ester            7.1880 2-Furancarbonitrile            16.6974 Glutaric acid, di(4-cyanophenyl) ester            24.0022 1-Dodecanamine, N-dodecyl            28.6250 9,12,15-Octadecatrienoic acid, methyl ester, (Z,Z,Z)            37.8775 Coumarine, 4-methyl-7-hydroxy-8-benzoyl-</p>	Khadeeja S, Ragunathan et.al. (2022)
<i>Excoecaria agallocha</i>		Khadeeja S, Ragunathan et.al. (2022)

(Methanol extract)	4.1048 Acetylacetone
	6.8916 Trifluoroguanidine
	8.1685 Picolinamide
	8.5621 p-Aminotoluene
	16.7231 Phthalic acid, hexyl 2-propylphenyl ester
	20.3128 Enanthamide
	20.3916 Cyclopentanecarboxaldehyde
	21.2097 Benzamide, 4-fluoro-N-allyl-
	22.0511 L-Leucine, ethyl ester
	23.5800 1,3-Dioxolane
	26.5490 Octanamide, N-(2-butyl)-N-heptyl-
	31.7868 2H-1-Benzopyran-2-one, 3,4-dihydro-6-hydroxy-
	37.7123 Glutaric acid, 2-methylpent-3-yl 2,2,3,4,4,4-hexafluorobutyl ester

Table 1: Bioactive compounds identified from different mangroves and their percent composition with retention times in minutes

GC-MS analytical studies proved that the leaf extract of *Avicennia alba* contain a high content of phenolic compounds. GC-MS chromatogram of methanolic leaf extract of *Avicennia alba* have showed 12 peaks indicating presence of 12 compounds (G. Eswaraiyah, K. Abraham Peele et al., 2020) The spectral fingerprint of each compound can be identified from the data library. From the chromatogram peaks, found different bioactive leads which includes: terpenoids, silicones, phenolic compounds and fatty substances (Table 1). Among all, one unknown compound was found i.e., 3-(3-Fluoroanilino)-1-(3-nitrophenyl)-1-propanone (7.954%), which was not reported previously and it is first time reported from mangrove plant *Avicennia alba*. In MTT assay, cell line viability of treated cells decreased gradually with increase of the sample concentration. The methanol extract showed potent cytotoxicity against Human breast adeno carcinoma (MCF7) and HeLa cell lines, the viability of cancerous cells is reduced to 44.68% for MCF 7 and 35.89% for HeLa cells.

### Conclusion:

Emergence of multidrug-resistant bacteria has become a major source of concern around the world, and pharmaceutical waste is a major reservoir of these bacteria. Pharmaceutical waste, which consists of unwanted or expired medicines that are thrown into the environment without being properly treated and disposed, is responsible for the emergence of multidrug-resistant bacteria in the environment. According to research findings, the four isolated strains of *Staphylococcus aureus*, *Staphylococcus sp.*, *Staphylococcus saprophyticus*, and *Aeromonas jandaei* were resistant to practically all antibiotics available as they acquired antibiotic resistance through gene transfer. Before being dumped, pharmaceutical waste should be processed and make them non hazardous (Amrun Naher et al., 2022). The developing enthusiasm for the complementary and alternative medicines is principally due to disadvantages related with the traditional chemotherapies and the supposed advantages of more natural treatment alternatives.

### ACKNOWLEDGMENT

I would like to acknowledge my gratitude to Andhra University, TDR-HUB, Visakhapatnam for giving this opportunity to do research. I would like to thank my supervisor Dr. Ch. Lalitha, HOD – Department of Microbiology, Government College for Women (A), Srikakulam for giving constant support and guidance. I would also like to thank my organisation A.S.D. Govt. Degree College for women (A), Kakinada

Finally I wish to acknowledge my family members and God almighty for continuous encouragement for this work.

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