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Exploring Uncharted Marine Bacteria as a Source of Novel Antimicrobials

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Abstract

Marine microbes are defined by their habitat as microorganisms living in the sea or ocean. The term "marine microbes" includes viruses, protozoa and fungi. This microbial life constitutes 70% To 90% of marine biomass. More than 15000 bioactive compounds have been isolated from marine fungi, and other organisms and used as anti-inflammatory, and anticancer leads. Among the microorganisms of marine, bacteria are the least explored ones.
Marine actinobacteria have adapted to high hydrostatic pressure, high concentration of Sodium Chloride, low concentration of organic matter, and low temperature. The phylum actinobacteria is a Gram-positive, nonmotile, and aerobic bacteria. Streptomyces and Actinomycetes are studied largely in this phylum due to their ability to produce a wide array of extracellular enzymes and secondary metabolites. Examples of active compounds isolated from Streptomyces include Fijimycins, etamycin A, Chlorinated bisindole pyrroles, and dynamics A–E. There may be diverse extremo enzymes hidden in the shadows that are currently unknown and, if discovered, may open up interesting new methods for the production and use of novel anti-microbials. In pharmaceutical research, a very small fraction of such organisms is studied. If discovered may open up interesting new ingenious, and cost-effective methods for the production and use of many novel anti-microbials.

Keywords: Marine Bacteria; Actinobacteria; Extremophile; Firmicutes; Proteobacteria

Introduction

Marine microbes are defined by their habitat as microorganisms living in the sea or ocean. The term "marine microbes" includes viruses, bacteria, microalgae, archaea, protozoa and fungi. This microbial life constitutes 70% to 90% of marine biomass [1]. Their diversity and number are far more than the macroscopic life on earth and many of them adopt unique life methodologies to survive in extreme conditions [2]. They form the very base of the food chain recycling organic matter and nutrients. The marine microbes, due to their diverse metabolic pathways, play a major role in the regulation of biogeochemical cycles that involve cycling of important elements like hydrogen, carbon, nitrogen, oxygen, sulfur, and phosphorus along with other microelements like potassium, sodium calcium, chlorine, and magnesium. This is the basis for the formation and production of new organic matter. Since the discovery of cephalosporins, there are many bioactive compounds have been isolated from various marine organisms for several diseases [3]. More than 15,000 bioactive compounds have been isolated from marine fungi, algae, and other organisms and used as anti-inflammatory, anti-diabetic, anti-microbial, and anticancer leads. Among the microorganisms of marine, bacteria are the least explored ones. The marine microbiota has been proven as a potential source for the development of new chemotherapeutic agents. A special focus has been given to the discovery of antimicrobials as the emergence of antimicrobial resistance is a severe concern due to the increase in the mortality rate [2].

Marine microbes have developed numerous metabolic pathways for the production of active secondary metabolites due to their capability to adapt to different and extreme conditions like high salinity, high temperature in the range of 80 °C to 90 °C, and extreme pH conditions. Because of the inability to culture such marine bacteria in the lab, an attempt to explore the metabolic pathways has remained unexplored largely and is the major source of new antimicrobials.

Marine Bacteria

Among the diverse marine microorganisms, secondary metabolites like steroids, peptides, terpenoids, alkaloids, polyketides, etc., [4]. Produced by marine bacteria have many biological activities, including antimicrobial properties. The six phyla of marine bacteria Actinobacteria, Bacteroidetes, Cyanobacteria, Firmicutes, Planctomycetes, and Proteobacteria were explored frequently anti-microbial leads. Among these, Actinobacteria, Firmicutes, and Proteobacteria Srinivasan R, et al. [5] are the chief contributors.

Actinobacteria

The phylum actinobacteria is a Gram-positive, nonmotile, and aerobic bacteria. Marine actinobacteria are exceptional because they have adapted to high hydrostatic pressure, high concentration of Sodium Chloride, low concentration of organic matter, and low temperature. In the course of adapting to such conditions, these bacteria biosynthesize various enzymes and secondary metabolites. Streptomyces and Actinomycetes are studied largely in this phylum due to their ability to produce a wide array of extracellular enzymes and secondary metabolites. Fijimycins, etamycin A, Chlorinated bisindole pyrroles, and dynamics A–E isolated from Streptomyces are a few examples that were found to be active against Multidrug-resistant Staphylococcus aureus and vancomycin-resistant Enterococcus faecium.

Firmicutes

It is a phylum of Gram-positive bacteria. Few of them have a permeable pseudo-outer membrane and it makes them take Gram-negative stains. The genus Bacillus is one of the main groups in Firmicutes. It has high-temperature tolerance and the capability to grow in liquid culture. A novel oxatetracyclo ketone isolated from the *B. stercoris* MBTDCMFRI Ba37 strain inhibited the growth of aquatic bacterial pathogens.

A new thiopeptide-class antibiotic, micrococcin, isolated from marine-derived *B. stratosphericus* exhibited potent antibacterial activity against Gram-positive bacterial pathogens without considerable cytotoxicity.

Proteobacteria

It is the largest phylum of Gram-negative bacteria having six subclasses. Marine γ-Proteobacteria, especially Pseudoalteromonas genus members are major producers of bioactives and potentially diverse secondary metabolites for example thiomarinol which is a potent antibiotic. Non-ribosomal peptides and their hybrids, alkaloids, terpenoids, and polyketides isolated from Myxobacteria, another major culture-resistant group of the phylum need to be explored for their mechanism of action [5,6].

Archaea

These are unicellular organisms known as extremophiles. They live near the hydrothermal vents where the temperature and chemical environment are extreme. They adapt to the surrounding environment by producing various biocatalysts that are generally called extremo enzymes because they are stable and active in extreme conditions. Such enzymes have industrial, and biotechnological applications, stable amylase, protease, and other enzymes have been isolated and effort is going on for their application in biotechnological processes. In pharmaceutical research, a very small fraction of such organisms is studied. The enzyme that is widely used is thermotolerant DNA polymerases in Polymerase chain reactions at temperatures higher than 95°C. This opens up a new way of interacting with the enzymes as they are not denatured at high temperatures which enables the pharmaceutical field to create more bioactive compounds which may prove beneficial for the overall wellbeing of human beings. There may be diverse extremo enzymes hidden in the shadows that are currently unknown and, if discovered may open up interesting new ingenious, and cost-effective methods for the production and use of many novel anti-microbials [6,7]. Some of the examples are listed in Table 1.

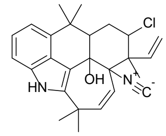
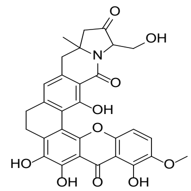
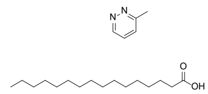
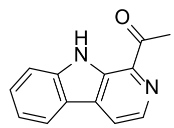
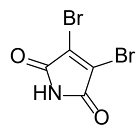
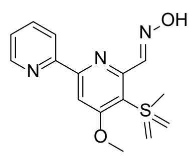
Sl. No.	Name of metabolites	Source organism	Structure	Antimicrobial activity	Reference
1	ambiguine-K isonitrile	*Fischerella ambigua*		*Mycobacterium tuberculosis*	[8]
2	citreamicin	*Streptomyces caelestis.*		*Staphylococcus haemolyticus*, Staphylococcus aureus	[9]
3	Ethyl acetate extract	*Streptomyces sp.* Al-Dhabi-90	 (Major components)	*Staphylococcus aureus, Pseudomonas aeruginosa*	[10]
4	1-acetyl-beta	*Pseudomonas sp.* UJ-6		Methicillin resistant, *Staphylococcus aureus*	[11]
5	3,4-dibromopyrrole-2,5-dione	*Pseudoalteromonas piscicida*		*Pseudomonas aeruginosa*	[12]
6	maipomycin A	*Kibdelosporangium phytohabitans* XY-R10		*acinetobacter baumanni; Pseudomonas aeruginosa*	[13]
7	exopolysaccharide B3-15	*Bacillus licheniformis* B3-15	Polysaccharide	*Pseudomonas aeruginosa; Staphylococcus aureus*	[14]

Table 1: Examples for metabolites derived from marine bacteria having anti-microbial activity.

Conclusion

Though bio-actives discussed cover only a few, the marine environment is a chemical storehouse and potentially abundant source. Marine microorganisms are nature-friendly and renewable resources for drug discovery. The first step is the isolation and culturing of novel strains, but all biosynthetic clusters cannot be expressed in laboratory conditions. Various methodologies and techniques like dereplication, use of cryptic gene clusters, next-generation gene sequencing, advanced mass and nuclear magnetic resonance spectroscopy, and advanced bioinformatic tools, can be combined with pathway engineering methods, new heterologous expression methods to explore the untapped resources. Along with this, the mechanism of actions of novel bioactives also needs to be established. Exploration of deep-sea organisms has taken much attention in recent years. A high level of innovation can only be the solution to the struggle against multi-drug-resistant organisms.

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