Bioprospecting Mangrove Endophytic Fungi for Potential Bioactive Compounds

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Abstract:

Mangroves are important – for the life on the earth. Coastal regions that are tropical or subtropical are home to mangrove forests, supporting a vast variety of animals, both above and below the water, that provide food and shelter. Mangrove plants are associated with the microorganisms of endophytes such as actinomycetes, fungi and bacteria in each part of their plant body which secretes potential bioactive compounds exhibiting properties like immunosuppressants, antimicrobial, anti-parasitic, anti-cancer, antioxidants etc. Of the various microbes, endophytic fungi of mangroves have been recognized as a novel and significant sources of naturally occurring bioactive compounds with varied activities. Bioprospecting endophytes from mangrove species could offer a great solution in discovering potential drug candidates. The current review mainly focuses on the endophytic fungi of mangroves as novel sources for potential bioactive compounds.

Keywords: Mangroves, Bioprospecting, Endophytic fungi, Bioactive compounds, Potential bioactive compounds, Biological activities.

1. Introduction:

Mangroves are woody trees or shrubs found along tropic or sub-tropical coastlines near the equator, unable to withstand freezing temperatures. They create a unique ecological environment with diverse species, some of which have evolved adaptations to survive in salty and oxygen-poor soil [7]. Mangroves, found in 112 countries, cover 18 million hectares, with 41.4% in Southeast Asia. The continents like Asia and Australia have the highest diversity of the mangrove varieties. They are divided into eastern and western groups, with the Eastern group having five times more species. The largest mangrove formations are in Indonesia, Brazil, Bangladesh, and India. The main plant species found in mangrove forests are trees and shrubs from various families, classified as red, white, and black, and include species like Hibiscus pernambuensis and Acrostichum speciosum, also known as mangrove cotton and mangrove fern [20].

Mangroves have enormous ecological value. They protect and stabilize the coastlines, enrich coastal water, yield commercial forest products, and support coastal fisheries [4]. The exploration of novel energy harvesting technologies, such as the plant-based triboelectric nanogenerator developed by Babu *et al.,* (2022), highlights the innovative applications of natural resources in advancing biotechnological solutions. They produce organic carbon, contribute to the global carbon cycle, and exhibit activity against pathogens. Mangrove endophytes, which include bacteria and fungi, are promising sources of bioactive compounds with medicinal applications. They are perfect locations for conducting experiments on ecological functioning and biodiversity

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[1] [55]. Mangroves contain endophytic microorganisms like bacteria, fungi, and actinomycetes that maintain symbiotic relationships with plants. These fungi produce immunosuppressants, antimicrobials, anticancers, and antioxidants, which are beneficial for the host plant under adverse conditions. These compounds are used in various applications, including antibiotics, immunosuppressants, and antioxidants [21].

This review explores the compounds from endophytic fungi which are potentially active, particularly those from mangrove ecosystems that are identified as potential sources of anticancer metabolites due to their diverse activities. Figure 1 shows the global distribution of mangroves.

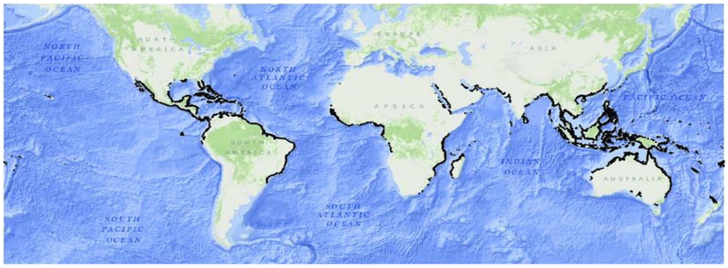

Figure 1: Global distribution of mangroves

2. Mangrove Endophytes:

Endophytes, or organisms living within plants, are often associated with mangroves like bacteria and fungi. They can prevent pathogenic organisms from colonizing, create a barrier effect, produce chemicals, stimulate plant growth, and modify plant biology for survival in extreme environments. Additionally, endophytes produce bioactive antimicrobial products and secondary metabolites, including immunosuppressive, antiviral, antidiabetic, anticancer, and antioxidant substances.

2.1. Endophytic fungi of Mangroves: Endophytic fungi, are marine fungi found in mangrove plants and soils [11]. They are the second largest ecological group, having unique survival mechanisms, such as high salt concentration growth through endophyte host interactions [82]. Fungal endophytes, including Aspergillus, Penicillium, Fusarium, Cephalosporium, Blastomyces, and Candida, exhibit potent activity against organisms and have the potential to produce bioactive compounds [60].

2.2. Importance of Endophytic fungi: Natural product development has attracted attention because of its cheap production costs, structural diversity, and medicinal chemicals used for a variety of disorders. Mycology is the study of fungi and their uses in agriculture, medicine, and the environment [2]. A widespread and varied class of microorganisms known as endophytic fungus produces bioactive substances that are comparable to those produced by their host plant [12,14,50,56,59]. The endophytic fungi contains two broad groups: C-endophytes (clavicipitaceous) found in grasses and transmitted through vertical transfer, and NC-endophytes (non-clavicipitaceous) found in the majority of angiosperms and cryptogamic plants asymptomatic tissues [13]. Both fungi and bacteria are common endophytes, producing a wide range of secondary metabolites with medicinal properties [57] [48].

Endophytic fungi produce bioactive metabolites like anticancer compounds, based on the genetics, environmental factors, and host species [61] [49]. Host plants provide nutrition to endophytes, which help plants grow and produce secondary metabolites which protect against plant pathogens [9] [77]. The metabolites produced by endophytes can sustain the mix of auxiliary metabolites that are naturally dynamic, such as phenol, citrinin, taxol, and piperine [68] [34]. Endophytes help the host plant by boosting immunity and producing secondary metabolites that are useful in a variety of industries [64] [30]. Plants, including roots, leaves, stems, fruit, and rhizome, contain biological compounds [13]. Recently, drug discovery has focused on microorganisms in mangrove plants [26], with the current review focusing on mangrove endophytic fungus and the bioactive substances they produce have a wide range of biological activity.

3. Bioactive Compounds from Endophytic Fungi:

Biologically active substances secreted by endophytic bacteria support host plants in challenging environments and shield them from diseases and predators. The manufacturing of growth hormones, enzymes, and antibiotics from endophytes has gained importance in agricultural and medicinal fields. Endophytic fungi secrete secondary metabolites such as alkaloids, benzopyrones, flavonoids, phenolic acids, quinones, steroids, terpenoids, xanthones, saponins, and tannins. These bioactive compounds act as strong immunosuppressants, antiparasitic, anti-inflammatory, antiviral, anticytotoxic, and antioxidants [3]. One of the most exciting and ambitious scientific advances of our day is the hunt for novel bioactive chemicals and their possible biological actions.

In addition to creating growth-promoting compounds and insect and pest repellents, endophytic fungus also help plants absorb nutrients [6]. Co-evolutionary processes have given these endophytes a vast metabolic capacity to produce highly bioactive chemicals that may be used for commercial purposes. Figure 2 shows Endophyte Bioprospecting and the identification of new, valuable metabolites with economic relevance are summarized in the following sessions.

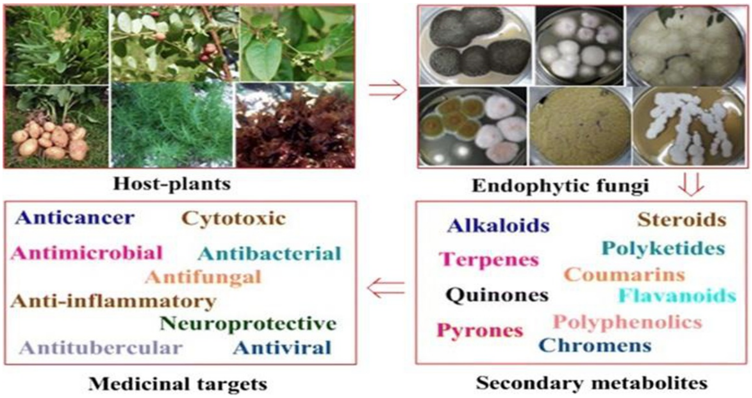

Figure 2: Schematic representation of Bioprospecting of endophytes and discovery of novel compounds, for their commercial significance

3.1. Antibacterial activity: Deshmukh *et al.,* (2014) investigated antibacterial compounds extracted from endophytic fungi. Many of the researchers have isolated compounds with antibacterial activity from various endophytic fungi with different host plants. These compounds include Phomoxanthone A, Dicerandrol C, Cycloepoxylactone and cycloepoxytriol B, Phomosines A–C, Phomosine A and G, Phomopsichalasin, 4-(2, 4, 7-trioxa-bicyclo [4.1.0] heptan-3-yl) phenol Colletotric acid, artemisinin, two Fusarusides, Fusapyridon A, Javanicin, Fusaric acid, Epoxydine B, Epoxydon, Flavipucine, Anhydrofusarubin, Javanicin, dihydrojavanicin, and solaniol. Mazlan *et al.,* 2019 studied endophytic fungi of Fusarium sp. and enlisted various compounds effective against E. coli and B. megaterium. Some of the endophytic fungi that have antibacterial properties are included in Table 1.

3.2. Antifungal activity: Strobel and Daisy (2003) have highlighted the various problems that today's pharmaceutical industry is facing. These include- the appearance of various drug-resistant bacteria and viruses, increased instances of infections caused by fungi, and the patients with transplanted organs are facing many problems with infections. Endophytic fungi are a new hope in all these as many endophytic fungi have antimicrobial potential. Literature shows abundant studies on isolating compounds with antifungal potential from endophytic fungi harbouring different host plants. These include- pentaketide [8], Glucoside derivatives – xylarosides [52], Cytosporone B and C [28], Cryptosporiopsis quercin [65], Cryptocin, a tetramic acid [38]. Pseudomycins L [5] etc. Many of the researchers reported that certain endophytic fungi of mangroves have shown activity against certain fungal pathogens and these include Phylotypes Lecythophora species 1, 2 and Fusarium oxysporum [58], Colletotrichum ovulariopsis, Phomopsis pestalotiopsi and Alternaria, Paecilomyces sp. [29]. Some of the endophytic fungi with antifungal properties are included in Table 1.

3.3. Anticancer activity: Cancer is a dreadful disease, and the search for an effective and low-cost anti-cancer drug has been one of the greatest challenges in today's world for mankind. Endophytes are naturally available compounds that contain anticancer properties [17]. Paclitaxel is the first significant class of anticancer drugs to be created and some of its derivatives from endophytes. Taxomyces andreanae, which has opened a new horizon for obtaining a cheaper product through microorganism fermentation [63]. Further investigations have led to the discovery of Taxol in many fungal endophytes either related to Yew trees or not associated with it, such as Wollemia nobilis [66], Taxodium distichum [39], Bartaliniarobillardoides [19], Phyllosticta spinarum [32], Botryodiplodia theobromae [51], Pestalotiopsis terminaliae [18], Tubercularia sp. [72], Sporormia minima and Trichothecium sp. [62]. Campthothecin, an alkaloid, is an important antineoplastic agent isolated from Campthotheca acuminate wood in China [69]. Ergoflavin, a compound from the ergochromes class, is isolated from an endophytic fungus from Mimusops elengi [16], Trametes hirsute, a Podophyllotoxin-producing endophytic fungus, has shown promising anticancer properties [53]. Strong anticancer properties have been demonstrated by secalonic acid D, which was extracted from the mangrove endophytic fungus. [81], other endophytic fungi or compounds with anti-cancer or anti-tumor properties include Aspergillus fumigates, Fresenius, Torreyanic acid, three novel cytochalasins, and Streptomyces microorganisms [33] [37]. Table 1 shows some of the endophytic fungi with anticancer activity.

3.4. Antiviral activity: It has been discovered that endophytic fungal antimicrobial compounds inhibit viruses [22], with Cytonaema sp. cytonic acids A and B functioning as inhibitors of human cytomegalovirus protease. An endophytic fungus called Pestalotiopsis theae was found on an unnamed tree in Jianfeng Mountain, China, and it generated Pestalotheol C, an anti-HIV drug [36]. Compounds Emerimidine A and B from Emericella species from Aegiceras corniculatum mangrove also showed effective anti-viral activity [80]. However, because of their exposure to severe environmental circumstances, mangrove endophytes provide a considerable need for the identification of new anti-viral drugs. Table 1 shows some of the endophytic fungi with antiviral activity.

3.5. Antioxidant activity: The antioxidant qualities of endophytic fungus from Rhizophora species, particularly Pestalotiopsis sp. and Diaporthe sp., from the South China Sea coast were examined by Jing [82]. They discovered that these fungus extracts can provide high-quality metabolites that are helpful in the search for new drugs. The DPPH (2, 2-diphenyl1-picrylhydrazyl) and ABTS (2, 2-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid) methods were used to examine the antioxidant activity of the fungal extracts. Mangrove sp. may be a sustainable supply of natural antioxidants, as the isolates showed strong antioxidant activity. Table 1 shows some of the endophytic fungi with antioxidant activity.

Table 1: The list of compounds that were separated from several mangrove species endophytic fungus and the associated bioactivities

S. No	Mangrove species and parts	Endophytic fungal Isolates	Bioactive compounds	Bioactivity	Ref
1.	Avicennia lanata (Root and Stem)	Lasiodiplodia theobromae	5-hydroxymellein and -mellein or 8-hydroxy-3-methylisochroman-1-one, Trans and cis 4,8-dihydroxy-3-methylisochroman-1-one	Antibacterial activity Antioxidant activity Cytotoxicity	[44]
		Fusarium sp.	Anhydrofusarubin, solaniol, Javanicin and dihydrojavanicin	Antibacterial activity	
2.	Avicennia officinalis (Leaves, Stem, Roots)	Alternaria longipe	2,4,6-triphenylaniline	Antidiabetic activity, Anticancer activity	[53]
3.	Rhizophora mucronate (Leaves)	Pestalotiopsis sp.	Pestalotiopsoid A, 3-hydroxymethyl-6,8-dimethoxycoumarin, cytosporone C, and dothiorelone B	Antibacterial activity, Anticancer activity	[54]
		Eurotium chevalier	Diaportheins BandEmodin	Antibacterial activity	[43]

		Fusarium napiforme	6 hydroxy-astropaquinone B, astropaquinoneD and3-O-methyl-9-O-methylfusarubin	phytotoxic	[67]
4.	Xylocarpus moluccensis (Leaves)	Aspergillus sp.	(7 R, 11 S) -7,12-epoxis acidoydonic; (7 S, 10 S)-7,10-acido epoxysydonic; acido 7-desoxi-7,14-didesidro-12-hydroxysydonic; € -7-desoxi-7,8-didesidro-12-acido hydroxysydonic Pestalotiopen A	Antibacterial activity	[70] [71]
5.	Bruguiera gymnorrhyiza (Leaves)	Nigrospora sphaerica	Nigronapthaphenyl	Antibacterial activity	[79]
		Aspergillus sp.	Spergillumarinas Aand B	Antibacterial activity	[35]
6.	Scyphiphora hydrophyllacea (Leaves)	Guignardia sp.	Guignardone B andGuignardoneI	Cytotoxicity	[45]
7.	Bruguiera sexangular (Leaves)	Phyllosticta capitalensis	Guignardone A andguignardoneJ	Antimicrobial activity	[25]
8.	Bruguiera sexangular Var. rhynchopetala (Leaves, stem, root)	Penicillium citrinum	Austinol Penicimarins GandH 2^{J}-acetoxy-7-chlorocitreorosein	Antimicrobial activity	[24]
		Daldinia eschscholtzii	8-Omethylnodulisporin F andnodulisporin H, Hydroxy-2-methoxy-6, 7dimethyl-1, 4-napthoquinone, 5-hydroxy-2-methoxy-6,7-dimethyl-1,4-naphthoquinone	Antibacterial activity	[40]

		Stemphylium sp.	2-O-acetylaltersolanol B, Altersolanols AandB Infectopyrones AandB	Antimicrobial activity	[31] [83]
9.	Pluchea indica (Leaves)	Ascomycota sp.	Dichlorodiaportintone, desmethyldichlorodiaportin, dichlorodiaportin	Anti-inflammatory, Antimicrobial activity	[10]
10.	Rhizophora stylosa (Leaves)	Pestalotiopsis sp.	PestalotiopisorinB	Antibacterial, cytotoxic activity.	[27]
		Aspergillus nidulans	Isoversicolorin C,versicolorin C	Antibacterial activity	[78]
11.	Kandelia candel (Leaves)	Penicillium aculeatum	8-dihydroxy-chromone, bacillisporinAand bacillisporinB	Antibacterial, cytotoxic activities	[76]
		Nigrospora sp.	Bostrycin,andDeoxybostrycin	Antibacterial, cytotoxic activity	[75]
		Pestalotiopsis vacinii	,3,8-dihydroxy- 6-methyl-9-oxo-9H-xanthene-1-carboxylate, pestalotiopsone F, pestalotiopsone B, and5-chloroisorotiorin	Antibacterial activity	[74]
12.	Pongamia pinnata	Nigrospora sp.	3,6,8-trihydroxy-1-methylxanthone	cytotoxic activity	[61]
13.	Avicennia marina (Leaves)	Penicillium brocae	Penicibrocazines B–E, Bbrocapyrrozins A and 4-hydroxy-3-phenyl-1H-pyrrol-2(5H)-one	Antimicrobial, cytotoxic activity	[46, 47]
		Neosartorya hiratsukae	Neosartoryadins AandB	Antitumor activity	[75]

14.	Rhizophora apiculata (Leaves)	Phomopsis sp.	2R,3S)-7-ethyl-1,2,3,4-tetrahydro-2,3,8-trihydroxy-6-methoxy-3-methyl-9,10-anthracenedione	Antimicrobial, cytotoxic activity	[31]
		Arcimonium strictum	Cytosporone E	Antimicrobial, cytotoxic activity	[23]
15.	Ceriops tagal	Colletotrichum gloeosporioide	(2S)-2,3-dihydro-5,6-dihydroxy-2-methyl-4H-1-benzopyran-4-one an4-ethyl-3-hydroxy-6-propenyl-2H-pyran-2-one	Cytotoxic activity	[42]
		Cytospora sp.	Cytospomarin	Antimicrobial, cytotoxic activity	[73]
16.	Aegiceras corniculatum	Emericella sp.	Emerimidine A and B	Antiviral activity	[80]
17.	Excoecaria agallocha	Penicillium expansum	Expansols A&B, Polyphenols	Cytotoxic activity	[41]

4. Conclusion:

The endophytic microorganisms found in coastal regions are abundant in mangroves with different species. The research that is now accessible makes it abundantly evident that Mangrove endophytic fungi can create novel bioactive compounds with a variety of effects. These substances address several human health issues, including medication resistance in malignancies, fatal viruses, fungal infections, and harmful human bacteria. They also hold promise for novel therapeutic molecules that can effectively cure illnesses in humans, plants, and animals. Because of their ability to survive in harsh environments, Research on the endophytic fungi that have been isolated from mangrove plants might lead to the development of novel medications.

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