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NATURAL BIOACTIVE PRODUCT OF ENDOPHYTIC FUNGI FROM VARIOUS MARINE SOURCES - A NOVEL APPROACH

Biotechnology

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ABSTRACT

Worldwide, ailments like cancer and infections are growing widespread, producing an urgent demand for new constructive compounds with different modes of action that may be used to combat these dreadful conditions. Endophytic fungi represent an source of great biodiversity for isolation of effective novel natural products for medical, agricultural, and industrial applications. Microorganisms associated with marine endophytic fungus by inter and intracellularly in marine source investigated (including algae, seagrass, driftwood, and mangrove plants), marine vertebrate (mainly fish), and marine invertebrate (sponges and coral). The specialized techniques of interaction evolved from the evolution of bacteria and eukaryotes to a greater level of complexity, as a consequence of their co-evolution with one another. The organism produce compounds that have anticancer, antiviral, anti-neuro-degenerative, antimicrobial, antioxidant, and immuno-suppressive. Furthermore, fungal endophytes possess a wide range of biological capabilities used in environmental and agricultural sustainability, among other things. Novel lead compounds must be discovered to progress in the creation of new pharmaceuticals. The ability of endophytes to produce bioactive metabolites widely investigated over the past decade. The current level of research on endophytes from a range of situations from 2000 to 2022, emphasizing metabolites discovered in endophytic plants.Our research will help to accelerate the development of new treatments for a broad spectrum of human ailments for future research and development.

KEYWORDS

Endophytes, Fungi, Algae, Bacteria, Sponge

1. INTRODUCTION

Over the past two decades, a new paradigm in marine biology has steadily emerged and expanded throughout a wide range of various fields of research in the field of marine biology. Symbiotic connections are formed between eukaryotic hosts and the microorganisms that coexist with them. Bacterial, archaeal, protist, microalgae, fungal, and viral symbiotic interactions are formed. Host-microbiome interactions and symbiotic relationships may be found in a variety of marine habitats, from coral reefs to the deep sea. These interactions are essential to the health of marine ecosystems[1] [1]. The seas provide a bulk source of the biological activity on our planet. Bioactive compounds from marine flora and fauna have a long history of use in the medical application, and has interest in natural and as synthetic application. They are also being looked at as possible medication candidates, which is exciting news. In clinical trials the advanced level of using chemicals isolated from a range of marine species, and the compounds have already received FDA approval for use as medications [2]. symbiotic Microbial consortia serves as a source of bioactive compounds having the potentiality to be used in the pharmaceutical sector. Bacteria and fungi from marine plants and the internal tissues of animals, and marine fungi are becoming more popular as study topics [3]. More recently, several bioactive compounds have been isolated from marine taxa, including tunicates, sponges, soft corals ,bryozoans, sea urchins, and sea animals, from the surrounding environment. Secondary metabolites from marine sources The anti-cancer compound, anti-infectious and anti-inflammatory activity are from the secondary metabolites of marine sources has also been proved [4] to be of major significance. The great majority of microorganisms isolated from the marine environment have the potential to produce a diverse variety of exciting natural compounds that might be employed as therapeutic leads, even though the vast majority of them are non-cultivable species[5]. Endophytic fungi in marine organism, have medical significance and used in pharmaceutical industry, due to significant and quantifiable component of fungal biodiversity and location of the host community [6]. One-third of 30,000 diseases can be treated symptomatically and a small number can be entirely cured is a source of great frustration. The discovery of novel therapeutic agents is necessary to meet medical needs that are currently unmet by current therapies. Historically, natural ingredients played a vital role in the creation of novel pharmaceuticals. In terms of land area, the marine environment accounts for more than seventy percent of the world's land area. with a rich source of powerful compounds, led to the identification in medicinal possibilities. In contrast, the diversity of marine microorganisms and its bioactive metabolites, have not yet explored [7].

2. Various Marine Sources for Bioactive Compound Production:

2.1 Mangrove Plants

A rich source of secondary metabolites, mangroves offer a broad variety of uses in pharmacological and medical research, and they may be found in abundance in the wild. Mangrove forests created by humans may be found in tropical and subtropical places all over the globe. Coastal habitats that are protected in estuaries, river banks, and lagoons [8] are examples of this kind of environment to survive in a range of severe climate conditions, mangroves have evolved to be resistant to low oxygen levels, high saline levels, and high temperatures, among other things. [9] It is possible that the development of different adaptive traits, as well as the creation of secondary metabolic pathways, are responsible for the synthesis of structurally diversified metabolites that enable mangroves to survive under harsh environmental conditions. Mangroves, like other plants, contain a variety of bioactive metabolites, including essential oils [10], limonoids [11], flavonoids [12], coumarins [13], terpenoids [4], glycosides [5], and alkaloids [6]. Essential oils [10], limonoids [11], flavonoids [12], coumarins [13], terpenoids [4], glycosides [5], and alkaloids [6] are among the total of 73 mangrove species are present in 123 countries throughout the globe, making them both commercially significant and having traditional folkloric medicinal importance [17]. In addition to being utilized as antibiotics, antiherpetics, and anthelmintic agents [18], the medications are also used to treat dyspepsia, hepatitis B and C, as well as diabetes, leukemia, and stomach disorders. They are also commonly employed in the treatment of malaria and syphilis, among other conditions. Insecticidal and gastroprotective effects of mangrove species have been shown in studies. Various research [19] has shown that the extracts of many mangrove species contain antioxidant, cancer-fighting, and anti-inflammatory capabilities, in addition to their other beneficial effects.

2.2 Seaweeds

Algae are a varied and complex group of animals that are distinguishable from other species by their photosynthetic nature and their basic reproduction system. Algae is classified into four groups based on the pigment: the ***Cyanophyta*** (blue-green algae), the ***Phaeophyta*** (brown algae), the Rhodophyta (red algae), and the ***Chlorophyta*** (green algae). Marine algae are found in complex ecosystems that are exposed to a variety of extreme environmental conditions. They may produce a vast variety of physiologically active

metabolites as a consequence of their capacity to adapt to their environment, which is unlike any other species. It is via the use of these metabolites that algae may survive in highly competitive environments [20], acting as chemical defense mechanisms. A wide variety of terrestrial and aquatic plants contain phytochemicals like phenolic compounds, which are important for the development and survival of organisms as well as their role in the defense against infections and predators. Among other mechanisms of synthesis, the pentose phosphate, and phenylpropanoid pathways are capable of producing these compounds [21].

2.3 Sponges

Members of the phylum "the pore bearers," sponges are spineless organisms that live in a watery environment (Porifera). They are the most basic multi-cellular species on the earth, having survived for millions of years and serving as a model for future evolution. [22] Marine sponges can assemble little quantities of food from saltwater that is beginning to rise through their bodies. They have a soft body, are sessile, and filter feed on the food they collect. Bioactive compounds from marine sponges is high compared to other living microorganisms. Due to the inability to move and lack of physical defenses make sponges very susceptible to marine predators and become extinct [22, 23]. According to recent research [24], bioactive substances derived from sponges or associated with other marine microorganisms are capable of acting against a variety of pathogens, including bacteria, viruses, fungi, and parasites. They are also immunosuppressive, relaxant, and anti-inflammatory agents.

2.4 Coral

Micro organisms are associated with corals found in the coral's skeleton, epidermis, gastrodermis, and outer mucus layer. Corals are a form of cnidarian that lives in the ocean and is classified as a cnidarian by the International Union of Naturalists [25]. In addition to host control, coral microbiomes may be quite varied, and the development of these microbiomes is regulated by environmental influences. There are many different types of algae and bacteria in the microbial communities. There are also different types of archaea, microeukaryotes, and viruses, all of which contribute to the supply of energy and nutrients that are vital to the health of coral reefs. To maintain host homeostasis, it is necessary for corals and the microorganisms that dwell beside them to form symbiotic interactions [26]. Coral-associated bacteria (CAB) plays role in host defense of the coral against pathogens [27].

3. What are endophytes?

Endophytes are microorganisms that live inside plants for at least a part of their life cycle. Endophyte definitions have changed in recent years, and it is expected that they will continue to evolve even more over the next several years. The term "endophyte" has historically been used to refer to fungus that grows inside plants, but researchers have recently discovered that the interior parts of plants may also be inhabited by microorganisms [28,29]. Phytoplankton endophytes are the diverse microbial groups that reside inside the 46 tissues of the plant in a commensal relationship with the host plant. Extensive biotic and abiotic stressors have been seen in endophytes, which have been established in scientific research over the years to aid host plants in their adaptation to a wide variety of agroclimatic conditions, including a wide range of abiotic stressors. Endophytes are also well-known for their capacity to stimulate plant development by synthesizing 49 metabolites that help in nutrient absorption [30], which are essential for plant growth. All plants have a diverse microbial community residing inside their interiors, which includes bacteria, prokaryotic organisms, actinomycetes, and protistic species. This group of endophytic microorganisms is crucial to the development and growth of plants, as well as to their fitness and variety, as well as to their survival. Endophytes are becoming more well-known, and there is more information accessible on them than ever before, providing insight into the complexity of the plant microbiota and its interactions with the environment. Depending on the nature of the interaction, interactions between plants and endophytes may be helpful or destructive. To do this, several environmental and biological factors must be considered, including the genotypes of plants and microbes, climatic conditions, and the extensive network of interactions that exists within the plant biome [31].

3.1 Endophytes from Algae

The endophytic fungus has been isolated from distinct marine algae that have been collected from mandapam and Kovalam in Tamil Nadu by Ahamed and Murugan. The antioxidant capacity of fungal extracts from ***Chaetomium sp., Phomopsis sp., Acremonium sp., Aspergillus niger, Xylaria sp., Cladosporium sp., and Fusarium sp***. was observed [32]

Host Algae Species	*Endophytes*	*Bioactive Endophytes*	*Epiphytes*	*Bioactive Epiphytes*
A) RED ALGAE				
1.Gracilaria salicornia	*49*	*22*	*24*	*8*
2.Hypnea musciformis	-	-	*26*	*14*
B) GREEN ALGAE				
1.Codium geppiorum	*19*	*5*	*29*	*6*
2.Caulerpa mexicana	*13*	*7*	*27*	*3*
c) BROWN ALGAE				
1.Turbinaria decurrens	*44*	*10*	*28*	*7*
2.Sargassum cristaefolium	*51*	*16*	*23*	*7*

The above table represents the marine Microbe Isolated From Marine Algae of Kenyan Indian Ocean[33]

3.2 Endophytes from Sponges

Phakellia Fusca was discovered to have Ascomycota sp., A. candidus in comparison to the coastal sponge Theonella swinhoei [34]. Coastal and Phakellia Fusca sponges were found to have different fungi. There were Ascomycota sp., A. candidus, in the sponge Phakellia Fusca An experiment by Gao et al. (2018) looked at the fungal diversity and sponge-microbe interactions in two sponges from one geographic region by altering the symbiotic fungus type that both sponges shared.

3.3 Endophyte from Mangrove

Around 39 distinct endophytic species were identified in accordance with Xing et al. (2011), of which ***Cytospora, Diaporthe, Fusarium, Glomerella, Mycosphaerella, Phoma, Phomopsis, and Stemphylium*** are prevalent depending on the host and tissue type studied. Alternaria sp., an endophytic fungus found in mangroves, produced cyclopentenone derivatives and ***Fischer xanthones*** that were inhibitory to ***Fusarium graminearum*** and antifungal to ***Colletotrichum musae***, indicating that these compounds could be used in the development of antifungal agents[35]. Wang et al. (2015) discovered that the endophytic fungus ***Alternaria sp***., found in mangrove The researchers at Xu (2015) gathered the diverse natural products created by mangrove-associated microorganisms over three years (January 2011 to December 2013), and discovered that phenols and lactones were produced by more than 50 different taxa of bacteria[36]. This species of Zygomycetes of the ***Rhizopus*** genera was discovered in a mangrove region of Nigeria and is similarly a filamentous fungus with branches on the ends of its mycelium bodies. It is primarily utilized in conventional food fermentation operations, as well as a source of enzymes for the breakdown of organic contaminants. It is also employed in pharmaceutical fermentation procedures[37].

3.4 Endophyte from Coral

Brevi bacterium sp. L-4 an coral-derived endophytic bacteria produces cyclic-(Tyr-Ala-Leu-Ser) and four naturally occurring compounds namely 3H-imidazole-4-carboxylic acid, 2-methyl-3H-imidazole-4-carboxylic acid, 3-ethylidene-6-isopropyl [38] observed in South China Sea.

4.Endophytic Micro organism

4.1 Endophytic Bacteria

Marine bacteria produces novel physiologically active compounds [39]. As a result of the advancements in marine microbe research, an increasing number of natural compounds with anti-pathogenic activity are being discovered. ***Bacillus*** is a significant component of marine ecology that is widely spread and diverse, and it has been used to isolate several important marine natural products [40]from the ocean. Two novel glycolipid molecules, ieodoglucomide C and ieodoglycolipid Occurs in ***Bacillus licheniformis*** an marine bacteria with antifungal action against plant pathogenic fungus [41]

4.2 Endophytic Fungi

Fungal endophytes from herbaceous plants, and marine algal thalli, including ***Fucus serratus, Fucus spiralis, Fucus vesiculosus, Ceramium sp., Laminaria sp., Ascophyllum nodosum, Enteromorpha sp., Halarachnion ligulatum,*** **and** ***Plumeria*** [38]. Terrestrial plants raise whether marine algae and seagrasses (the

principal angiosperm plants that are submerged in water) host endophytic fungus produce secondary compounds are similar but it was found by Kobayashi and Ishibashi marine endophytic fungi produce secondary metabolites, ,active primary metabolites, with enzyme activity compounds distinct from terrestrial sources [39]. There were two isolates of marine fungus having cellulase enzyme activity, namely ***Aspergillus terreus*** and ***Mucor plumbeus*** [13].

4.3 Endophytic Actinomycetes

Marine ***Streptomyces*** is another major natural product source of marine bacteria that may be found in the ocean. ***Streptomyces*** is the marine actinomycete that has been examined the most extensively, and it is responsible for 60 percent of the novel natural compounds produced by marine actinomycetes, according to research[42]. It was discovered by Buatong et al. that the marine Streptomyces sp. had produced a substance called oligomycin A. This potential biological fungicide can rupture the fungal cell membrane and organelles, as well as impede the germination of spores and the development of appressorium [43].

5. Various Methods Used for Isolation of Endophyte

5.1 Isolation of grass fungal endophytes

Endophytes are surface sterilized ,the plant material to eradicate potential pollutants (mostly bacteria) and fungal epiphytes and molds because fungal epiphytes found in leaf and other plant components. A surface sterilization phase is followed by repeated washes to eliminate any foreign material before plating, which is the most frequent isolation process for fungal grass endophytes. Preparation is needed depending on the plant component that is being utilized. Pretreatment of the plant might include cleaning plant parts with sterile water or alcohol, removing glumes, and other procedures. Sodium hypochlorite is the most often used sterilizing solution, however, there are a variety of additional options available. A few extra actions may improve outcomes, such as regular shaking of the material during all of the phases to ensure that the material is cleaned uniformly and to aid in the loosening of any material from the surface of the material. Chopping the material's ends to promote mycelial development is an additional optional step that may be performed. A nutrient media is plated onto the material after it has been dry-blotted on paper to remove any remaining surface contaminants. Because grass-endophytes develop at a sluggish rate, mycelia begin to appear on the borders of the plant material 7-10 days after plating[44].

5.2 Plant Material

The sterilization and isolation were followed, with minor modifications in accordance with Araujo et al. The leaves cleaned using 70% alcohol,sodium hypochlorite (2.5 percent Cl-), ethanol and finally with distilled water. TSA (1.5 g/L of tryptone; 0.5 percent soy peptone; 1.5 grams of NaCl; 15 grams of agar; pH 7.3) plates were evaluated for the presence or absence of microorganismal growing colony.[45].

6. Endophytic Fungi Yielding New Compounds (Secondary Metabolites From Various Microorganism)

Too far, a variety of biologically active chemicals from marine sources have been identified, each with a different mode of action, including anti-tumor, anti-cancer, anti-microtubule, anti-proliferative, cytotoxic, photoprotective, antibiotic, and antifouling characteristics, among others[4]. A significant supply of novel microorganisms (bacteria, fungus, actinomycetes, microalgae-cyanobacteria, and diatoms) capable of producing bioactive secondary metabolites has also been discovered in the marine environment, even though it is a relatively untapped resource. Bioactive potential of marine microorganisms (both free-living and symbiotic) found astoundingly varied and fruitful in findings

Compound	Biological Activity	Endophytic Bacteria	Source	Reference
Edecomycins		*Pseudomonas viridiflava*	leaves of lettuce (Lactucasativa)	[46]
Griseofulvin	Antifungal	*Abies halophila (Manchurian fir)*	Xylaria sp.	[47]
		Pinus strobus (white pine)	Xylaria sp.	[48]
		Vaccinium angustifolium (blueberry syrup)	Penicillium sp.	[49] [50]
		Taxus brevifolia		
quoiatones	Antitumor (breast cancer)	*Sequoia sempervirens*	Aspergillus parasiticus	[51]
Nodulisporins A,B,C	Antifungal	*Juniperus cedrus*	Nodulis porium sp.	[52]
Brefeldin A	Antifungal ,antiviral and anticancer, protein transport inhibitor	*Texus mairei Torruvia grandis*	Paecilomyces sp. Aspergillus clavatus	[53]

6. Endophytes as Source Of valuable Biopolymer In Drug Delivery

6.1 Nano Sponge

Nanosponges are a modern sustained and controlled release drug delivery system. They are composed of nano-structured hyper branched polymers and cavities that are only a few nanometers wide, allowing for the encapsulation of a wide range of substances, including hydrophobic and hydrophilic substances. A medical researcher has been working on converting a medicine into a targeted drug delivery system for a long time. The challenge is how to put the drug in the correct location in the body while also controlling the release of the drug to prevent overdose. Nanosponges are one of the most effective medication delivery systems available today for dealing with this issue. The nanosponge delivery of drugs platform is made up of a network of specialized polymers that progressively break down and release the medication of some time od of time[54]. Nanosponges are tiny sponge-like structures with a nanoscale size. By their inclusion and non-behavior behavior, they are spherical and colloidal, and they have an extremely high solubilization capacity for poorly soluble medications compared to other pharmaceuticals[55].

In a contemporary dosage form, nanosponges are poowater-solubleuble pharmaceuticals that have been encapsulated and released over a longer periperiodile also enhancing the solubility and bioavailability of the medication[54]. Because of their internal hydrophobic chambers and exterior hydrophilic branching, nanosponges are capable of loading both hydrophilic and hydrophobic medicinal molecules, providing them with unprecedented versatility. The size of the nano- sponge virus in nature is less than 1 micrometer in diameter, and it seems to be a scaffold structure made of naturally degradable polyester[56].

7. CONCLUSION

Diverse endophytic fungal biodiversity with pharmacological and therapeutic properties has been observed in the maritime environment. Marine microorganisms have been used as a source of novel pharmaceuticals and marine fungal endophytes to manufacture a number of unique bio-products with a wide spectrum of bioactivities. Bioactive compounds with various chemical structures are produced in nature, whether indirectly or directly, by complex and dynamic environmental interactions, as shown by marine organisms and related fungi's diverse chemical structures. Bio-resources from endophytic fungus may be used to generate innovative anticancer, antibacterial,

antioxidant, and antifungal drugs, as well as high-yielding or other biotechnological purposes.

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