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BREAKTHROUGH OF BIOLOGICS FROM MARINE MICROORGANISMS

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ABSTRACT

Marine microorganisms anticipate growing interest in bioactive metabolites and offer a unique opportunity to both increase the quantity of aquatic natural foods used in clinical studies and hasten their advancement. This study focuses in particular on those marine microorganism-derived compounds that are now under development for use in medicine and have been found or are highly anticipated to be such based on mounting incidental evidence. Specifically, chemicals of the karlotoxin class that were identified from the dinoflagellate *Karlodinium veneficum* provide opportunities to develop novel medicines for the prevention and treatment of cancer and excessive blood cholesterol.

KEYWORDS: Marine, bioactives, marine microbes, biofilm.

INTRODUCTION

The field of microbiology is particularly crucial for the creation of drugs.[1] Even though more than 70% of Earth's surface is covered by seas, little is known about the natural foods produced by aquatic microbes. Diverse unique bacteria that produce bioactive complexes, or biologically active substances, call the aquatic environment home. For thousands of years, people have used plants and plant extracts to treat a variety of human illnesses. Their utilization is also evidenced in many earlier archaeological artifacts.[2,3] In contrast, the 20th century saw the discovery of microorganisms as producers of medicinal compounds. Despite this little history, microbial origins account for roughly 10% of all currently known biologically active natural meals and products. These mostly antibiotics show how microorganisms may be a growing and promising source for the development of biologically active compounds.[4] Undoubtedly, the bioactives produced by microorganisms in the 20th century served as the foundation for modern medications. Marine microorganisms have gained recognition as a large and unexplored source of new bioactive chemicals and complexes over the past ten years.[5] To allow for the continued identification of unique microorganisms, it is important to do study on the maritime environment. Numerous recent investigations of the microbial variety in the marine environment, particularly those microorganisms that coexist with marine animals and plants, may lead to the discovery of a new bioactive source. Numerous studies have shown that "living surfaces" represent a habitat that is abundant in the epibiotic bacteria that produce bioactive substances. However, the vast biotechnological potential of the marine epibiotic bacteria has not been fully investigated. The physiological needs of the majority of marine microorganisms are currently poorly understood. However, a deeper comprehension of their growing environments will provide fresh perspectives into the intricate world of marine microbiology.[6] Therefore, increased investment in the advancement of marine biotechnology will result in the production of new chemicals that might have a substantial impact on medicine development during the coming ten years. We have spoken about how important it is to look into new sources that might be rich in bioactives and emphasize how important it is to take into account the chemical ecology of marine microorganism-host interactions for the targeted separation of microorganisms that produce bioactives. According to the source's examination of medical theory, natural foods and associated medications are used to treat 87% of all human ailments, including those that function as anticancer, antibacterial, antiparasitic, anticoagulant, and immune-suppressant agents, among others. Antihistamine, antianginal, anesthetics, chelator, anxiolytic and diuretic, antidote, and hypnotics were the seven drug categories that had no entries of any innate or natural foodstuffs or related medications prior to the year 2000.[7,8] Natural products and other foods have contributed significantly to the development of antibacterial medicines, either directly treating bacteria or serving as models for synthetic alterations. According to species analyzed, more than 79% of the medications that were commercially accessible in the United States or were formally approved globally between 1982 and 2002 may be linked back to a natural product origin. Most novel chemicals discovered in marine microorganisms come from species that can potentially be separated from both the water and the land. Although all of these maritime facultative organisms are definitely a valuable source of novel metabolites, nothing is known about how well-adapted they are to the marine environment or what ecological functions they play.[9,10]

1. Drug Development Using Marine Organisms

1.1 Marine microbes

The main way that marine bacteria are described is in terms of the amount of sodium or sea water that they need to grow. We discovered that a large proportion of marine bacteria produce antibiotic compounds when they are subjected to the screening procedure after being removed from the surface of invertebrates and marine algae. The first antibiotic was created by marine microorganisms in 1996.[11] Additionally, more bacteria that manufacture antibiotics are discovered in biofilms, which are produced on the surface of marine microorganisms, than in any other marine habitat. Some marine epiphytic bacteria have revealed that they create antimicrobial secondary metabolites that slow down the resolution of prospective rivals when combined with nutrient-rich invertebrate surfaces and marine algae. Recent studies have shown that many surface-associated bacteria generate a variety of antibiotics. Nowadays, Bacillus species isolated from marine worm in Papua New Guinea are used to make the new cyclic decapeptide antibiotic loloatin B, which prevents the growth of VRE (vancomycin resistant Enterococcus) and MRSA (methicillin resistant Staphylococcus aureus). A sea bacteria called Alteromonas rava produces the novel antibiotic thiomarinol. Numerous antibiotics, such as loloatins, sesbanimides, and agrochelin from the agrobacterium pelagiomicins and pyrones from Pseudomonas, have been linked to Bacillus.[12,13]

1.2 Marine sponges

The secondary metabolites of several marine creatures have been extensively researched during the past 35 years. A small group of chemists started to identify and isolate new substances from the marine source in the 1970s. Research on developing drugs from marine microorganisms has advanced, and now multidisciplinary fields such as biochemistry, ecology, biology, pharmacology, and organic chemistry are now engaged.[14] Marine microorganisms have drawn a lot of interest because of the richness of life that can be found in the oceans and seas that span more than 70% of the globe. Novel and structurally unique secondary metabolites from marine microorganisms have been extracted and identified. As a result of this conflict, several drugs using a novel chemical model were created and released in 2004, while the majority of the other competitors are still undergoing clinical studies.[15] By the finding of phylogenetic complex, sponge-specific microbial communities in the sea sponges, including unique lineages and candidate phyla, proven to be a significant step forward. Since microorganisms are more accessible than those found in seawater in a number of ways, new opportunities for research have emerged. The majority of marine sponges function as microbial fermenters, opening exciting new paths for marine microbiology and biotechnology.[16]

1.3 Aquatic fungi

Sorbicillacton A is one of several substances obtained from marine fungus that are now being tested in human trials. This substance, which is derived from a fungus connected to sea sponges, represents an advanced level in medical treatment development. Numerous marine fungus generate antioxidant compounds include 4,5,6-trihydroxy methylphthalide from *Epioeeum* species, Xanthenes derivative from *Wardomyees anomalus*, and *cremonin* from Acremonium species. These antioxidants prevent the oxidative damage associated to conditions including cancer, atherosclerosis, and dementia. They might potentially be useful as food additives or medicines.[17] Among the bacteria that produce antibiotics, marine actinomycetes, in especially the *Salinospora* group of the family Micromonosporaceae, hold great promise. These microbes are discovered to be a strong source of anticancer drugs that essentially target the proteosomes function. The commercial viability of Nereus Pharmaceutical's plan to create these anti-cancer drugs has been confirmed. Recently, certain research teams have successfully discovered and isolated from marine bacteria agricultural fungicides, shrimp feed supplements, biofertilizers, and medications that lower cholesterol.[18] These studies are all restricted to easily cultivatable marine microorganisms. Even marine bacteria that are impossible to cultivate may now have their potential metabolic and biochemical skills shown thanks to genome sequencing. Bioactive compounds generated from non-culturable marine microorganisms must be one of the future research themes.[17] While researching fungi that inhabit sponges, most prokaryotes from marine sponges have been comprehensively described. *Scalarispongia scalaris* (also known as *Cacospongia scalaris*) is a wild sponge that was found on the Greek island of Lesvos in shallow seas.[19] isolated and described a fungus strain from this sponge. Based on the findings of the phenotypical and molecular study, the fungus was identified as Alternaria sp. In several forms of growth medium, it displayed nearly identical growth kinetics in both the absence and presence of NaCl. Bacterial (*Escherichia coli, Pseudomonas species,* and *Bacillus subtilis*) and yeast (*Saccharomyces cerevisiae*) strains were used in antagonistic experiments to study the fungal antimicrobial activity in vitro. Clear inhibitory zones were seen for all of the aforementioned strains, making this fungus a potential source of antibacterial compounds.[20]

1.4 Nematodes marines

According to a hierarchical diversity index-taxonomic distinctness index, the production of gas and oil, among other anthropogenic factors, may affect the Bohai Bay and adjacent coastal areas. In other words, we may claim that these benthos elements in these places were being impacted by an anthropogenic disturbance. And because of the substances excreted by marine species, particularly nematodes, many shore sample locations in the center of the Bohai Sea were clear, pure, and unpolluted.[21]

1.5 Cyanobacteria of the sea

It was hypothesized that marine cyanobacteria might cause acute myeloid leukemia cells to die. Nearly half of the 41 examined cynobacteria strains showed malignant cell death.[22] Apoptosis activity is seen in several Cyanobacteria strains against acute myeloid leukemia cells; however, it has no effect on non-malignant cells such hepatocytes and cardiomyoblasts. One of these strains, M44, is particularly promising because it has activity that reduces the risky effects of LEDGF/p75, which is overexpressed in acute myeloid leukemia. It accomplishes this action by combining with the anthracycline anticancer drug daunorubicin in AML cells, which shields cardio myoblasts from the anthracyclines' toxic effects. By reviewing recent studies, it is possible to draw the conclusion that culturable benthic cyanobacteria from temperate marine settings provide a promising but underutilized source for new leukemia medicines.[23,24]

1.6 Marine weeds

A variety of metabolites produced by marine algae are naturally halogenated and have potential commercial use. Such compounds' structures progress from simple and straightforward polycyclic molecules to complicated acyclic entities with linear chains. Their pharmacological and medical devices have been studied for a few decades.[25] Numerous novel chemicals have been found during the last few years, and research has continued, however most algae species have not been sufficiently screened. The emphasis is mostly on the hitherto unnoticed ecological function of halogenated metabolites of marine algae. New studies in this area will provide fresh ways to comprehend biodiversity as well as several unique and practical insights into the dynamics of marine ecosystems. But the challenging goal for the upcoming years will be to comprehend the relationship between the creation of halogenated compounds and environmental changes, such as changes in the planet's temperature.[26] In recent years, studies on the formation of halogenated metabolites have been more concentrated on macro algae than phytoplankton. However, phytoplankton may hold promise since it forms the basis of marine food chains and adapts quickly to environmental changes, which surely affect secondary metabolism.[27,28]

1.7 Chitins

Natural marine biopolymers chitin and chitosan are biodegradable, non-toxic, and biocompatible. The appealing aspect of these biomaterials is their ease of transformation into other forms, such as gels, membranes, sponges, microparticles, scaffolds, nanofibers, and nanoparticles, for use in a variety of biomedical applications, including tissue engineering, gene therapy, wound dressing, and cancer targeting drugs. Recent research on two- or three-dimensional chitinous scaffolds derived from marine sponges is ongoing, and these scaffolds' potential uses are being explored.[29,30]

1.8 Seafood that is useful

The chemical and biological diversity in the maritime environment is quite diverse. Alginate, marine polysaccharides, carrageenan, and agar are the most popular compounds produced from the marine environment that are utilized as food and food components. Recent bioactive additions to food lists include glucosamine and marine oils for their enhanced health advantages. Functional foods containing omega-3 fats are now widely consumed, and every year, a range of new products are released globally.[31,32] Additionally, a number of other marine elements, including glucosamine and omega-3 fatty acids, are being investigated as functional food components.[33,34]

2. Marine Medicines in Development

Numerous drugs originating from marine microbes and other substances are being tested in clinics.[35] Solblidotin, Tasidotin, Dolastatin, Salinosporamide A, Bryostatin, Plinabulin, Phenylahistin, Halimide, Trabectedin, Cyanosafracin B, Eribulin mesy- late, Halichondrin B, Tetronamycin, Nigericin, K41A, Manzamine A, Ircinal A, and Karlotoxin are molecules currently These substances are used in a number of ways.[36,37] Others include Aplidine, Bryostatin, Didemin B, Ecteinascidin 743, Kahalaide F, Mycaperoxide B as an anticancer drug, Cyclodidemniserinol trisulfate as an HIV inhibitor, Lamellarin A 20 sulfate as a nematode infection preventative, Dithiocyanates as an asthma medication, and Conotoxins as a pain reliever.[38–42] Recently, the cancer therapy drug trabectedin was authorized. It is generated by symbiotic bacteria. The ring system of the antibiotics Zalypsis and Trabectedin is strikingly like that of bacterially generated saframycin. Trabectedin might also be manufactured semi-synthetically using Cyanosafracin B and Pseudomonas fluorescens.[39,41] Eribulin mesylate, a variation of the sponge that is essentially isolated polyether Halichondrin B.[43] Nigericin, Tetronamycin, and K41A are examples of polyether produced by bacteria whose structures are almost identical to those of Halichondrin family compounds, suggesting the possibility of microbial synthesis.[43,44]

3. CONCLUSION

Beginning in the late 19th century, the study of marine microbiology has developed into one of the most exciting and engaging areas of biology. Ocean missions and trips conducted between 1855 and 1890 laid the groundwork for later ocean microbiological investigations. Between 1975 and 1980, the functions of marine microorganisms in several areas, including productivity, ecology, biofilm creation, and food chain generation, were found. After 1980, the study of marine microorganisms was given focus by the developing discipline of biotechnology for biotechnological applications including microbial medicines and genetic identification. Between 1989 and 2005, these factors received a lot of attention, which ultimately led to the creation of new goods and methods. The development of fluorescent probes and scanning electron microscopes has made it much easier to comprehend how bacteria behave and act. Advanced tools are being used in research. Future advancements in marine microbiology will depend on newly developed tools and approaches.

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