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BIOPROSPECTING MARINE MICROORGANISMS FOR THE PRODUCTION OF ANTIBIOTICS AND ITS FUTURE PERSPECTIVES

Gayathiri G. S.*, Precilla Jennifer R. D. and Arun P.

Department of Biotechnology, Dr. N. G. P. Arts and Science College (Autonomous), Coimbatore, Tamil Nadu, India.

***Corresponding Author: Gayathiri G. S.**

Department of Biotechnology, Dr. N. G. P. Arts and Science College (Autonomous), Coimbatore, Tamil Nadu, India.

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ABSTRACT

Marine microorganisms are fascinating resources due to their novel natural products with antimicrobial activities. With the emergence of new diseases, it is necessary to develop antibiotics from natural resources. Marine microorganisms are unique and have the ability to produce antibiotics. Marine antibiotics are the antibiotics that are obtained from marine sources most probably marine microorganism. Scientists have reported the discovery of antibiotics; Asplasmomycin, himalomycin, pelagiomycin, cycloedusemol, prepacifernol, marinomycins – C and D. This indicates that marine biodiversity is rich in species that can produce antibiotics for various pathogens or diseases.

KEYWORDS: Marine microorganisms, marine antibiotics, marine biodiversity, pathogens, diseases.

INTRODUCTION

Marine antibiotics are the antibiotics that are obtained from marine plants, animals, microorganisms. It is reported that marine biodiversity is rich than terrestrial and other biodiversity. Marine microorganisms have unique properties. It has resulted in compounds that are been developed to treat cancer, resistant bacteria and viruses. These compounds were discovered by applying recent advances in understanding the genetics of secondary metabolism in microorganisms, exploring the marine environment and applying new screening technologies. Marine organisms have long been recognised as a source of novel metabolites with applications in human disease therapy. In last 50 years, over 30,000 marine natural products have been found and approximately 2% of those have been isolated from deep sea organisms. The discovery of novel antibiotics is necessary to encounter pathogens and in the treatment of diseases. The development of novel antibiotics includes isolation, screening and developing the bio active compounds.

Biodiversity of Marine Microorganisms

The marine environment is the largest habitat on Earth. It is a source of a plethora of many organisms with unique properties, extremely rich in bio active compounds for medical, industrial and biotechnological applications. Still these marine microorganisms remain underexplored and understudied. Nowadays marine sources are clearly one of the most important natural reservoirs of bioactive compounds. Ocean contains various different habitats for bioprospection. Marine microorganisms living under extreme conditions have also been the focus of bioprospecting efforts as novel sources of biomolecules with biotechnological applications. Marine invertebrates comprising about 60% of marine fauna were seen to generate bioactive natural products which can be considered as beneficial therapeutic agents for human. Through billions of evolution, marine microorganisms from the three main domains of life: Bacteria, Archea and Eukarya produced novel metabolic activities. Bacteria are abundant in all parts of the ocean. Archea is the simplest and most primitive forms of life. It is found in the extreme marine environments such as deep sea, highly acidic or alkaline conditions. Marine eukaryotes may be unicellular or multicellular which includes algae, diatoms, dinoflagellates, ciliates, marine fungi, etc.

Need For Marine Antbiotics

According to the database created by Hu *et al*, a pool of 12,322 new compounds has been isolated from marine microorganisms. Marine bacteria were noted to generate compounds such as salinoporamide – A which have the ability of acting as antitumor antibiotics, Apratoxin – exhibiting anticancer capacities. The scaffold which is present in the marine environment is isolated to produce antibacterial compounds which could be developed and clinically tested for therapeutic remedies and medical purposes. Marine actinobacteria are considered as a fruitful generator of potent natural products. The surface of marine microorganisms is more nutrient rich than sediments and strains of microorganisms. This urges the biotechnological and other pharmaceutical companies to tap this new found resources since it have potential in the development of pharmaceuticals, cosmetics and other nutraceutical supplements. Hence marine antibiotics can

fulfil the needs of current pharmaceutical and biotechnological companies.

Antibiotics From Marine Bacteria

A great diversity of bacteria can be found in different marine sources, including both biotic and abiotic substrates. Some marine bacteria produce antimicrobial substances active on a broad range of target organisms. The marine bacteria is easily isolated from water, sediments, etc., Advanced studies on some species of tunicates and their associated bacteria, such as *Streptomyces* sp. , exhibited increased production of secondary metabolites also with antibacterial activity when co cultured with human pathogens *Pseudomonas aeruginosa.* Some of the antibiotics derived from marine bacteria are as follows,

1. Rifamycin

Rifamycin, previously known to be produced only by soil bacteria, has now been found to be produced by marine bacteria *Salinispora* which is isolated from marine sponge *Pseudoceratiana clavata.* Rifamycin is a group of antibiotics that belongs to ansamycin family. They are clinically important antibacterial agents that are active against gram positive bacteria.

2. DD – Diketopiperazines

It is obtained from the bacterial strains CF 20 (CECT5719) and C-148 (CECT5718). The strains are isolated from the cultures of larvae of molluscus. This antibiotic showed stron activity against *Vibrio anguillarium.* It is the first series of DD-diketopiperazines that has been isolated from single marine source.

3. Thiocoraline

It is a novel bioactive depsipeptide. It was isolated from the mycelia cake of marine actinomycete strain L- 13 – ACM2 -092. The antibiotic is reported to have antitumor activity. It is produced by marine micro monospora. Thiocoraline showed strong antimicrobial activity against gram positive microorganisms.

4. Pelagiomicins

It is isolated from the marine bacterium *Pelagiobacter variabilis.* This antibiotic showed the properties of anticancer activities. Pelagiomicin A exhibits activity against gram positive and gram negative bacteria. It also showed antitumor activity in both *in vitro* and *in vivo* studies.

Antibiotics From Marine Algae

Marine algae have been recognised as a promising biomass for the production of drugs, food and energy. Many bioactive compounds have been isolated from various algae including fatty acids, terpenes, bromophenols and halogenated compounds. Studies have reported that green algae, brown algae and red algae are known to produce antibiotics.

The green algae, *Dunaliella primolecta,* exhibited highest antibiotic activity. The crude extract of these algae strongly inhibited the growth of *Staphylococcus aureus, Bacillus subtilis, Bacillus cereus, Enterobacter aerogenes.* Studies reveal that the algal cells of *D. primolecta* contain a number of different antibiotic substances. Some of the antibiotics derived from marine algae are as follows,

1. Iso-laurinterol

Laurinterol and iso-laurinterol, two cuprane derived sequiterpenes isolated from Japanese *Laurencia,* a kind of red algae, exhibited strong inhibitory activity towards the marine bacteria *Alteromonas* sp., *E.coli, Azomonas agilis, Erwinia amyiovora.* Iso-laurinterol was found in *L. Intermedia.*

2. 7-hydroxylaurene

It was isolated from the marine red algae *Laurencia okamurai.* The structures of these compounds were established by mass spectroscopic techniques. It exhibit potential anti bacterial activity. It was found to be the major antimicrobial metabolite of *L. subopposita.*

3. Cycloedusemol

The sequiterpene cycloedusemol was isolated from *Chondria oppositiclada.* It was found to be strongly antibiotic towards *S. aureus* and *C. albicans.* It is an antibiotic cyclopropane containing sequiesterpene from the marine algae.

4. Pachydictol A

It was isolated from the brown algae *Pachydicton coriaceum.* This alga produces the antimicrobial compound Pachydictol A, which was found to have mild antibiotic activity against *S. aureus.*

5. Chondriol

It was isolated from a red algae orginially identified as *Chondria oppositiclada* but later known as *Laurenia yamada*. It is a halogenated acetylene. This antibiotic showed activity against *S. aureus* and *M. Smegmatis.*

Antibiotics From Marine Fungi

Marine fungi are recognised as a prolific source of biologically active secondary metabolites. The structure of the first new metabolite, leptosphaerin, from marine fungus was reported in 1986 and 437 new metabolites from 149 strains have been reported in 182 scientific journals. These new compounds were mostly obtained in the course of studies on biologically active metabolites for searching new drug candidates and their leads, and there were very few reports describing ecological significance of marine fungi and their metabolites. Research in the field of marine derived fungi aided the discovery of several metabolites. Since the discovery of penicillin, fungi have been established as good producers of antibiotics which are low molecular weight organic natural products with antibiotic activity. Fungi are considered as not only sources of antibiotics but also

producers of anti inflammatory inhibitors, anti cancer drugs and hypercholesterolemia treatment agents. Some of the most promising molecules derived from marine fungi, particularly from deep sea sediments, also have antitumor activities.

1. Asperolide – E

A new tetranorlabdane diterpeniod, asperolide E was isolated from deep sea sediments derived fungus *Aspergillus wentii* SD-310. It showed cytotoxicity against cervical, breast and lung cancer cell lines. This fungal genus also produces Asperethers A-E, five new 20-nor-isopimarane diterpenoids. This displayed cytotoxicity towards human pulmonary adenocarcinoma cell line.

2. Wentilactone A and B

Aspergillus dimorphicus SD317, isolated from deep sea sediments of South China sea, whose genus identified in DHABs, produced antitumor agent Wentilactone A and B. Wentilactone A induced apoptosis inhibiting G2/M cell cycle through the stabilisation of the p53-p21 dimer within human lung carcinoma cells. Wentilactone B blocked proliferation and migration of human hematoma cells.

3. Circumdatin G

It was produced from the marine fungus *Aspergillus westerdijkiae* SCSIO 05233. The cultures were isolated from deep sea sediments which own antiproliferative activity against myelogenous and promyelocytic leukemia cell lines. The crude extract of the broth of *Aspergillus ochraceus* was found to inhibit the final stage of polyprotein processing during hepatitis C virus replication.

4. Lovastatin

It is isolated from *Aspergillus terreus*, which was the first agent to be approved by the food and drug administration. Lovastatin is a lactone metabolite with cholesterol lowering and potential antineoplastic activities. It is proven to reduce the coronary heart disease in the patients by lowering the plasma cholesterol level. It also reduces proliferation of lung cancer, breast cancer, liver cancer and cervical cancer.

Future Perspectives of Marine Antibiotics

The diversity of natural products from marine microorganisms clearly demonstrates that there are potentials for transferring these compounds into clinical trials for future development of anti-infective drugs or antibiotics. Marine antibiotics must be developed to stem the rise in global bacterial resistance. The major challenges in future will be the large scale production of marine antibiotics, to meet the demand for drug development. To overcome the challenges of marine natural products development a multi disciplinary strategy can be adapted which utilizes nascent technologies and tools for developing novel antimicrobial agents. The ocean is the treasure of cure for infectious diseases and only awaits to be discovered. Novel antibiotics from marine microorganisms are attracting attention because of the growing demand for antibiotic to combat infectious diseases. Already some of the marine metabolites being tested clinically. Researchers believe that metabolic engineering has the potential to be used for the production of antibiotics.

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CONCLUSION

In this review, it is clear that the marine environment will play a vital role in the future development of antibiotics. Efforts are still needed in terms of large scale production and exploitation through biotechnological application for future supply of these natural products from marine environment. The activity of compounds derived from marine microorganisms is comparable with existing antibiotics and can address the problem of resistance and re-emergence in infectious diseases in addition to molecular novelty and bioactivity, marine microbes present a secure and renewable supply of targeted metabolites for scientific enquiry and commercial development.

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