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Marine Bacteria: A Potential Tool for Antibacterial Activity

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Abstract The marine environment possesses a wide range of diverse habitats from which novel sources of natural products can be derived. Marine microorganisms produce a diverse array of metabolites with novel chemical structures and potent antibacterial activities. Now-a-days, microbial pathogens show antibiotic resistance. Marine bacteria have been shown to produce antibacterial compounds as extensively as terrestrial bacteria. It was reviewed that the bioactive metabolites extracted from bacteria had broad range of antibacterial activity against various antibiotic resistance bacteria which requires more attention in terms of discovery of drugs.

Keywords: *marine bacteria, antibacterial activity, bioactive compounds*

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1. Introduction

Various dreadful diseases are caused by viruses, bacteria and fungi which are serious threat to public health although there is remarkable progress in medical sciences for the management of such microorganisms. Due to the unavailability of medicines, their impact is broad in developing countries and the rising of extensive drug resistance. As a result of the adaptation of microbial pathogens towards antibiotic, there is demand for the development of new and effective antimicrobial compounds. New drugs, mainly antibiotics, have been searched against antibiotic resistance bacteria. The marine environment has been considered for varied and plentiful source of potent bioactive chemicals [1,2] which can be represented as drug [3]. Now-a-days, isolation of promising and new source of bioactive compound from marine microorganisms are increased rapidly [4].

Marine bacteria are distributed in sediment, [5], animate [6] inanimate surfaces [7] and the internal spaces of invertebrate [8]. Because of the complex nature of marine environment, marine microorganisms, such as bacteria, fungi, micro-algae, have developed complicated biochemical and physiological systems with which they can be adapted to extreme habitats and unfavorable conditions of marine environment. They live in a biologically competitive environment with unique conditions of salinity, pressure, temperature, light, oxygen, pH and nutrient. For the survival and defense mechanisms, microbes produce unique secondary metabolites. Even though these biologically active compounds are produced in response to stress, many have shown value in pharmaceutical and biotechnological applications [9].

A number of various bioactive compounds show different action such as cytotoxic, antimicrotubule, anticancer, photoprotective, antiproliferative, antitumour, as well as antifouling and antibiotic properties, have been isolated from marine bacteria [10,11,12]. Some of these biologically secondary metabolites of marine source with antiviral, antifungal and antibacterial activities are now-a-days in intense use as antibiotics and may be effective against infectious diseases such as AIDS and conditions of multiple bacterial infections. Members of various classes of metabolites, such as ribosomal and nonribosomal polyketides, terpenes, peptides, and alkaloids have been shown to exhibit antimicrobial and antiviral activity [13,14,15].

In this review, we will present the antimicrobial activity of natural compounds isolated from the marine bacteria.

2. Antibacterial Activity of Marine Bacteria

A marine bacterium, *Marinomonas mediterranea*, was isolated from the Mediterranean Sea at the Murcia coast. *M. mediterranea* showed antibacterial activity against nosocomial strains such as *Pseudomonas* sp. and *Staphylococcus aureus* resistance to respective antibiotics ceftazidime and meticillin [16]. Bacitracin is produced by *Bacillus licheniformis* which is active against many Gram positive organisms, anaerobic cocci, but not against other Gram negative bacteria [17]. *Pseudomonas* was isolated from India in 2009 showed antimicrobial activity against many pathogenic microbes [18]. In 2012, *Pseudoalteromonas piscicida* was isolated by Tawiah and coworkers from Iran [19] and *Pseudomonas aeruginosa* was isolated by Darabpour and coworkers from Ghana [20] with antimicrobial activity. A large number of the strains were isolated from marine environment with antimicrobial activity against the most common pathogenic bacteria

MRSA (methicillin resistant *Staphylococcus aureus*). *Pseudoalteromonas phenolica* was isolated by Isnansetyo and Kamei which showed antibacterial activity against methicillin-resistant *Staphylococcus aureus* [21]. Radjasa *et al.*, [22] isolated a coral-associated bacterium, TAB4. 2, was idendentified as *Pseudoalteromonas luteoviolacea* which showed inhibitory effect against both pathogenic and coral bacteria. Holmstrom and Kjelleberg [23] showed antibacterial activity of *Pseudoalteromonas* spp which was isolated from tunicates.

Table 1. List of antibacterial activity of marine bacteria against some pathogenic organisms

Sl. no	Marine bacteria with antimicrobial activity	Test strain	Reference
1.	*Pseudomonas putida*	*Bacillus subtilis* *Vibrio parahaemolyticus* *Escherichia coli* *Serratia marcescens* *Aeromonas hydrophila* *Rothia.* sp. *Staphylococcus aureus* MRSA	[24]
2.	*Actinomycetes*	*Staphylococcus aureus* *Bacillus subtilis* *Escherichia coli* *Saccharomyces cerevisiae* *Candida albicans* *Aspergillus niger* *Pseudomonas aeruginosa*	[25,26]
3.	*Pseudomonas aeruginosa*	*Aeromonas punctata* *Kokoris marina* *Rothia.* Sp. *Vibrio.* Sp. *Staphylococcus aureus* *Staphylococcus epidermidis* *Escherichia coli* *MRSA* *Proteus vulgaris* *Bacillus thuringiensis* *Bacillus subtilis* *Enterococcus faecalis*	[12]
4.	*Pseudoalteromonas* sp	MRSA *Staphylococcus aureus*	[20,21]
5.	*Pseudomonas* sp.	*Klebsiella pneumoniae* *Staphylococcus aureus* *Shigella flexneri* *Pseudomonas aeruginosa* *Bacillus subtilis* MRSA/ORSA	[18]
6.	*Bacillus* sp	*Kokoris marina* *Rothia.* sp. *Aeromonas punctata* *Rothia.* sp. *Vibrio.* sp. *S.aureus*	[27]
7.	*Brevibacterium frigoritolerans*	*Rothia.* sp. *Vibrio.* sp. *Staphylococcus aureus*	[27]

3. Anti-bacterial Compounds from Marine Bacteria

Microorganisms, mainly bacteria have too much influenced the development of medical science. Since the discovery of Penicillin, a large number of studies on marine bacteria have shown that they are a rich source of structurally unique, bioactive chemicals. About 50,000 natural products have been discovered from microorganisms in the last six decades. Over 10,000 of these compounds are biologically active and about eight thousand are recognized as antitumor agents as well as antibiotics [28,29]. Nearly hundred microbial products have now found clinical applications as antitumor agents, antibiotics and agrochemicals [30,31,32]. Marine microorganisms produce different types of biologically active secondary metabolites. The metabolites are chemically divided into peptides, saponins, terpenoids, alkaloids, nucleosides, polycyclic ethers, sterols, amino acids etc. It is not possible to follow a specific technique for the separation of the constituents from complex mixture of bioactive compounds which is unknown. Fractionation with organic solvents method was used for broad separation of complex mixture. Alcoholic extracts of marine microorganisms showed biological activities could be a mixture of several classes of compounds. Mainly two different procedures are followed for separation of the bioactive fractions of different diverse group. In the first step the fractions of low or medium polarity contain lipophilic organic compounds that can be separated generally by standard normal or reverse phase column chromatography and high performance liquid chromatography (HPLC) to get the individual components. Another method is based on high-polarity fractions that contain the water-soluble organic compounds. The organic material is chromatographed on Sephadex. The individual components of the active fraction are further separated by countercurrent chromatography (i.e., DCCC) and HPLC on the appropriate column packing (C18, amino, cyano,

etc.). The primary extraction of natural compounds from the bacteria was done with an adequate solvent system (generally acetone or methanol). In the first step, the screening of a bioactive compound from the extracts consists of a sequential gradient partition with solvents such as hexane, dichloromethane, ethyl acetate, chloroform and carbon tetrachloride. The fractions were obtained according to their polarity. Thus the water-soluble organic material is found in the *n*-butanol fraction, mainly alkaloid salts, amino acids, polyhydroxysteroids, and saponin. The active compounds at early stages were fractionated by solvent partitions which eliminates much of the weight of inactive material. The wide fractions, thus procured, are fractionated further by column chromatography of several types (absorption on gel permeation or ion change, alumina, partition, silica gel) using a wide variety of solvent systems adapted to the polarity of the active fraction. Thus different chromatographic techniques are needed before the active fraction can be concentrated to a state of purity. Phenolic compounds such as 4,4,6-tribromo-2,2'-biphenol ,CMMED 290 had been isolated from marine bacteria, *pseudoalteromonas* sp, which displayed significant antimicrobial activity against methicillin-resistant *Staphylococcus aureus* [33]. From other *Pseudoalteromonas* species, the marine bacterium *Pseudoalteromonas phenolica*, was isolated 2,2',3-tribromo-biphenyl-4,4'- dicarboxylic acid by Isnansetyo and Kamei [21]. This compound showed antibacterial property towards methicillin-resistant *Staphylococcus aureus* with MIC values between 1 and 4 µg/ml. The compound was also highly effective against *Bacillus subtilis* and *Enterococcus serolicida*, but showed no activity against Gram negative bacteria and fungi. These results demonstrated that this bromophenyl compound has high *in vitro* activity against *Staphylococcus aureus* and might be useful as a lead compound in developing new antimicrobial substances. The marine resistant to methicillin bacterium *Pseudoalteromonas haloplanktis* INH strain can produced another antimicrobial compounds namely bromophenyl compounds [34]. Cetina *et al*., [35] in their experiment, seven bioactive compounds producer strains were isolated which indicated that a likely association exists between pigments and toxicity in several marine heterotrophic bacteria with pigmentation. For example, a number of biosynthetic enzymes involved in the synthesis of inhibitors were identified for pigment synthesis in *Pseudoalteromonas tunicate*. However, when they tested yellow pigment of strain (MS-3/48) against target pathogen bacteria, no antimicrobial activity was observed which indicated that pigment had no antimicrobial activity against target bacteria. Lu *et al*., [36] have found diketopiperazine and macrolide are the two important bioactive secondary metabolites by the screening for bioactive principles from marine microorganisms. The smallest cyclic peptides, Diketopiperazines (DKPs), had been isolated from marine microorganisms. These have been found as cell-cell signalling compounds. Recently some L, L-diketopiperazines had been known as quorum-sensing bacterial sensors, which are used by Gram-negative bacteria for cell-cell communication and to regulate expression of genes in response to population density. Three phenolic compounds, 7-methylcoumarin, and two flavonoids, rhamnazin and cirsimaritin, were isolated from a marine *Streptomyces* sp by El Gendy *et al.* [37]. These isolated compounds are reported to be antimicrobial products. The other antimicrobial phenolic compounds included ammonificins A and B, which are chroman derivatives from *Thermovibrio ammonifican*, a marine hydrothermal vent bacterium [38]. Zhang *et al.* [39] isolated two new cyclic maribasins A and B, lipopeptides from the fermentation broth of the marine microorganisms *Bacillus marinus* B-9987 from Suaeda salsa on the Bohai coastline of China. These compounds exhibited broad-spectrum antifungal activity against phytopathogens by the antifungal bioassay. From deep-sea sediments, *Bacillus* species and *Bacillus amyloliquefaciens* SH-B10 produced two different antifungal lipopeptides which were purified by bioactivity-guided fractionation [40]. Both compounds were reported to have significant inhibitory activities against five different plant fungal pathogens in paper-agar disk diffusion assay. The marine bacterial isolate *Brevibacillus laterosporus* PNG276 from Papua New Guinea had been isolated tauramamide, a new lipopeptide [41]. Antimicrobial peptides, tauramamide, ethyl ester, thiopeptides and depsipeptides, from marine bacterial origin showed effective inhibition of human pathogenic *Enterococcus* sp. These compounds had been isolated by bioassay-guided fractionation. Activity-guided fractionation of organic extracts of the marine *Nocardiopsis* sp. TP-1161 showed the identification and purification of the active compound [42]. Structure elucidation revealed that this compound was a new thiopeptide antibiotic with an unusual aminoacetone moiety. Unnarmicine A and C were found to be new antibacterial depsipeptides synthesized by *Photobacterium* MBIC06485, a marine bacterium [43]. These compounds particularly inhibited the growth of two strains of *Pseudovibrio*. Another antimicrobial peptides found in the marine environment are hybrid polyketide-nonribosomal peptide. Marine myxobacteria are rare culture-resistant microorganisms, a large number of strains of which have been studied and identified by research groups in Asia. A slightly halophilic myxobacterium, *Paraliomyxa miuraensis*, was discovered in Japan, produces the cyclic hybrid polyketide-peptide antibiotics known as miuraenamides A and B [44]. The antimicrobial activity relationships of these compounds were demonstrated the significance of the macrocyclic structure as well as the β-methoxyacrylate moiety. From a marine gliding bacterium of the genus *Rapidithrix* Ariakemicins were produced A and B which linear hybrid polyketide-nonribosomal peptide antiobiotics [45]. The ariakemicins were composed of threonine, two Ω-amino-(Ω-3)-methyl carboxylic acids containing diene/triene units, and δ-isovanilloylbutyric acid. The antibiotics selectively inhibited the growth of Gram positive bacteria. Dofourcq et al [46] obtained 493 marine isolates from various environments and samples of which 63 (12·8%) presented an antibacterial activity against a panel of reference pathogenic strains (Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli and Enterococcus faecalis). Graca *et al.* [47] reported antimicrobial activity of the bacteria Cellulomonas and Proteus sp. isolated from marine sponge Erylus deficiens. Sinimol et al [48] observed antimicrobial properties of 24 bacteria, 4 actinomycetes and 8 fungi isolated from diverse marine sources.

4. Conclusion

The search for novel antimicrobial agents which have clinical and pharmaceutical importance against many antibiotic-resistant pathogenic bacteria such as *Enterococcus* spp., *Mycobacterium tuberculosis, Streptococcus pneumonia, Pseudomonas sp*. and *Staphylococcus aureus* is a great challenge. Many researchers have identified bacteria in biological samples that resist all currently available antibiotic drugs. The emergence of antibiotic resistant bacteria can be a natural process and a human mediated one. Most of the natural antibiotics available are derived from terrestrial microbes. Microbial resistance against them intensifies the necessity of new bacterial strain with novel antibiotic production. In this review was recorded that bacterial strain which isolated from marine sources found to be promising antibiotic producing agents that can be further use to control the spreading of antibiotic resistant pathogens, which cause life threatening infections. This study also highlighted the role of other sources apart from soil community in screening of potential candidates that might be helpful for the discovery of new antibiotics.

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