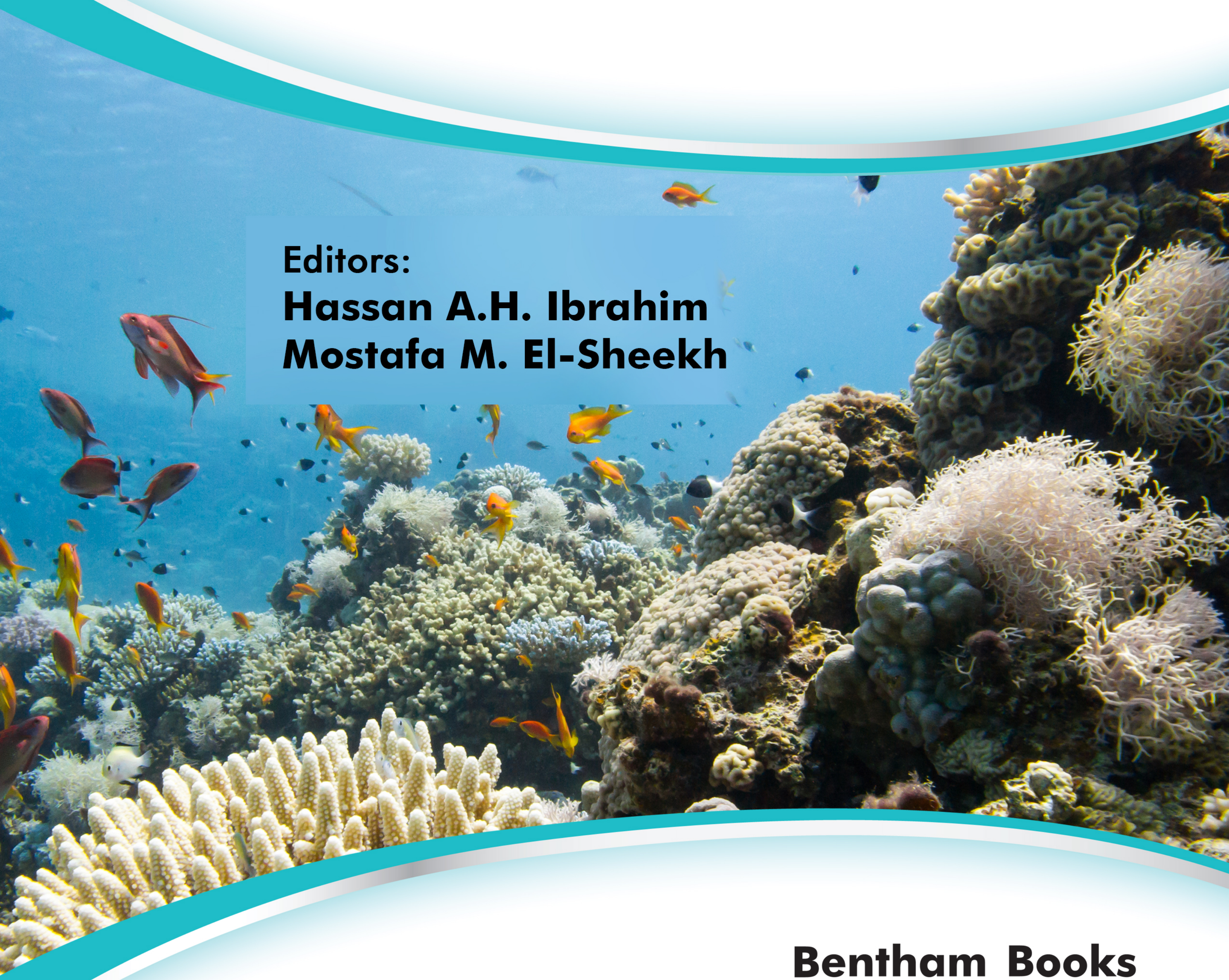
MARINE ECOSYSTEMS: A UNIQUE SOURCE OF VALUABLE BIOACTIVE COMPOUNDS



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Marine Ecology: Current and Future Developments

(Volume 3)

Marine Ecosystems: A Unique Source of Valuable Bioactive Compounds

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PREFACE

Each marine ecosystem, including the open ocean, the deep-sea ocean, and coastal ecosystems, has different components with different physical and biological characteristics. Therefore, marine ecosystems have variability with a wide array of habitats involving mainly seaweeds, seagrasses, coral reefs, and mangroves besides estuaries and various protected areas.

Primarily, the productivity of a certain marine ecosystem refers to the organic matter production by producers or autotrophs (phytoplankton and algae), where the produced organic carbon is supplied to heterotrophs, which obtain their energy only from the organic matter respiration.

Mangrove environment microorganisms provide a large supply of antimicrobial substances creating a broad spectrum of major health chemicals such as enzymes, antitumors, insecticides, and immune modulators. Although the ecology of mangroves is highly diverse in microbiological conditions, less than 5% of species are characterized. In many cases, their ecological role and their potential application are unknown. Recently developed molecular biology and genetics technologies hold a great promise for exploring the potential of microbial diversity. In addition, the antimicrobial potential of the "macroalgal epiphytic microbiome" and the application of "meta-omics" approaches are significant for further exhaustive exploitations of this unique microbiome for future drug discovery.

Most marine biota can survive under stress conditions, as a result, they produce complex metabolites with unique biological properties. These natural substances could be used as functional constituents in the food sector. Moreover, they could aid in the treatment of a wide range of different diseases, including antitumor, anti-inflammatory, antimicrobial, etc.

Microalgae and phytoplankton are rich sources of various pigments like carotenoids, beta-carotene, and polyunsaturated aldehyde. Seaweeds are abundant in vitamins A and C, and also in phenolic compounds, terpenes, etc. Primary consumers like crustaceans and mollusks are reported to produce steroids having high medicinal potential. Carnivorous fishes like herring, shad, and mackerel are the secondary consumers. Mackerel is a great source of the amino acid taurine, which is considered to have beneficial effects on heart health. Top carnivorous fishes like the haddock or cod belong to the category of tertiary consumers. Cod is popular for its "cod-liver oil" which has high contents of vitamins A, D, and E and omega-3 fatty acids whose health benefits are familiar to all. Even the decomposers like marine bacteria and fungi are effective manufacturers of alkaloids, terpenes, peptides, and mixed biosynthetic compounds derived from polyketides. Thus, it will not be an exaggeration to say that the marine ecosystem has a plethora of bioactive compounds, and it can easily be proclaimed that collective efforts in the form of copious research and documentation are required to enable sustainable utilization of this untapped bioresource. This confirms that marine organisms offer a delicate, yet plentiful source for a vast array of novel products whose unique structural features make them suitable drug candidates.

Many challenges threaten the marine ecosystem like climatic change, biological invasions, overexploitation, overfishing, and water pollution. These challenges negatively affect marine biodiversity and then productivity. Human activities, also, place diverse stresses on marine ecosystems, which are predicted to increase, resulting in great impacts on marine ecosystems and then on biodiversity. So, they must be overcome for the potential preservation of various lives in the marine environment. Moreover, numerous challenges threaten the marine natural system, particularly in the field of marine drug discovery. The primary issues include the impact of climate change on marine biodiversity, biological invasions, overfishing, pollution, and habitat destruction, often occurring together in time and space, and have a cumulative effect. Although the additional costs, like specialized services for divers, submarines, staff safety, and costs, can add up quickly, several marine-based medications are actively being developed for commercial use.

Natural bioactive products are up against vast chemical libraries and combinatorial chemistries in the fight for market share. As a result, each stage of a natural product program, from environmental sampling and strain selection to metabolic expression, genetic exploitation, sample processing, and chemical dereplication, must be more effective than ever. Oceans and their immense biodiversity have gifted humanity with a pathway out of the obstacles of health care. The constant need for innovation has been a great challenge for the pharmaceutical industry especially finding new sources for active compounds.

The development of a certain marine drug involves the creation and analysis of large amounts of data, requiring the interaction of scientists from the scientific and industrial communities. Efficiently, the collaboration shares the knowledge, tools, finances, and administrative processes, hence increasing the innovation potential of all parties than a single one. Specifically, at the academic level, the quality of collaboration is evaluated in the number of co-authored articles over some time.

Collectively, the current book has twelve chapters to highlight the biodiversity and productivity of marine ecosystems covering their protected areas and explaining all biotic and abiotic factors that affect the viability of this ecosystem. In addition, it spotlights the potentiality of the biological activities that have been detected by marine organisms. Moreover, it presents an effective strategy for drug discovery from these features. Indeed, this book aims at researchers' students, ecologists, microbiologists, pharmacologists, and biotechnologists working with the living components of the marine environment providing those with the recent information and strategies in the field of drug discovery from unique marine features and resources.

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CHAPTER 1

Biodiversity of Marine Ecosystems

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Abstract: The water covers about 71% of the earth's surface and occupies an area of about 361 million km^2 and a volume of about 1370 million km^3 of water. Oceans and seas are responsible for maintaining the global climate by regulating air temperature and supplying moisture for rainfall. They play a major part in the global carbon cycle, removing almost 25% of the carbon dioxide released by human activity. Furthermore, life would not have begun on Earth without seas, which support the planet's highest biodiversity. They also offer social and economic goods and services, as well as tourism and recreation, maritime transportation, security, and coastal protection. Marine ecosystems include the open ocean, the deep-sea ocean, and coastal marine ecosystems, each of which has different physical and biological characteristics. The variability of the marine ecosystem is the result of the wide array of habitats in seas and oceans. Coral reefs, seagrasses, estuaries, and mangroves are the most important types of marine ecosystems. Variations in the characteristics of the marine environment create different habitats and influence what types of organisms will inhabit them. The marine environment can be divided into zones based on physical features such as depth, temperature, light penetration, and other several factors. There are two main marine realms or provinces, a pelagic realm that includes the water column and a benthic realm that represents the sea floor. Each of these two domains has also been divided into other smaller domains or regions based on the prevailing environmental conditions. Pollution, habitat alteration, and overfishing are the most destructive impacts on the marine environments and their threats are very clear. So, marine ecosystems in oceans and seas should be protected through planned management in order to prevent the over-exploitation of these resources.

Keywords: Marine Ecosystem, Diversity, Oceans, Conservation.

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1. INTRODUCTION

Since ancient times, man has been eagerly looking forward to the sea to reveal its mysteries. The sea was and still is an important source of food and entertainment for people in coastal areas. Although man is not a marine creature, he comes at the top of the marine food chain, where he extracts hundreds of species of fish, invertebrates, and algae on which he depends for his food. The value of what man extracts from the sea has been estimated at about 100 million tons.

In recent decades, several marine organisms such as sponges, marine algae, soft corals, jellyfish, and others are utilized to extract thousands of compounds of medical and therapeutic significance that are used in the treatment of many fungal, bacterial, and viral diseases. The word ocean means the sea surrounding the world and it is derived from the Greek word "*Okeanus*" and the ocean is the largest body of water on the surface of the earth. It was previously well known that there are four oceans.

The water covers about 71% of the earth's surface and occupies an area of about 361 million km^2 and a volume of about 1370 million km^3 of water. Hence the earth is called the water planet or the blue planet. Marine water constitutes 98% of the water on the surface of the globe distributed among 5 oceans, the Pacific Ocean, the Atlantic Ocean, the Indian Ocean, the Arctic Ocean, and the Southern Ocean arranged according to their area. The largest and deepest ocean, the Pacific Ocean, has an area of about 165 million km^2, a maximum depth of 11,000 meters and an average depth of about 4000 meters. The Atlantic Ocean has an area of about 76 million km^2 and a maximum depth of 9000 meters and an average depth of 3000 meters. As for the Indian Ocean, its area is about 68 million km^2 and the average depth is 3000 meters. The area of the Arctic Ocean is about 14 km^2. The Southern Ocean covers an area of about 20 million km^2 [1].

The distribution of marine waters on the earth is uneven, as it covers 60.7% of the earth's surface in the northern hemisphere and increases to reach 80.9% in the southern hemisphere. It covers about 62.1% of the Eastern hemisphere and about 81.2% of the surface of the western hemisphere. Freshwater constitutes only 2% of water around the world and includes rivers, fresh lakes, mountains, ice masses around the poles, and groundwater [2].

Healthy ocean ecosystems are essential for the mitigation of climate change [3] and life would not have started on Earth without oceans [4]. Rising ocean temperatures and ocean acidification mean that the capacity of the ocean carbon sink will gradually get weaker. Oceans play an important role in the global climate by regulating the air temperature and by supplying moisture for rainfall.

They also play a role in the global carbon cycle by removing large amounts of (about 25%) of the carbon dioxide emitted by human activities.

The marine environment is considered as one of the most complex ecosystems on the earth, because it contains many chemicals, physical and biological features that interact together and lead to the creation of this unique ecosystem. Water currents, waves, tides, salinity, light, and sediments as well as the feeding and reproduction habits of marine animals, control the distribution of marine organisms in different zones and at different depths of the marine environment. Marine Environments contain about 90% of the animals on the surface of the earth, so it represents a very important vital stock for life on earth. Marine organisms represent all the different living phyla from the smallest organisms such as fungi and bacteria to the largest species such as whales, dolphins, and sharks such as the whale shark with about 13 meters in length [5].

The marine environment supports many ecosystems in coastal and open ocean habitats that in turn support biodiversity in these ecosystems. Examples include coral reefs, rocky and sandy shores, mangroves, estuaries, kelp forests, and polar seas. These ecosystems provide many services to the society where a significant proportion of the world's population depends intimately on these services. However, the pressure on marine ecosystems and the resources they provide is increasing and threats caused by land-use change, climate change, the invasion of non-native species and other impacts of anthropogenic activities affect biodiversity. As environmental conditions change, species need to evolve and adapt to these changing conditions [5].

Marine ecosystems are closely related to the global climate and studying these ecosystems allows scientists to predict the impact of climate change on marine biodiversity. Monitoring of biodiversity and species distribution and density in the marine ecosystems help managers and policy makers respond to protect, and manage the threatened ecosystems [6].

2. COMPARISON BETWEEN MARINE AND TERRESTRIAL ECOSYSTEMS

Life has started in the oceans much earlier than on land and the diversity at higher taxonomic levels is greater in the ocean than land. Because life began in the oceans, oceans are believed to have more diversified genetic resources than land. A total of 14 animal phyla are restricted to the ocean compared to only one phylum on land (Tables **1** and **2**).

CHAPTER 2

Productivity of Marine Ecosystem Components

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Abstract: The marine ecosystem is the greatest of all ecosystems. Marine ecosystems cover approximately seventy-one percent of the Earth's surface; moreover, they contain approximately ninety-seven percent of the planet's water. Thirty-two percent of the world's net primary production is generated by them. There are many marine ecosystems environmental problems, which include marine pollution, unsustainable exploitation of marine resources (as overfishing to certain species), building on coastal areas, and climate change. From the trophical standpoint, a marine ecosystem has two groups of components: autotrophic components and heterotrophic components. The primary or basic productivity of an ecosystem could be defined as the storing rate of radiant energy by producers (chemosynthetic and photosynthetic) activity as an organic substance that can be utilized as food. The productivity of marine ecosystem greatly refers to the organic matter production by producers or autotrophs “phytoplanktons and algae,” the produced organic carbon is supplied to “heterotrophs,” which obtain their energy only from the organic matter respiration. There are many carbon-nested cycles associated with marine productivity including Grass and Net Primary Productivity (GPP and NPP, respectively) as well as Net community and Secondary productivity (NCP and SP, respectively). Fisheries depend on secondary productivity; thus they rely on both Net primary productivity and the organic matter transferring efficiency to the food web. Environmental factors as well as the change of climate may strongly impact NPP in many ways that rely on the regional as well as local physical settings, ecosystem structure, and functioning medium.

Keywords: Fisheries, Habitats, Human, Marine, Productivity.

1. INTRODUCTION

The Marine water (oceans and seas) forms approximately seventy percent of the Earth's surface that equals about 360000000 km^2 which has a rich wealth of marine life. The marine ecosystem serves as a source of food, energy, and

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minerals. Although the conditions are slightly different than on the land, most, marine organisms' tolerance limits are relatively narrow and their distribution issue primarily controlled by the interrelation between water latitude, distance from shore and depth. Some marine organisms are found in very large depths but the most of species occur in the shallower marine water which encircles the continents: these shallow marine waters form approximately eight percent of the total area of oceans. On the other hand, marine habitats are also classified according to depth Zones into three zones namely, Continental shelf, continental slope, and deep ocean basins [1].

The continental shelf extends from the coast to 200 m depth~~.~~ and about 75 km width averages. This shelf zone collects much of the sediments (deposits of sand and mud) that are carried by the rivers from the land. The slope (continental slope) begins just at the outer edge of the continental shelf. The continental slope is much steeper than the shelf and plunges to great depths of 3.6 km. The width ranges from 20 to 100 km. Submarine canyons extend into these slopes. The canyon heads may form some deep sea fans and levees. The area between the continental slope and the deep ocean floor is known as continental rise. The deep ocean basin is called the abyssal plain. Abyssal hills, gyots, sea mounts, and deep sea trenches are the physiographic features of the basin. The deep ocean basins consist of deep-sea peaks, valleys, and plains which lie beyond the continental margin of the ocean basin. The mid-ocean ridges are the unique features of the ocean basins. Deep valleys also cut across the ridges in many places. Frequent volcanic activity is also expected in some valleys. The two chief sources of deep-sea sediment are the land itself and marine life. Marine life sediment consists mainly of tiny shells and the remains of dead organisms of the plankton. When such matter makes up a large part of sediment, they are called oozes. Comparing marine ecosystem productivity to terrestrial ecosystems (land) revealed certain unique features of the marine ecosystems. In an area of 135.0×10^6 km^2 of terrestrial ecosystem, the Gross primary productivity is 51.2 $kcal/m^2/year$ and the Total gross productivity is 57.4×10^{16} kcal/year, compared with an area of 362.4×10^6 km^2 of marine ecosystem in which the Gross primary productivity is 29.0 $kcal/m^2/year$ and the total gross productivity is 43.6×10^{16} kcal/year). On the other hand, the marine ecosystem is characterized by:

i. Wide marine environment (covering about 75% of the earth's surface).
ii. Very deep as life presents in all depths.
iii. Seas and oceans are continuous.
iv. Continuous water movement in vertical as well as horizontal dimensions.
v. Salty water with 35% an average salinity.
vi. Low dissolved nutrients concentration.

2. ECOSYSTEM COMPONENTS

An ecological system (ecosystem) is a unit consisting of all organisms (*i.e.* the community) present in a certain region and their interaction with the physical environmental conditions, so in the ecosystem, the energy flow leads to a clear well defined biotic diversity, trophic structure as well as material cycles within the ecosystem (Fig. **1**). According to the trophic structure, ecosystems have two groups of components: autotrophic components and heterotrophic components. To describe an ecosystem component, it includes; firstly, biotic components (Fig. **2**) which include: i) Producers (autotrophs: largely algae and green plants), ii) Macro consumers (heterotrophs: chiefly animals), and iii) Micro consumers (saprotrophs: chiefly bacteria and fungi). Secondly, abiotic components include: i) Inorganic substances (*e.g.* C, N, CO_2, and H_2O), ii) Organic substances (compounds) (*e.g.* carbohydrates, proteins, lipids, *etc.*), and iii) The climate (*e.g.* the wind direction, temperature, *etc.*) [1]. However, ecosystems could be classified according to various methods as shown in Fig. (**2**).

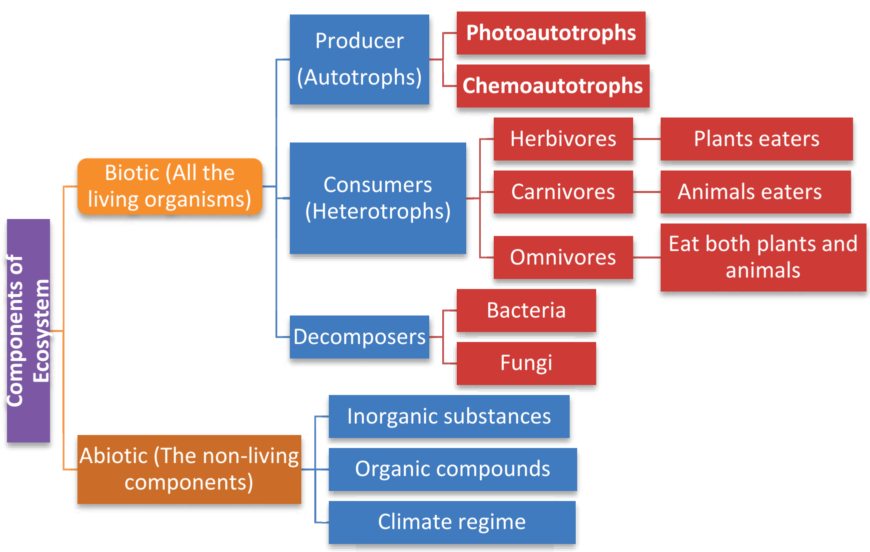

Fig. (1). Components of ecosystem.

CHAPTER 3

Biotic and Abiotic Components of Marine Ecosystem

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Abstract: An aquatic ecosystem is a water-based environment. Aquatic ecosystems include the marine ecosystem and freshwater ecosystems. Two-thirds of the total surface area of the planet is covered by marine water. These ecosystems can be classified into two main categories; i) water/pelagic environment (including; neritic and oceanic zones) and; ii) bottom/benthic environment (including; supra-littoral, intertidal/littoral, and sublittoral zones). Biotic and abiotic factors mean all the living and non-living components of any ecosystem. Biotic factors also include the interactions between organisms and the way they live with or rely on each other. Abiotic factors include all the non-living components, which the living inhabitants rely on to live, grow and thrive. Factors affecting aquatic biomes greatly differ from one water body to the other as the water itself has different properties. Abiotic factors that influence aquatic biomes include light availability, depth, stratification, temperature, currents, and tides.

Keywords: Interactions, Living Components, Non-Living Components, Pelagic, Benthic, Marine Ecosystems.

1. INTRODUCTION

Almost all life forms we are seeing nowadays either on land or in the water first emerged from marine habitats nearly billions of years ago. Marine ecosystems are one of the largest and most prevalent aquatic ecosystems on Earth. They are considered the highly variable and diversified aquatic ecosystems of the Earth and almost make up most of the Earth's surface with about 71% covered by oceans

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(*i.e.* 361 million square kilometers or 140x10^6 square miles), while all other water resources constitute less than 30% (Table **1**), with the depth average of 12,000 feet [1]. The deepest point of which (32,800 feet) located in the Pacific Ocean at the Mariana Trench with a depth of about, being salty with a salt concentration (mainly NaCl) of 3.5% (35 ppt) in an open sea. An ecosystem is made up of the living organisms, the habitat they live in, the non-living structures present in the area, and how all of those relate to and influence each other [2].

Table 1. Distribution of the Earth's water [1].

Water Source	Water Volume (km^3)	% of Total Water	Nature/Availability of Water
Oceans, Seas, & Bays	1,338 x 10^6	96.54	Saline water distributed among various marine ecosystems or/and habitats.
Glaciers, & Permanent Snow	24,064 x 10^3	1.74	Freshwater, locked up in ices and glaciers (unavailable for use).
Groundwater	23,400 x 10^3	1.69	Fresh water, kept under the ground.
Soil Moisture	16,500	0.001	Mostly fresh water, however salinity level determined by the source and the proximity to the sea.
Lakes	176,400	0.013	Some lakes are of fresh water (0.006 out of 0.013%) while others are of saline or brackish water (0.007 out of 0.013%).
Rivers	2,120	0.0002	Fresh water, although the minute amount (1/1000th), it is the most available source for human use.

Ecosystems may vary in size, but all the parts of the ecosystem depend upon each other. If one part of the ecosystem is removed, it affects everything else. Despite some debates around a sole categorization of marine ecosystems, the classification that is largely accepted by most marine scientists is having; estuaries/lagoons, salt marshes, mangrove forests, coral reefs, the open ocean/deep-sea ocean, and the sea floor. Marine ecosystems are a unique set of habitats with a combination of various and well-interacted components of biotic/living and abiotic/nonliving factors. The living component comprises aquatic/marine plants, animals, and microbes/microorganisms, while important the non-living components or factors include sunlight oxygen and nutrients water temperature, depth within the ecosystem as well as the relationship with the land nearby. According to the geographical location, marine habitats show a wide range of temperatures which varied between 0°C to 30°C in the polar regions and the tropical/subtropical regions, respectively [2].

Values in Table **1** show the world's total water supply is about 332.5 x 10^6 million m^3 of water, of which > 96% is saline water (marine). Of total freshwater, over 68 percent is locked up in ice and glaciers [1], and another 30% of freshwater is in the ground. Rivers are the source of most of the fresh surface water people use, but they only constitute about 509 mi^3 (2,120 km^3), about 1/10,000th of one percent of total water as stated in the pamphlet of the United State Geological Survey No.198.

This chapter contains an overview of the marine environment and its various ecosystems and their major components or controlling attributes, types of habitats in accordance to various basis of classification with a referral to its diversity and the various organisms' types live in each type and how they interact with each other and with the habitat/environment surrounding them.

2. IMPORTANCE OF MARINE ECOSYSTEMS

Marine habitats occupy a portion of almost 65-70% of the total planet's surface area, knowing that both marine (saline) and freshwater constitute about 71% of that surface area the oceans hold about 96.5% of all Earth's water (The Hydrologic Cycle, as stated in the pamphlet of the United State Geological Survey No.198). The most of vital gases exchanges are made by marine ecosystems, producing almost 50-80% of the oxygen for human survival (most of this oxygen is made by oceanic plankton "phytoplankton); besides secreting carbon dioxide to help to breathe fresh oxygen [3]. The marine ecosystem is the largest ecosystem and it is of the greatest biodiversity on earth, with nearly 50% of living species on Earth (*i.e.,* 700,000 - 1 million species live in the oceans) and maybe another 1 million yet to be discovered [4].

In addition, almost 57% of atmospheric carbon is mainly captured by marine organisms, including mangroves, salt marshes, seagrasses, and seaweed, which are called "blue forests", however, these vegetated habitats only cover > 0.5% of the seabed [5].

Generally speaking, oceans play an important role in regulating the global climate of the earth, as they absorb almost all heat radiated from the sun and re-distribute it by their currents [6, 7]. Most of this heat is used during the evaporation process, which consequently forms rain and sometimes thunderstorms or hurricanes, so it is fairly said that most of the precipitation is typically originated from the oceans. The climate is an engine that uses heat energy to keep the atmosphere and ocean moving. Evaporation, convection, rainfall, winds, and ocean currents are all part of the Earth's heat engine [8]. In addition to oceans, marine ecosystems include also shorelines, estuaries/lagoons, tide pools, islands as well as some specific habitats; such as mangrove forests, and salt marshes.

CHAPTER 4

Protected Areas in Marine Ecosystem

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Abstract: Marine ecosystems encompass around 70% of the earth's surface and contribute significantly to human well-being by giving social, economic, and environmental advantages to the world's growing population. Marine ecosystems provide a variety of different services that are crucial for human well-being, in addition to being a major source of food, income, and employment. Coastal protection, marine biodiversity, and carbon sequestration are among them. Human activities, on the other hand, place diverse stresses on marine ecosystems, which are predicted to increase, resulting in cumulative impacts on marine ecosystems and biodiversity. As a result, significant efforts have been made around the world to create marine protected areas (MPAs) in order to safeguard and preserve biodiversity, as well as natural and cultural resources. They're usually made by designating zones and prescribing permissible and prohibited activities within those zones. MPAs include the Open Ocean, coastal areas, intertidal zones, and estuaries, among other habitats. The United Nations Convention on the Law of the Sea (UNCLOS), which established the worldwide framework for marine governance in 1982, obligated all governments to protect and conserve the marine environment. In 2000, MPAs covered 0.7% of the Ocean; since then, MPA coverage has increased by more than tenfold to 7.68%. The MPA network will need to be ecologically representative, equitably and efficiently maintained, and of particular importance for ecosystem services in order to meet the aim.

Keywords: Marine Ecosystems, Protected Areas, Human Activities, Cumulative Effects, Biodiversity, Effective Management.

1. INTRODUCTION

The types and geographical extent of marine ecosystems vary greatly. Oceans, seas, intertidal zones, estuaries, lagoons, mangroves, salt marshes, coral reefs, the deep sea, and the sea floor are all part of these ecosystems [1] which occupy approximately 70% of the earth's surface and contribute significantly to human well-being by offering many advantages namely; social, economic, and enviorn-

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mental to the world's growing population. In addition to being a major source of food, revenue, and employment, they provide a variety of other functions that are beneficial to human well-being, such as coastal zone preservation, marine biodiversity, and carbon sequestration.

Mangroves and coral reefs, for example, provide vital shelter from catastrophic weather events like hurricanes and inundations, and the oceans have sequestered one-third of the carbon dioxide produced by human activities [2]. Seagrass meadows are well-known for their valuable ecosystem services [3]. They are one of the most important sources of carbon, with part of it being transferred to the deep oceans, where it provides a vital supply of organic matter in a food-scarce habitat [4]. Seagrass, on the other hand, influences currents and waves by capturing and storing both sediments and nutrients, thereby efficiently filtering nutrient inputs to the coastal ocean [5]. They're also used as a nursery for juvenile stages.

However, human-caused stresses on marine ecosystems have increased considerably and are predicted to continue to rise. These stressors can reinforce one another, having a cumulative effect on marine ecosystems and biodiversity. Among these pressures and their impacts are discussed below:

The rise in sea surface temperature, sea level, carbon dioxide cycle, frequency and intensity of storms and associated surges and swells, regional shifts in water quality [6], and localized impacts due to excess of sediment, contaminants, and nutrients reaching coastal environments are all threats posed by the global climate change [7]. Noticeably, climate change will intensify the severity of extreme weather events, affecting a variety of biota. An estimate of 50 % of salt marshes, 35% of mangroves, 30% of coral reefs, and 20% of seagrass have been lost or deteriorated as a result of climate change influences on marine ecosystems [8]. On the other hand, strong winds, currents, and wave movement, can aid the dispersal of invasive species at regional and global scales [9]. Changes in a species' geographic distribution, phenology, photosynthetic rates, carbon uptake, and productivity have all been observed as areas of influence [10]. These dynamics, when combined, will have an impact on species interactions as well as community composition, trophic webs, and ecosystem functioning.

Marine pollution occurs when chemicals, particles, industrial, agricultural, and residential waste, noise, or the migration of invasive species into the ocean result in negative or potentially detrimental impacts. The majority of marine pollution (80%) originates from land, generally from nonpoint sources like agricultural runoff [11]. However, pollution is a severe problem that endangers marine life and has several impacts on marine organisms. The signs are variable, starting with organisms' weakness, sickness, slow population decline, scarcity, and finally extinction of the species. This decline in biodiversity [12] causes in turn marine ecosystems' degradation. [13].

In 2013, an estimate of 31% of fish stocks were evaluated to be fished at levels that were considered overfished, compared to 10% in 1974. Fully-fished stocks made up 58% of the total number of stocks assessed in 2013, while under-fished stocks accounted for 11% [14]. Fishing that is illegal, unreported, and unregulated (IUU) is also an issue. According to Agnew *et al.* [15], every year, between 11 and 26 million tons of fish are lost to IUU, accounting for an average loss of 18% across all fisheries. Hazardous fishing practices such as trawling or dynamite fishing, as well as land misuse practices in agriculture, coastal development, and other human activities such as anchoring caused habitat degradation along the coast and in the ocean [11].

Tourism can have dramatic effects on both the maritime environment and surrounding islands if it is not regulated or restrained, especially in high-use areas. Tourist ships anchoring in the same spot repeatedly, for example, can destroy coral habitats and seagrass meadows. However, sewage discharge by all users, comprising tourism processes, may be requested if land-based facilities are not enough to meet the area's pump-out requirements. Forecasts of increased tourism numbers, as well as expectations of increased effects of use, should be factored into tourism planning [16].

Mariculture has the potential to disrupt trophic systems, consume natural seed stores, spread diseases, and limit genetic variability, as well as change, damage, or destroy maritime ecosystems. The spread of mariculture along the coast can result in considerable physical changes to coastal habitats, as well as a decline in coastal protection and other ecological functions. Mariculture also has other implications, such as nutrient contamination, antibiotic use, and antifouling agents [16].

Dredging and subsequent dumping of dredge spoil at sea can have severe consequences, particularly in terms of altering the marine ecosystem's hydrographic characteristics. A variety of factors influence the magnitude of the effects, including the site of the dredged area and dumping area, the method and rate of extraction, and the type of gear employed, as well as the characteristics of the seafloor surface, sediments, coastal processes, and the sensitivity of habitats and species. Seabed disturbance, pollutant transmission or re-suspension, sediment movement alterations, and changes in coastal processes can all be caused by dredging or the development of port infrastructure. These consequences have the potential to have a profound impact on local communities (both ecologically and socially) [16].

CHAPTER 5

Mangrove Ecosystem Components and Benefits

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Abstract: There is a wide variety of plant, animal, and microbial life in mangrove forests because of their location at the boundary between terrestrial and marine environments. Because of their central role in the development and upkeep of the mangrove ecosystem, microbes also serve as a useful and significant source of biotechnologically engineered materials. Microbes are essential to the health of the mangrove ecosystem's productivity by aiding in the decomposition and mineralization of leaf litter at a number of different phases of the process. They are capable of recycling nutrients; they can generate or consume gases affecting the global climate; they can remove contaminants; they can process anthropogenic trash. Mangrove environment microorganisms provide a large supply of antimicrobial substances and also create a broad spectrum of major health-boosting chemicals such as enzymes, antitumors, insecticides and immune modulators. However, unlike other ecosystems, mangrove ecosystems have never had their microbial diversity described. Despite the rich diversity of microbiological conditions in mangrove ecosystems, only around 5 percent of species have been classified, and many of them remain enigmas in terms of their ecological importance and practical use. Microbial diversity must be fully utilised to reach its potential, and modern molecular biology and genetics technologies show considerable promise. This Chapter, therefore, attempts to examine and analyze the microbial diversity of mangrove ecosystems in many aspects, such as agricultural, pharmaceutical, industrial, environmental, and medical possibilities.

Keywords: Mangrove, Ecosystem, Microbial Diversity, Floristics, Food Web.

1. INTRODUCTION

Mangroves are special intertidal ecosystems found in tropical and subtropical locations that provide habitat for a wide variety of aquatic and terrestrial creatures. About 60–70% of the world's tropical and subtropical coastlines are covered by mangroves, giving this type of ecosystem a huge ecological footprint. Despite their vulnerability and limited range, these ecosystems are among the

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most productive on Earth [1, 2]. They safeguard and stabilize coastal zones, as well as nutrient-rich coastal water. Periodic tidal flooding characterizes these ecosystems, making environmental elements due to factors that are unexpected, such as salinity and nutrient availability, and different and specialised features are produced. Apart from plants and animals, one of the most important groups in these ecosystems is microbial diversity. The mangrove ecosystem supports a vast range of microbial populations that can adapt to moderately saline and variable environmental circumstances due to the supply of carbon and other nutrients. These microbial populations play a crucial role in the cycling of nutrients including carbon, nitrogen, sulfur, and phosphorus, and consequently manage the mangrove ecosystem's chemical environment [3].

Within mangrove ecosystems, microbial activity is also responsible for important nutrient changes [3, 4]. In tropical mangroves, bacteria and fungi make up 91% of the microbial biomass, while algae and protozoa only make up 7% and 2%, respectively [5]. These bacteria' complex interactions maintain the balance of several biogeochemical processes, as well as the nutritional condition and ecological equilibrium. In mangrove ecosystems, free-living bacteria, fungi, and yeasts have been found to play an important part in the creation of detritus [6]. Bacteria of various types are commonly found in the ecosystem [7], where photosynthesis, nitrogen fixation, and methanogenesis are the activities that take place [8]. Several investigations have demonstrated the distinct microbial makeup of mangrove sediments [9].

Microbial diversity in mangrove sediments has a key role in understanding the biogeochemical cycle and pollution removal processes [10]. Mangrove ecosystems' microbial abundance can also provide information on their ecological significance as well as their particular biotechnological possibilities in agriculture, industry, medicine, and pharmaceuticals [1b, 11]. The advent of modern molecular techniques based on nucleic acids has led to numerous recent discoveries in the field of microbial ecology [12]. For measuring microbial diversity in natural habitats, this method eliminates the constraints of classic culture procedures. Even though we now comprehend microbes and microbial activities, we are just beginning to scratch the surface of microbial variation. This natural resource needs to be investigated in order to make the greatest use of it. The unique characteristics of a mangrove, as well as bacterial species' adaption to those environments, constitute a significant source of biotechnological potential resources to be tapped [13]. Beneficial enzymes, proteins, antibiotics, and salt-tolerance genes have been found in microorganisms from mangrove ecosystems. This review brings together the most recent results on mangrove microbial biodiversity from several fields of study to examine the enormous biotechnological potential of mangrove microbial flora.

2. FACTORS INFLUENCING MANGROVE DISTRIBUTIONS

While the genetic makeup of today's mangrove flora is clearly influenced by current climatic and geographical conditions [14]. It appears to be mostly obsolete. Past events and circumstances have shaped where species are today. As a result, today's distributional patterns aren't always explicable solely by present deterministic reasons. Furthermore, a variety of factors influence each mangrove plant type, including distinct physiologies, ecology, dispersal ability, propagule stability, and persistence. Ten overarching elements (divided into three categories) with the greatest influence on mangrove biogeography and evolution are presented below. These criteria are determined by a number of authors' findings, including [14c, 15], which have been amended further here.

2.1. Floristics and Biogeography

Although the number of species in the 80 taxa is not particularly large, mangrove taxa are found across a wide range of plant family lineages [15]. They mostly consist of a small but diversified group of shrub and tree species from 18 plant groups, total 69 species and 11 hybrid intermediates. There are 32 genera in total, with all but one of them being flowering plants. Mangrove species' distributional ranges are extremely diverse [16]. Others have distributional ranges that are more localized over the world. The Indo-Malesian (Fig. **1**) area now serves as the primary diversity hotspot for mangroves, analogous to other shallow water, and tropical marine environments such as seagrass and coral species [17].

Fig. (1). Mangrove area in Malaysia image: Missgioia.com.

CHAPTER 6

Macroalgal Epiphytic Microbiome: A Potential Source of Novel Drugs

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Abstract: In the marine rocky intertidal ecosystem, macroalgae (seaweeds) serve ecosystem engineers that create, modify, or maintain the physical habitat for their own and other species. Intriguingly, most marine macroalgal species evolved with microbial colonization and biofilm formation on their surface. The macroalgae (basibiont) and associated epiphytic microbiota (epibiont) act as a functional unit known as a "macroalgal holobiont," characterized by its complex chemical interactions. In this non-trophic association, the epiphytic microbial biofilm forms a protective layer essential in host defense against foulers, consumers, or pathogens. In addition, antimicrobial activity is widespread among these epiphytic microbes. However, due to their thinness and often negligible biomass, the chemo-ecological impact of this epiphytic microbiome is severely underestimated. This chapter aims to review the antimicrobial potential of the "macroalgal epiphytic microbiome" and introduce the application of "meta-omics" approaches for further exhaustive exploitations of this unique microbiome for future drug discovery.

Keywords: Bioactive compounds, Epiphytic bacteria, Macroalgae, Meta-omics, Seaweeds, Secondary metabolites.

1. INTRODUCTION

Over the last few decades, our society has faced major public health crises due to the newly emerging and re-emerging infectious diseases. Emerging infectious diseases are newly identified infections that cause local or global public health problems, for example, Chikungunya, Zika, and SARS-CoV2. The re-emerging infectious diseases were a major health problem globally or locally in the past and then declined remarkably, becoming health problems at present due to the reappearance or increase of the infection. Some examples of re-emerging infectio-

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us diseases are Diphtheria, Malaria, Tuberculosis, and Cryptosporidiosis. In addition, the emergence of antimicrobial-resistant pathogens has recently become a global public health crisis. Antimicrobial resistance (AMR) occurs when pathogens evolve mechanisms to evade the effects of antimicrobials. Overuse or inappropriate use of medicines contributes to the increase of AMR. The pathogens acquire this "purpose-built ability" by rapidly evolving cellular and molecular mechanisms and transmit it to their community quickly [1, 2]; consequently, we are rapidly running out of treatment options for common infections. Finding new drugs has become a global health priority to prevent these epidemics.

Over the last fifty years, the marine environment has represented a promising source of natural bioactive compounds with pharmaceutical relevance. More than 30,000 defined chemical compounds were reported from about 13,000 sampled marine organisms [3]. Eventually, the most marine-originated drug-lead compounds isolated and identified in higher organisms are the products of associated microbes (endophytic or epiphytic microbes) [4]. So far, nine marine-originated drugs have been approved by the FDA and multiple compounds are in clinical trials, which suggests a success ratio of 1 in 3300, which is orders of magnitude better than synthetic molecules. Notably, all these drug discovery successes come only from the study of 0.02% of organisms of about half a million extant marine species. Thus, most marine species remain unexplored in the context of drugs from the sea. It is now paramount to turn our attention to the least studied marine biota to discover the novel drug molecules' new source for our sustainable future. One such unexplored marine microbiota is the "macroalgal epiphytic microbiome", which exhibits antimicrobial potential against pathogens and could be a potential source of novel drug molecules for our sustainable future.

Macroalgae are multicellular aquatic photosynthetic plant-like organisms easily observed without a microscope, also known as Seaweeds. They lack the characteristic structure of higher plants, such as rooting systems, true leaves, and encased reproductive organs. The macroalgal's main body is termed the thallus, characterized by holdfast for attachment at the substratum, blades (a flattened branch of the thallus), and strips (a stem-like structure that does not have proper vascular tissue). They are most commonly found in marine intertidal zones, where the ocean meets the land. The marine intertidal ecosystems are the most temporally and spatially variable marine habitats. It is continuously experiencing the fluctuation of temperature, salinity, tides, and nutrient supply; consequently, the organisms living in this habitat have evolved with strong biotic interactions that enable them to cope with environmental stresses. In this hostile environment, the marine macroalgae serve the role of "ecosystem engineers" who create, modify, and maintain the physical habitat for their own and other species [5].

Taxonomically, macroalgae are not a single entity; they are distributed in three major groups of eukaryotic algae: Rhodophyta (red algae), Phaeophyta (brown algae), and Chlorophyta (green algae). According to the seaweed site (https://www.seaweed.ie/), more than 10,000 macroalgal species have been described to date; about 7000 species are red algae, about 2000 species are brown, and about 1800 species are green algae. In addition, the prokaryotic colony-forming cyanobacteria are also considered macroalgae.

In nature, most higher eukaryotic organisms maintain a stable relationship with the microscopic organisms, associated either on the surface (epiphytic microbes) or inside (endophytic microbes) host organisms. Purposefully, most marine macroalgae secrete various organic exudates to attract diverse microorganisms for colonization on their outer surface. Upon successful colonization, these microorganisms form a thin layer of biofilm on the outer surface of macroalgae, which acts as a second skin of the host organism. The macroalgae (basibiont) and associated epiphytic microbiome (epibiont) evolved as a functional unit known as "macroalgal holobiont" (Fig. **1**). In this non-parasitic association, the epiphytic microbiota secures the nutrients from macroalgae and protects their host by secreting the bioactive compounds. Moreover, the nutrient-rich microalgae surface ultimately leads to high competition among the pelagic microbial communities for colonization, particularly the bacteria [6]. The bacterial species that successfully colonize on the macroalgal surface might evolve to produce certain antimicrobial compounds to sustain competition from other pelagic bacteria (Fig. **1**). These suggest that the macroalgal epiphytic microbiome could be a potential repository of novel antimicrobial compounds for future drug discovery. However, the antimicrobial potential of this unique microbiome is least explored due to its slimness and often negligible biomass. This chapter aims to review the antimicrobial potential of the "macroalgal epiphytic microbiome" and to introduce the application of "meta-omics" approaches that can be implemented to explore their full antimicrobial potential for future drug discovery.

2. BIOTIC INTERACTIONS WITHIN MACROALGAL HOLOBIONT

The concept of holobiont was initially rooted in symbiotic research to refer to a simple biological entity involving a host and a single inherited symbiont [7]. Later, it was extended to define a host and its associated microbial communities, which act as a functional unit and characterize complex chemical interactions. In holobiont, the microbial association can be either endophytic or epiphytic. Endophytes live within the host without causing apparent disease, whereas epiphytes live on the surface of the host. Macroalgae harbor both types of microbial association.

CHAPTER 7

Bioactive Compounds from Components of Marine Ecosystem

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Abstract: With the advent and rapid progress of the novel blue economy, the prospect of large-scale commercial production of diverse natural bioactive compounds from aquatic biota is likely to be realized in the near future. The biodiversity of the marine biota represents a potentially abundant source of new biomolecules with potentially different economical applications. Most of these biotas are able to survive under stress conditions, as a result, they produce complex metabolites with unique biological properties. These natural substances could be used as functional constituents in the food sector. Moreover, they could aid in the treatment of a broad range of different diseases, including antitumor, antioxidant, antiaging, anti-inflammatory, and antimicrobial. The special properties of these compounds make them an attractive group deserving increasing scientific interest. It is interesting to note that there are some biomolecules exclusively found in marine biota, including phlorotannins and sulfated polysaccharides. This chapter explains the bioactive molecules from different marine biota as well as illustrates their chemical structure and highlights their new biologically active form.

Keywords: Biopolymers, Bioceramics, Marine biomaterials, Marine biota.

1. INTRODUCTION

Oceans, marine habitats, are characterized by their biodiversity due to containing nearly 97% of all organisms on Earth. About 178,000 species belong to 34 phyla according to the Global Biodiversity Assessment by the United Nations Environment Program [1]. They have a wide range of products and services for humans and play important roles in the worldwide preservation of nutrients and climate regulation. Knowingly, life in oceans produces 30% of the oxygen nece-

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ssary for breathing, while human fish intake accounts for 16% of our source of animal protein especially in developing nations (IUCN, Europe).

In addition, the marine world is a rich natural resource for many biologically active compounds relating to the oceans' phenomenal biodiversity. Also, marine organisms live in complex habitats and are exposed to severe conditions, therefore producing a wide variety of potent bioactive substances that cannot be found elsewhere [2].

Moreover, in contrast to terrestrial organisms, marine macro- and microorganisms (including marine bacteria, fungi, sponges, microalgae, seaweed, crustaceans, mollusks, fish, and small vertebrates) are composed of biomaterials and secondary metabolites with a wide variety of distinctive structural and functional characteristics [2, 3] with both environmental and economic advantages which support their possible applications in many fields, such as, biomedicine, healthcare, food preparation, and tissue engineering devices [2, 4].

The Dictionary of Marine Natural Products and MarinLit database (http://pubs.rsc.org/marinlit/) contains more than 30,000 marine compounds [5] and around 1200 new marine biomolecules are detected yearly and only 5% of them are of European origin [6]. About 150-200 new compounds are now extracted from marine fungi per year [6]. While, marine bacteria produce over 100 new biomolecules like fatty acids, polyketides, alkaloids, and terpenes marine bacteria yearly [7]. Around 40 novel metabolites like macrolides, terpenes, brominated aromatics, and alkaloids were isolated from Ascidians (Tunicates) yearly [7]. Previously, more than 3000 compounds are isolated from Cnidarians species which most of them are terpenoids [8].

In general, marine biomaterials are categorized upon more levels, but they can be classified into; pigments, toxins, fatty acids, phenolic compounds (terpenes, flavonoid, tannins), polysaccharides (such as, chitin, chitosan agar, alginates, carrageenans, *etc.*), peptides (enzymes, collagen, and bacteriocins), glycosaminoglycans (chondroitin sulphate, heparin, and hyaluronic acid), ceramics (biosilica, calcium, and phosphorous complexes), and others [7 - 9].

2. CATEGORIES OF MARINE BIOACTIVE COMPOUNDS

In general, marine bioactive compounds are categorized according to their nature, chemical composition, role, and efficacy. Nevertheless, there is no clear and standard classification for such a proposal in the literature. Therefore, the current chapter presents for more effective categorization of marine bioactive compounds and all marine-origin biomaterials. However, they are classified depending on their nature and role into four general classes, such as marine pigments, marine ink, marine toxins and defense secretions, and marine storage food.

Several marine natural pigments, toxins biopolymers (*e.g.* proteins and polysaccharides), unsaturated fatty acids, bioceramics, and other bioactive substances (like antibiotics, enzymes, nanoparticles, *etc*.), have been isolated and tested in several ecomical fields, such as; food processing, tissue engineering, drug delivery, as well as other vital applications based on their major unique properties [10]. Moreover, all of these compounds play significant biological roles in their habitat.

3. TYPES OF MARINE BIOACTIVE COMPOUNDS ACCORDING TO NATURE AND ROLE

3.1. Marine Pigments

Natural pigments such as carotenoids, chlorophylls, and phycobiliproteins are known to be abundant in marine biotas. Several investigations have reported that natural pigments have a significant potential for pharmaceutical uses [11]. Marine pigments are widespread in marine algae and other living organisms like; bacteria, fungi, mammals, and invertebrates. In general, pigments, besides their colors, are made up of different chemical contents such as melanins and terpenoids, which are found in particular in bacteria and algae. In addition, these pigments have received specific attention because they show many biological properties *e.g.* antimicrobial, antioxidant, antitumor, anti-angiogenic, anti-inflammatory, and neuroprotective activities [12]. Furthermore, both sessile and non-sessile invertebrates commonly possess beautifully coloured aquatic species, particularly those from tropical regions. These spectacular natural colors are dominant in species inhabiting shallow waters, in animals exposed to bright light, and also in those living in dark areas. Also, these organisms show variances in color with depth and geographical location and display great variety in their color modeling. These color characteristics serve many purposes. Clearly, the distribution and function of pigments seem to differ among invertebrate classes playing a significant role in marine organism's interaction and may be involved in their physiological processes. However, in marine biotes, pigments from all the main structural classes of natural products are present [13].

The secondary marine bacterial metabolites, especially the colored species, have various biological abilities such as antibiotics and anticancer efficiency. In particular, numerous bacterial species have been studied, including marine actinomycetes, pseudoalteromonas, and cyanobacteria [14]. On the other hand, the bacterial pigments mainly are one of the following types:

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CHAPTER 8

Potentiality of Marine Ecosystem Bioactive Compounds

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Abstract: Of the several types of aquatic ecosystems, marine ecosystems are the largest and are characterised by high salt concentrations. Therefore, aquatic flora, fauna and microbes which are highly halophilic can be found here abundantly. Apart from oceans and seas, there are various other types of marine habitats like salt marshes, estuaries, intertidal areas, coral reefs, lagoons and mangroves . Bioactive compounds are those chemicals produced typically in small quantities by plants, animals or microbes for their own protection or functioning, but have beneficial effects on human health. Since marine ecosystems are exceptionally rich in biodiversity, the prospect of availability of the bountiful bioactive agents can easily be conjectured. Primary producers like microalgae and phytoplanktons are rich sources of various pigments like carotenoids, beta-carotene and polyunsaturated aldehyde. Sea-weeds are abundant in vitamins A and C, and also in phenolic compounds, terpenes, *etc.* Primary consumers like crustaceans and molluscs are reported to produce steroids having high medicinal potential. Carnivorous fishes like herring, shad and mackerel are the secondary consumers. Mackerel is a great source of the amino acid taurine, which is considered to have beneficial effects on heart health. Top carnivorous fishes like the haddock or cod belong to the category of tertiary consumers. Cod is popular for its "cod-liver oil" which has high contents of vitamins A, D and E and omega-3-fatty acids whose health benefits are familiar to all. Even the decomposers like marine bacteria and fungi are effective manufacturers of alkaloids, terpenes, peptides and mixed biosynthetic compounds derived from polyketides. Thus, it will not be an exaggeration to say that the marine ecosystem has a plethora of bioactive compounds, and it can easily be proclaimed that collective efforts in the form of copious research and documentation are required to enable sustainable utilisation of this untapped bioresource. This review is presented here as a small step to reach that goal.

Keywords: Bioactives, Marine Ecosystem, Bioresource, Phytochemicals, Toxins.

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1. INTRODUCTION

Blue biotechnology (or marine biotechnology) is a new field that uses marine resources as either a source or a target for biotechnological applications [1]. Seawater occupies approximately 361,000,000 square km (139,000,000 square miles) of the Earth's surface, accounting for approximately 71% of its total area [2]. The marine ecosystem supports the most complex and abundant faunal and floral communities and thus has borne abundant biologically active agents but has been only partially explored till date. The European Union's maritime frontier is the world's largest, with a 25 million-square km economic zone. Apart from the marine ecosystems, other large oceans including the Indian Ocean, the Pacific Ocean, and the Arabian Sea has also been considered as hotspots for bioactive compounds [2]. When all sea-dependent economies are included, the European Union's marine economy employs 5.4 million people. The sea and its coasts are significant contributors to the economic structure. For instance, India has 8,118 km coastline with an exclusive economic zone (EEZ) [3]. The geographical, morphological and climatic diversity of the Indian terrains has resulted in a highly diversified coastal flora and fauna.

Like all other ecosystems, the marine ecosystem also has two components: biotic and abiotic (Fig. **1**). The biotic components are classified as producers, consumers, and decomposers, while the abiotic components consist of the nutrient availability, moisture content, soil type, wind or water currents, temperature, available sunlight, dissolved oxygen, *etc.* In sea water, numerous types of salts are present, of which Na, Ca, Mg, and K salts are found in the highest concentrations. The broad categories of aquatic ecosystems include: the freshwater ecosystem, the transitional ecosystem and the marine or ocean ecosystem, of which the last one is the largest and most complex. Marine ecosystems are characterised by a high salt content in their waters and marine habitats are the most common of all the forms of ecosystems on the earth. They are teeming with life, supplying oxygen and acting as the habitat for a diverse variety of animals. Marine ecosystems are usually divided into six categories: estuaries, salt marshes, mangroves, coral reefs, open-sea and deep-sea [1].

The word "bioactive" is a shortened version for "biologically active". To put it simply, a bioactive compound is a substance that has biological activity. It is characterized as a compound that affects, causes a reaction, or triggers a response in living tissues. Depending on the drug, the dosage, or the bioavailability, the effects of a bioactive agent may be positive or negative. Marine life is interesting and has a lot of potential for drug research and development. The number of natural products isolated from marine species is steadily increasing. Natural products of unique structure and function originating from marine invertebrates are used in the current concept of human ailment care. Cephalosporin, cytosine, saxitoxin, didemins, and other clinically important biodynamic agents derived from the sea are some of them. This review presents a bird's eye view of the marine bioactives including marine toxins [1].

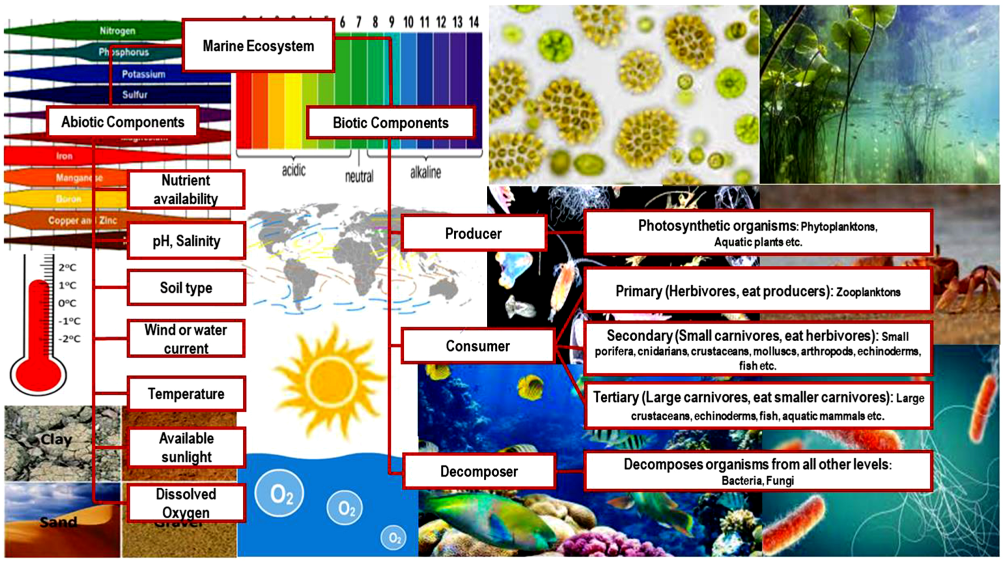

Fig. (1). The abiotic and biotic components of the marine ecosystem.

2. OVERVIEW OF BIOACTIVES AND MARINE ECOSYSTEMS

To study the occurrence of bioactive agents, which are the results of thousands of years of evolution and natural selection, it is important to have an overall idea of the different zones of marine ecosystems and the organisms inhabiting them. Lotic ecosystems which are most commonly found in unidirectionally flowing, fast-moving waters including springs, creeks, rivers and streams and has high contents of dissolved oxygen. These habitats are home to several insect species such as beetles, mayflies, and stoneflies, as well as many fish species such as trout, eel, and minnow. The term lentic is used to describe water that is stagnant or relatively still and they provide habitat to organisms that can survive or thrive in stagnant water. The key examples of the lentic ecosystem are lakes and ponds [4].

Cyanobacteria, green algae, frogs, plants, alligators and water snakes can all be seen in these habitats. Wetlands are basically marshes. Insects like dragonflies and damselflies, as well as birds like the heron and fish make up the animal life of this habitat. The marine ecosystem occupies the bulk of the earth's surface area. Salt

CHAPTER 9

Challenges and Opportunities in Marine Ecological System and Drug Discovery

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Abstract: Marine organisms offer a delicate, yet plentiful source for a vast array of novel products whose unique structural features make them suitable drug candidates, pesticides, marine anti-fouling agents, and more. There are many challenges that threaten the marine ecosystems like climatic change, biological invasions, overexploitation, overfishing, and water pollution. These challenges negatively affect the marine biodiversity and then productivity. So, they must be overcome for potential preservation of various lives in the marine environment. The current chapter will present various opportunities in marine drug discovery and will also discuss the problems encountered in marine drug discovery.

Keywords: Marine Ecosystem Development, Drugs Development.

1. INTRODUCTION

The resources already available for pharmaceuticals are already in use due to the rapid increase in the global population. Due to the rising demands of the global population, drug makers are therefore constantly searching for new sources to provide efficient and secure medications [1].

The ocean is home to all lives on Earth, and contains 32 of the 33 known animal phyla, 15 of which are entirely marine. Over the past 50 years, more than 20,000 natural compounds have been found in the marine environment [2].

The antibacterial, immunomodulator, antifungal, anti-inflammatory, anticancer, antimicrobial, neuroprotective, analgesic, and antimalarial characteristics of aquatic species are screened. All across the world, they are heavily utilised in the

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development of novel drugs. Research on these medications with marine origin is possible thanks to marine pharmacology. Few institutions in India provide these chances, which can aid in our search for new medications [1].

The increase in isolated marine natural products (MNPs), from a number close to 20 per year in 1984 to a number of over 1,000 per year in 2010 demonstrates the increased interest in MNP-based drug discovery [2]. Over the past few decades, marine-based drug discovery has advanced significantly in the urgent search for new pharmaceuticals. As a result, we now benefit from a number of approved marine natural products (MNPs) to treat cancer and pain, and a further group of promising leads are currently being tested in clinical trials. The structural complexity and low bioavailability of MNPs, however, have made their identification and supply difficult. Their production is mostly dependent on chemical synthesis and source extraction from marine sources, both of which have significant prices, are not sustainable, and have serious environmental issues [3].

Several challenges pose a threat to the marine natural system, limiting options, particularly in the field of marine drug discovery. The challenges and issues that arise as a result are numerous. They primarily include the impact of climate change on marine biodiversity, biological invasions, overfishing, pollution, and habitat destruction, often occurring together in time and space, and have a cumulative effect. Such changes in the ecosystem can have a significant impact on species abundance and distribution, marine biodiversity, ecosystem functioning and services, and ecosystem functioning and services [4]. Many marine species are found in isolated regions, and traveling to and from these locations can cost a lot of money. Additional costs, such as specialized services for divers, submarines, staff safety and costs, can add up quickly. The ship and submarine cost $14,500 per day, as an example of the prohibitive costs involved in collecting marine organisms [5].

Seven authorized drugs and 12 agents have been found in clinical trials as a result of continued advances in the field of MNPs. These molecules are either natural products, engineered natural products, or molecules based on the structures of natural products [6].

Mostly, MNPs are obtained from marine species found in shallow water tropical habitats. Algae, sponges, corals, and other invertebrates, as well as microorganisms, have made significant contributions to the discovery of new MNPs. Clinical trials have shown that marine invertebrates are a major source of MNPs [7]. Furthermore, increasing evidence indicates that several compounds belonging to the biomass of macroorganisms including sponges, tunicates and mollusks are synthesized by or associated with symbiotic microorganisms, or derived from a diet of prokaryotic microorganisms, rather than produced by the organism itself. In contrast to terrestrial plants, which have a higher concentration of secondary metabolites, marine invertebrates, and microorganisms produced significantly more biologically active natural compounds than marine plants [2].

With such a diverse range of organisms and virgin areas for marine life, the potential for more new products to emerge from the sea is great. The oceans are an outstanding source of new potential drugs, due to the curiosity of research and industry. As mentioned earlier, scientists have developed drugs in a variety of classes, the most important of which are anticancer, anti-inflammatories, analgesics, and antivirals. Worldwide, these lead compounds are in various stages of preclinical clinical research. Several marine-derived drugs are showing promise in treating a variety of chronic and incurable disorders, such as cancer. As a result, it may prove to be a new chapter in making chronic disease treatment affordable and effective. On the other hand, the marketing of promising micronutrient products is based on preclinical and clinical data [8].

Existing active natural product screening should be expanded, as well as a large and rapid random screening approach. Many universities and research institutes are creating new departments and educating people to work in this field. Furthermore, technology must be improved for drug development, approval, and commercialization. Medical pharmacologists around the world should consider further study in marine pharmacology to discover new drugs. Advances in marine pharmacology will assist in the efficient use of abundant marine resources [8].

2. CHALLENGES THREATENING MARINE ECOLOGICAL SYSTEM

The challenges of preserving and sustaining the marine environment are enormous, and the world must move quickly to overcome them. A variety of global, regional and local human pressures are gradually changing marine ecosystems worldwide [9, 10]. Climate change, biological invasions, overexploitation, pollution, and habitat degradation are examples of stressors that often occur in time and place and have a cumulative effect. Such environmental changes can have a significant impact on species abundance and distributions, marine biodiversity, and ecosystem functioning and services [4]. Despite advances in understanding the effects of individual stresses on marine populations, habitats and ecosystems, the cumulative effect of many stressors remains poorly understood [11]. Environmental changes also affect marine populations, habitats, and ecosystems. As a result, it is critical to understand how multiple human hazards, marine creatures, and ecosystems interact and influence each other [12].

CHAPTER 10

Effective Strategy of Drug Discovery from Marine Ecosystem

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Abstract: The bulk of today's medicines have been derived from natural sources in the past. In the last 50 years, more than 20,000 inspirational natural resources have been found in the aquatic world. The field of marine natural product chemistry is a relatively new field, with roots in the 1960s and an emphasis on drug development in the 1980s. Marine species constitute a significant portion of the oceanic community, and they play an essential role in the production of medicinal molecules and cosmeceutical with naturally effective moieties. They're full of potential antimicrobial, immuno-suppressive, anti- carcinoma, anti- viral, and protease inhibitory compounds that could be used in new therapeutics. Numerous compounds which care possibly about the photoprotective mechanisms of strong pharmaceutical and cosmeceutical value have previously been isolated from diverse marine sources like cyanobacteria strains, lichens, fungi, algae, animals, plants and phytoplankton. Due to public concern about ecosystem health and the consequent increase in aquaculture's supply of seafood in industrialized nations, several marine-based medications are actively being developed for commercial use. *Corallina pilulifera* extracts, for example, showed anti-photoaging properties or photoprotective properties derived from marine sources. To combat UV-A-induced oxidative stress in human dermal fibroblast (HDF) cells, these extracts were developed to provide high antioxidant activity and protection against DNA damage while also inhibiting matrix metalloproteinases (MMPs), a key player in skin photoaging caused by UV-A exposure. Natural bioactive products are up against vast chemical libraries and combinatorial chemistries in a fight for market share. As a result, each stage of a natural product program, from environmental sampling and strain selection to metabolic expression, genetic exploitation, sample processing, and chemical dereplication, must be more effective than ever. Hence, in the presented review, attempts have been made to illustrate more on the effective strategy of drug discovery from the marine ecosystem.

Keywords: Natural bioactive Product, Cyanobacteria, Marine Ecosystem.

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1. INTRODUCTION

Many of the new molecular chemical entities used as medicines are derived from or stimulated by natural bioactive compounds [1 - 6]. Human diseases have been treated since the birth of medicine with chemical substances derived from plants, microorganisms, and animals. Between 1970 and 1980, Western pharmaceutical industry research into natural bioactive products peaked as a source of new human treatments, culminating in a pharmaceutical world dominated by non-synthetic compounds. There are 877 novel chemical entities (NCEs) based on natural bioactive compounds, semi-synthetic analogues, and synthetic formulations disclosed between 1981 and 2002, accounting for over half of the total [7 - 9].

The aquatic ecosystem is the last major frontier in terms of natural medication supplies. Marine ecosystems were only recently recognized as having the ability to produce a wealth of experimental new products, perhaps due to the difficulties of living underwater for long periods. Chemists have been deciphering the fine structures of novel organic compounds formed by marine plants and animals since the 1970s. They were taken aback when they discovered a very different world for biosynthesis, with novel building blocks and unprecedented enzymatic reactions. As a result, it was realized that marine sources have a lot of scope for developing new medicines. Numerous collaborations have been formed in the latest years to promote academic marine science's connection with the worldwide pharmaceutical industry. The medicinal trade currently knows the world's oceans as an important frontier for medicinal skill, even though this relationship is still incomplete. The advent of this new field often referred to as marine pharmacology, has piqued the scientific community's interest. Great progress has been made in the exploration of underwater drugs since the early 1970s trials. In the 1980s, several studies collaborated and started to look at the oceans' potential and the bioactive agents derived from them for medicinal purposes. The vast majority of originally discovered drugs were ineffective in treating diseases. Some molecules, on the other hand, have been discovered to have significant biochemical properties that have affected our understanding of human diseases. Pharmacological probes, as these molecules are known, can revolutionize our understanding of disease's underlying biochemistry. For example, manoalide (Luffariella variabilis) and okadaic acid (Halichondria akadai) are two unique marine sponge molecules with an enzyme inhibitory impact, which are commercially available for biochemical researches [7, 10, 11].

Natural bioactive compounds, their selectivity, potency, and mechanisms of action have developed as critical adaptations naturally, serving as predator defence, warding off competitors, pests, and diseases, and influencing reproduction and alimentary activity. As a result, their relevance as drug candidates stems from natural selection [12]. While a comprehensive discussion of the potential natural roles of biologically active compounds would be lengthy, it is worth mentioning that knowledge of the chemo ecological status of natural bioactive compounds is scant. Chemical ecology is a relatively recent field that studies chemically mediated ecological relationships between species [13]. As an alternative, the conventional man-centered view on natural bioactive products, which emphasizes probable drugs, has ancient origins and continues to be a major driving force in natural food science. However, during the past years, the significance of natural products in medication findings has shifted significantly. With pharmaceutical companies shifting their focus away from natural product analysis and toward building huge chemical libraries using combinatorial chemistry in the mid-century, the discipline briefly recovered before falling out of favor. Though natural products or derivatives have accounted for 70% of all authorized pharmaceuticals in the previous 25 years, just a handful of new combinatorial compounds have been recognized as medicines [14 - 16]. According to Harvey and colleagues (2015), the development of therapeutics based on natural bioactive products has remained constant throughout the genomic era, despite the introduction of numerous innovative techniques that facilitate the detection of biologically active products and aid in the identification of novel mechanisms of action [17].

Several of such methods include a recapitulation of tumor ecosystems in three-dimensional culture models [18], the use of quantitative high-throughput screening [19], patient-oriented screening, the use of cut tissue slices [20], and “organs-on-chips” approaches [21], among others. Hence, in this chapter, the attempts were applied to review some of the marine origins of natural compounds and possible effective methods of drug discovery.

2. MARINE ECOSYSTEM

2.1. Marine Chemical Ecology

Nature-inspired drug development is linked to the discovery of new natural biodiversity, including those in the ocean, which covers 70% of the earth's surface and is the world's richest untapped resource. During the first Census of Marine Life (2000-2010), scientists discovered an incredible quantity of marine biodiversity. Natural product-based drug research has traditionally focused on substances derived from terrestrial species such as bacteria, fungi, and, in particular, Trachaeophyta, many of which use chemical defences to avoid herbivore predators. However, the application of aquatic natural chemicals in medication research is a relatively new practice. The oceans and seas include

CHAPTER 11

Drug from Marine Sampling to Factory

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Abstract: The marine world expresses a great scope for diverse novel scaffolds with unusual skeleton nature. Polyphenols, phycocolloids, pigments, fucoidans, peptides, pigments, and phlorotannins are the main classes of compounds provided by marine resources. Some of these structures displayed astonishing biological activities and successfully proceeded to marketed drugs for the treatment of different human diseases. There are many examples of successful commercially available marine-derived drugs such as cytarabine (Cytosar-U®) for acute myelocytic leukemia, trabectedin (Yondelis®) for ovarian cancer, Eribulin (Halaven®) for metastatic breast cancer, Ziconotide (Prialt®) for severe chronic pain, and Vidarabine (Ara-A) for viral infections. Oceans and their immense biodiversity have gifted humanity with a pathway out of the obstacles of health care. The constant need for innovation has been a great challenge for the pharmaceutical industry especially in finding new sources of active compounds. This chapter discussed the clinically approved marine-derived compounds and their impact on different diseases, focusing on those with granted approval in the last decade from 2011 to 2021. We also highlighted the underlying mechanism of actions through *in vivo*, *in vitro*, and computational *in silico* studies. Hopefully, this chapter will help scientists to develop a novel marine-derived drug.

Keywords: Marine, Phycocolloids, Fucoidans, Cytarabine, Leukemia, Vidarabine, Pharmaceutical Drugs, Natural Products (NPs).

1. INTRODUCTION

Marine life is a potential source of novel molecules, characterized by their long evolutionary history [1]. Marine organisms possess a greater molecular diversity in comparison with terrestrial natural sources [2, 3]. The earth's surface constitutes about 70% of oceans and seas with unexplored marine organisms and aquatic-derived microbial natural drugs [4]. Over the last decades, many academic resea-

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rch groups and pharmaceutical companies explored the aquatic environment with its treasures of soft corals, hard corals, algae, microorganisms, and sponges which provided interesting biologically active bioactive drug leads [5].

Marine-derived compounds tend to possess a diverse collection of active structures with chiral centers that are essential for substrate binding [6, 7]. The marine environment continues to be a major source of bioactive compounds that are effective against challenging disorders, such as cancer and autoimmune diseases [8]. The majority of known drugs are obtained from natural origins as their effectiveness is incentivized by their high target affinity, enhancing their suitability as effective pharmaceutical drugs [9]. The constant need for innovation has been a great challenge for the pharmaceutical industry because not all novel sources of active compounds are feasible to be developed as successfully marketed drugs [10, 11]. As a result, the focus has shifted towards the hydrosphere and its abundance of organisms [12]. Drugs of marine origin have become useful resources of secondary bioactive metabolites with distinguished roles in modulating cell proliferation, viability, and induction of reactive oxygen species (ROS) [13].

Marine organisms have constantly adapted to their harsh environment both chemically and physically to ensure survival [14]. The differences in environment seen in changes in salinity, aeration, and radiation in addition to their ability to combat infection and negative impacts of mutation resulted in the production of a plethora of secondary metabolites with potent biological activities [15]. The challenges faced by marine pharmacognosy have been reduced with the technological advancement in the processes of discovery and feasibility of isolation over the past 46 years. Oceans and their immense biodiversity have gifted the industry with a pathway out of the obstacles facing health care. Many marine-derived drugs proved effective against many diseases such as cytotoxic (anti-neoplastic), anti-inflammatory and cardiovascular drugs [16, 17].

In recent years, drug discovery from marine natural products has experienced a revival [18]. In December 2004, Ziconotide was approved as the first peptide analgesic drug isolated from a tropical cone snail in the United States [19]. After this marvelous discovery, Trabectedin was discovered as the first marine anticancer drug to gain approval in the European Union [19]. Other various classes of marine-derived compounds showed remarkable anticancer properties and entered clinical trials [20].

This book chapter aimed to summarize the history of clinically approved drugs discovered in the marine environment in the period from 2010 to 2020. We described the difficulties associated with their translation into pharmaceutical markets. We also provided an outlook into the mechanism of action, the recommended effective doses, and common side effects. Hopefully, this information will help scientists in their continuous search for novel biologically active compounds from the marine environment.

2. CATEGORIZATION OF MARINE PHARMACOLOGY

Essentially, the classification of marine pharmacological science is based on candidate drug origin/source into; genetically engineered marine organisms, pharmaceutical manufacturing and nutraceuticals of marine origin and pharmaceutically applicable substances found in marine organisms or produced by them [21]. Furthermore, marine drugs can be categorized more broadly according to their actions as follows:

2.1. Antimicrobial Agents

Cephalosporins are among the most known antimicrobial agents derived from marine sources. For instance, cephalosporin C was isolated from a marine fungus, namely *Cephalosporium acremonium* [21]. Moreover, a polyunsaturated fatty acid, known as Eicosapentaenoic acid derived from the marine diatom; *Phaeodactylum tricornutum* which exhibited activity against a collection of Gram-positive and Gram-negative bacteria, comprising a multidrug-resistant variety of a strain of *Staphylococcus aureus* [22].

2.2. Antiviral Agents

High molecular weight exopolysaccharides were obtained from a French marine sponge known as *Celtodoryx girardae* with associated symbiotic bacteria. They were found to display an anti-herpes simplex virus-1 (HSV-1) effect [23].

A gorgonian *Echinomuricea indomalaccensis* was obtained from the South China Sea and exposed for phytochemical studies [24]. A new oxygenated guaiane lactone namely, 5-*epi*-menverin was isolated and showed an anti-HSV-1 effect with an inhibition rate of 69.2% at a concentration equal to 25 µmol/L.

A marine sulfated polysaccharide namely, fucoidan was isolated from seaweeds and reported for its inhibitory effect against coronavirus disease-19 (COVID-19) [25]. Mechanistically, it could interfere with various phases of viral infection like the virus' entry into host cells.

CHAPTER 12

Future Perspectives for Developing Marine Drug Discovery

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Abstract: Many opportunities, from many marine secondary metabolites including some of the most interesting candidate drugs, have to be used for development in marine drug discovery in parallel to the updated technologies, procedures and protocols. The hope and the net result, in such a manner, are related to the acceleration and management of marine drug discovery as an integrated process from obtaining the sampling until the launch of the drug. The recent protocols targeted gene sequencing methods for identifying secondary metabolic pathways to be used in the biosynthesis of marine natural products (MNP) discovered from marine isolates. Afterward, the synthesis processes for replenishing inventories of compounds and analogs is a critical step. Moreover, the cheminformatics and computer screening of MNP for protein targets have been used to some extent. On the other hand, the collaboration allows sharing of knowledge, tools, finances, and administrative processes, therefore increasing the innovation potential of all parties, playing a greater role. Seriously, the future prospects for developing marine drug discovery involve the collection of relevant information and the evaluation of available opportunities to establish goals through government initiatives and finally to invest and market the drug products from marine origin. In the current chapter, the advanced approaches to marine drug discovery will be explained. Furthermore, this chapter will present both collaboration and innovation in marine drug discovery to increase the effectiveness of drug discovery and advance the production process.

Keywords: Future Perspectives, Marine Natural Products, Marine Drugs, Biodrug.

1. INTRODUCTION

The marine habitats have been researched for lead medication compounds that have shown to be novel therapeutic targets since they are a rich source of bioac-

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tive substances. Many structurally different pharmaceuticals and their secondary metabolites have been isolated from marine sources over the past 70 years. The medications derived from marine sources have demonstrated outstanding promise in the treatment of a broad range of illnesses, from acute to chronic problems. Recently, it has been suggested that marine medications may have a positive impact on human health [1].

Actually, the ocean provides a plethora of opportunities for new compounds' discovery, with over 13,000 distinct molecules, 3,000 of which have useful activities. More than 60% of novel drugs are derived from natural resources either a modified or unmodified natural product (NP), or a synthetic compound with a natural product) [2]. Surprisingly, from four in 2010 to seven in 2014, the total number of marine-approved drugs has consistently increased [3].

For example, Cytarabine (Cytosar-U®), as the first marine-derived drug, was approved in 1969 by the US Food and Drug Administration (FDA) for use as an anticancer drug. It was isolated from *Cryptotheca crypta* a Caribbean sponge. Recently, there are marine natural products (MNP) that have been subjected to clinical trials and were approved as pharmaceuticals, including the analgesic peptide ziconotide (Prialt®) from marine snails and the anticancer macrolide eribulin mesylate (Halaven®) derived from a sponge. In addition, other MNPs were approved with anticancer, antiviral and anti-hypertriglyceridemia properties [4].

Of newly discovered 23 compounds derived from water, 21 of them were included in various stages of clinical development as anticancer therapies, while only two were evaluated for the treatment of chronic pain and neurodegenerative diseases such as Alzheimer's disease [5]. Furthermore, a variety of additional compounds that possess antibacterial, antifungal, anti-inflammatory, antiviral, antiviral, and other compounds that may affect the nervous system, have been investigated for application in clinical trials [6].

Understanding of the metabolic pathways has been used to manufacture marine derived-drugs, or MNP as well as developing numerous genotypic means besides analytical methods, have supported the systematic and rigorous development of microbes to improve the production of their drugs. In addition, this may be ideal to manufacture drugs in their final form, in some cases the biosynthesis of drugs is also experimental and cost-effective [7].

Many workers discuss the significance of MNPs in various fields, including an update of FDA-approved medications and those that are currently undergoing clinical trials and could be viewed as MNP derivatives. The significance of marine microorganisms in current research and the application of cutting-edge methods and tools in this area are emphasized [8].

The potential of MNPs in drug discovery is incalculable when you consider the marine environment's extraordinarily high biodiversity. In comparison to synthetic substances, the success ratio of currently licensed medications and the overall number of MNPs recorded (about 28,500) is still quite high, and the clinical trial pipeline is very encouraging [8].

In the anticancer field, where the majority of the marketed and candidate medications fall, the development of new antibody-drug conjugates (ADC) and their combination with other anticancer treatments give an intriguing opportunity to investigate the amazing potential of MNPs. The MNPs are examined in the widest variety of biological tests, which is increasingly made possible by developing technologies, in order to ensure the broadest development of their structural diversity and bioactivity [8].

Valuable work has been performed by Moreira *et al.* (2004) [9] on uncultivated marine sediment and spongy microorganism *via* metagenomics-based technology for developing recombinant-secondary metabolites. The novel methodology emphasizes flexibility and cost-effectiveness besides high-quality test materials that have been examined in exciting areas of disease biology [10]. Surely, a targeted gene sequencing procedure, through specific genetic probes, for identifying secondary metabolic pathways is sometimes time-consuming and sometimes misleading [11].

On the other side, the samples are usually collected on such a small scale because the organism produced itself is small and difficult or impossible to collect. So, the significance of synthesis processes for replenishing inventories of compounds and analogs is critical. Also, the structures, estimated at the nanoscale and more abundant pure compounds, require independent methods in order to characterize their structure and stereochemistry accuracy. Nowadays, both cheminformatics and computer screening of MNP for protein targets have occurred to some extent [12].

The development of a particular marine medicine must involve the creation and analysis of large amounts of data. This requires the interaction of scientists from the scientific community and the industrial sector. Effectively, collaborations share knowledge, tools, funds, and managerial processes, thus increasing the innovation potential of all parties [13]. Particularly, at the level of academics, the quality of collaboration is assessed by the number of articles co-authored over a period of time. The Nature Index measures a database of the collaboration at various levels of different institutions, besides national and international levels

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Hassan A.H. Ibrahim

Prof. Hassan A.H. Ibrahim has published 91 research articles in peer-reviewed journals. The majority of them are in SCOPUS and others are impacted. In addition, he has shared in writing 6 books and 7 book chapters in marine and environmental biotechnology. On the other side, he has already written 12 books in Arabic, besides 14 Arabic review articles. He has completely supervised 21 MSc theses and 15 PhD theses around 9 Egyptian universities. He has revised many articles for international journals and also he judged several master theses. He has shared as PI or CO-PI in 20 projects between 2002 and 2023. Among them, there were 3 international projects. Finally, he has shared in 21 international conferences from 2008 to 2023. He was the head of the Marine Natural Product and Biotechnology Department and now he is the head of the Marine Microbiology Department, Marine Environment Division, NIOF.

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