# An Overview of Antibiotic Production from Marine Fungi: A Review

*Dr Santosh Kumar Singh, Assistant Professor*

*Department of Health & Allied Science, Arka Jain University, Jamshedpur, Jharkhand, India*

***ABSTRACT:** Filamentous fungus are quite well for their potential to manufacture natural antibiotics. Recent research has revealed the potential of antimicrobials derived from marine fungi with broad chemodiversity. The conversion of such natural materials into active molecules necessitates a long-term supply. At many stages of the processing chain, including discovery, manufacturing, intermediate processing, and lead development, aquatic biotechnology can make a substantial contribution to the creation of novel antibiotics. The number of biotechnological approaches described for better volume from marine fungi, on the other hand, is significantly less than the increase in the number found natural antibiotics. The techniques and methods used in marine fungal biotech are generally derived from equivalent terrestrial procedures, and they rarely represent the unique requirements of marine fungi. This review summarizes the current state of biological production of aquatic fungal antibiotics, antibiotics derived from natural sources, oceanic fungi, biotech for the long-term creation of new antibiotics, different stages of the production process for developing antibiotics from marine fungi, chemical structural elements of metabolic pathways from marine derived fungi, and biotechnology for the long-term production of new antibiotics. Recent research on marine filaments fungus in search of physiologically active secondary metabolites has revealed that they have enormous promise as a source of novel medicines. The uniqueness of marine-derived chemicals, as well as their broad range of uses, may pave the way to a treatment for many terrible diseases such as AIDS (acquired immune deficiency syndrome), cancer, Alzheimer's, and arthritis, which are harder to cure.*

***KEYWORDS:** Antibiotics, Bacteria, Biotechnology, Fungi, Marine.*

## 1. INTRODUCTION

The rise of multidrug-resistant (MDR) bacteria has been linked to the overuse and abuse of antimicrobial drugs, which has been linked to a rise in the death rate linked with infectious illnesses. Multidrug resistance and related mortality necessitate a redoubled effort to develop new effective antibiotics from non-traditional sources. This has involved the creation of new antibiotics from several Nano compounds in the recent decade. Furthermore, because natural chemicals account for around half of all novel antibiotics in development, researchers chose to look at marine microorganisms [1]. Active natural chemicals with biological and pharmacological characteristics abound in the aquatic environment.

Every year, the quantity of metabolically active chemicals found in the marine ecosystem grows, and fungus play a significant role, with around 200 new active ingredients discovered each year, the nature of which varies by fungal species [2]. Marine fungus may be susceptible to distinct difficulties than their terrestrial counterparts based on the nature of aquatic ecosystems, which encourage the synthesis of biologically active compounds as defensive strategies [3]. Such active metabolites from ocean fungus recovered from diverse geographical areas can be nucleoside compounds, terpenoids, polyether's, alkaloids, macrolides, or peptides having anti-inflammatory, anti-cancer, and antibacterial characteristics, among other pharmacological processes.

Considering the paucity of success in getting powerful synthetic antibiotic to the medical, discovering novel microbial natural ingredients (NPs) is the best chance for generating a new generation of anti-infective medicines. These molecules are unrivalled in their chemical variety and efficacy as antibiotics. Filamentous actinomycetes are responsible for 64 percent of all known NP antibiotic groups, with the rest coming from fungi and bacteria (Figure 1).

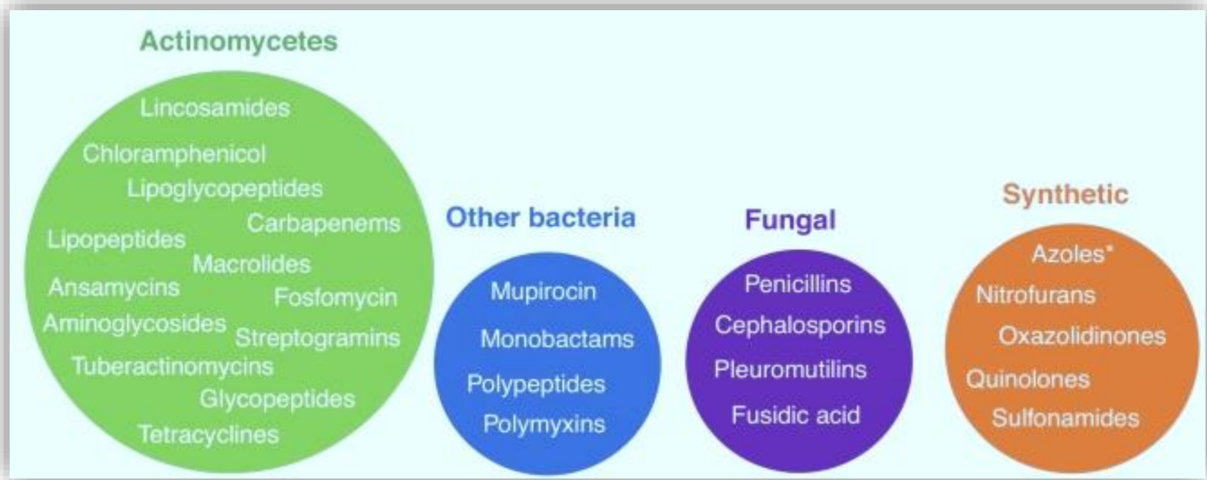


**Figure 1: Most Clinically Related Groups of Antibiotic Derived from Natural Origins**[4]**.**

*1.1 Marine Fungi:*

Fungi may be found in a wide range of marine habitats, from the ocean depths to the polar ice caps. They are present in sediment and all types of alive and dead organic materials. In comparison to bacterium, their quantities in ocean waters are very modest, and most research on marine fungus have focused on those linked with sediment samples, specialized substrates such as driftwood, microalgae, coral, and, in particularly, sponge [5]. It is necessary to understand the phylogenetic variety of marine fungus, the biosynthetic capacity of different strains, and the phylogeny of natural substance biosynthesis in order to evaluate the total potential of marine fungi for natural substance biosynthesis. One-third of a total of 30 investigations on secondary metabolites from deep ocean fungus was recognized as belong to Penicillium, one-third to Aspergillus, and the rest was allocated to several other species.

Aquatic fungi are a rich source of bioactive compounds that can be used in medication development. Despite the fact that marine fungi are less researched than their planetary counterparts, a number of important hits have been acquired from a drug development standpoint, highlighting their significance in natural substance invention, which has produced a huge spectrum of chemically diverse operatives with antimicrobial, antiviral, and anticancerous properties in experimental animals. Marine fungus has given different chemical skeletons that may be utilized to generate medicines of therapeutic relevance, beginning with the well-known examples of cephalosporins [6]. Many medicines in use have been isolated from fungus, including paclitaxel, camptothecin, vincristine, torreyanic acids, and cytarabine, to mention a few. Marine is therefore essential not only as a supply of novel medicines, and also as a source of potential scaffolds that may be further changed to achieve the required effect[7].

Despite considerable progress in drug development, which has resulted in the treatment of certain major illnesses, minor infections, and outbreaks, new medicines are needed to battle worldwide resistance to treatments for current diseases and novel infectious diseases that have just been identified. Aside from medication tolerance in illnesses like TB and malaria, cancers and HIV-AIDS have been major targets for therapeutic research with mixed results. Figure 2 depicts several of the marine fungus species that are developing in the culture medium for antibiotic synthesis[8].

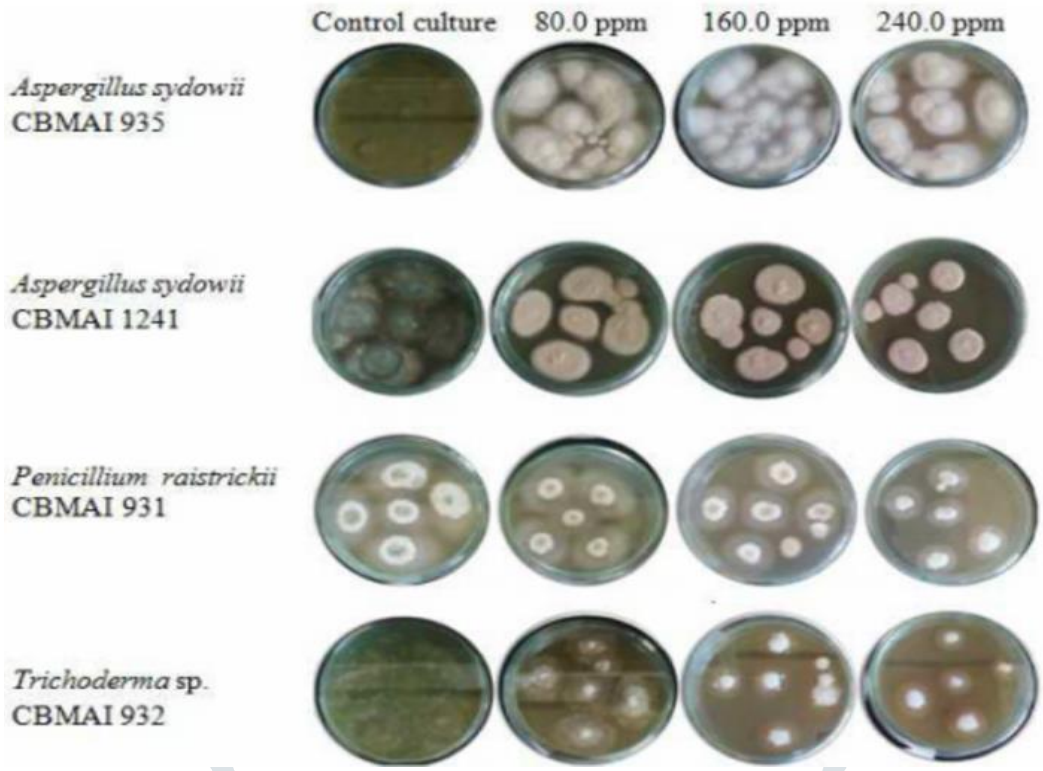


**Figure 2: Aquatic Fungi Mounting On Solid Culture Mediums**[9]**.**

*1.2 Biotechnology for Sustainable Production of New Antibiotics*:

Microbes, unlike macro organisms, have the benefit of being able to produce vast amounts of anti-infective natural compounds through large-scale culture at low prices. This is represented in the global antibiotic manufacturing fermentation products, which is in total 100,000 tons and include 60,000 tons of penicillins, 5,500 tons of tetracyclines, and 2,500 tons of cephalosporins. -lactam medications are antibiotics that are organic or produced from natural materials. Despite this, there are significantly fewer positive stories in aquatic biotechnology than in any other industrial biotechnology sector. Just some of the hundreds of bioactive chemicals discovered in marine fungus have been commercialized. The shortage of transference from the discovery stage to a suitable biotechnological production process has hampered the availability of adequate amounts of substances for clinical studies or early-stage lead generation, including such biochemical or biocatalytic modifications.

Bioprocess engineering in aquatic biotechnology, like biopharmaceutical biotech, begins to move from research to commercialization with a number of different beginning points and ways to move the molecule to next emerging stage [10]. Biotechnology, as shown in Figure 3, has a huge potential for producing antibiotics from marine fungi in a productive approach, starting with methodologies that effectively increase and recognize the chemical space in a targeted way, through traditional full fermentative and semi-synthetic processes, to metagenomics altering the genetic background as a grounds for generating "biological" derivative products[11].

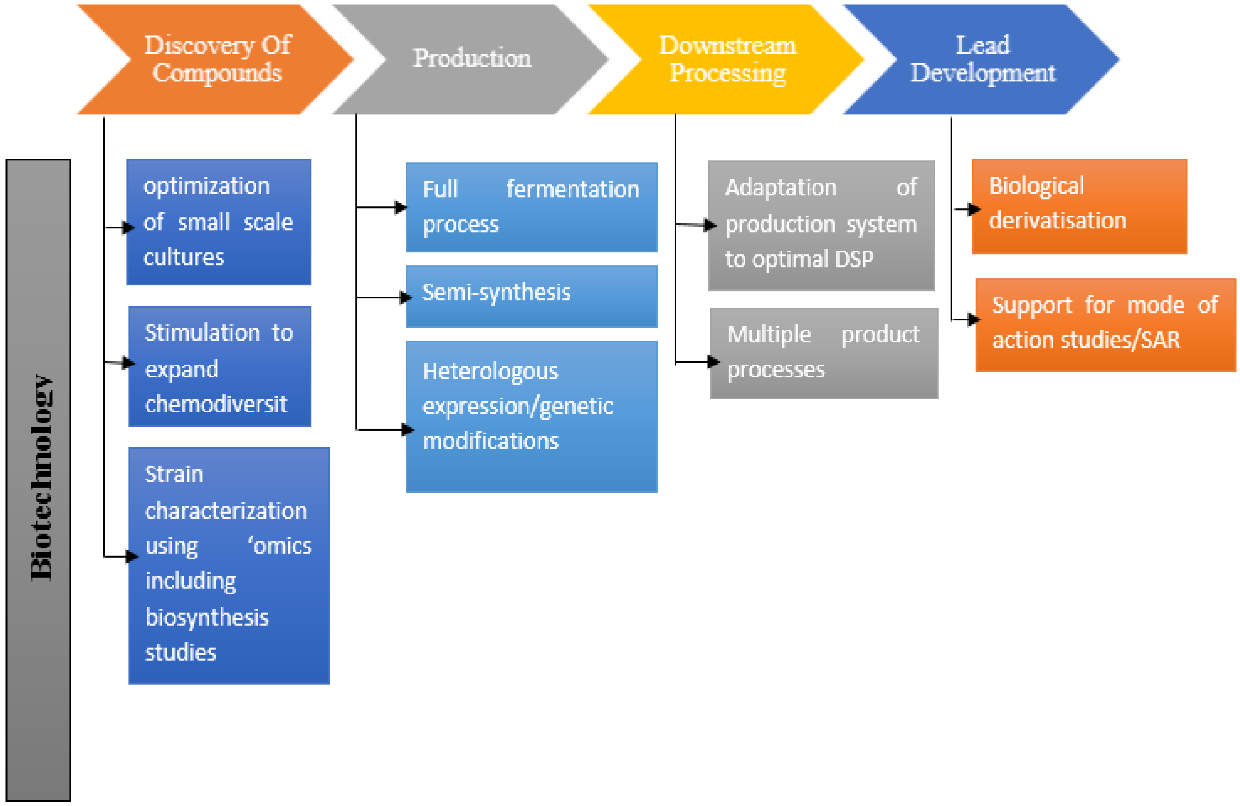


**Figure 3: Biotechnological Methodologies at Different Steps of the Procedure Chain for Emerging Antibiotics from Aquatic Fungi**[11].

*1.3 Current Status of Natural Products from Marine Fungi:*

Due to current trends in antibiotic resistance amongst different bacterial strains, that are generating severe issues in the management of infectious illnesses, it is in need of the research and development of new groups of antimicrobial chemicals. As a result of developing antimicrobial resistance, there is a growing need to create novel antibacterial chemicals. Antimicrobial substances such as 14, 15-secocurvularin, hirsutanol-A, and others have been discovered in marine fungus. This section addresses natural compounds derived from marine fungus that have antibiotic characteristics and might be used in clinical studies.

Pestalone is a novel chlorinated benzophenone chemical discovered from the marine fungi Pestalotia sp. It is demonstrated as significant antibiotic action against methicillin-resistant S. aureus and vancomycin-resistant Enterococcus faecium, hinting that it may be tested extensively in more advanced communicable diseases models (Figure 4). This antibiotic was generated particularly when a single celled marine bacteria type CNJ-328 was co-cultured in a fungal fermenter, indicating that microbial competitiveness is the catalyst for its synthesis. Speradine A, a 1-N-methyl-2-oxindole ring cyclopiazonic acid congener derived from the ocean fungus Aspergillus tamarii, exhibited antibacterial activity towards Mycrococcus luteus. Many gram-positive and gram-negative bacteria are inhibited by Zopfiellamide A, a pyrrolidinone derivatives derived from the facultative coastal ascomycete Zopfiella latipes[12].

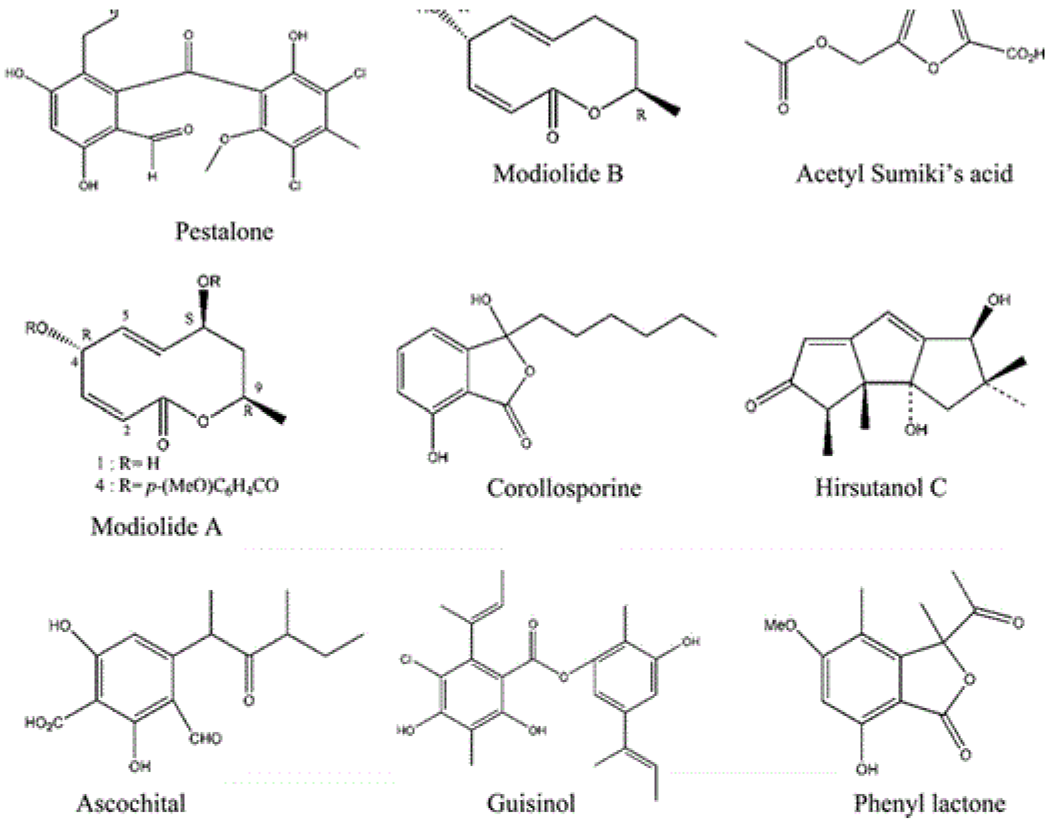


**Figure 4: Chemical Structures of Metabolites from Aquatic Derived Fungi Presenting Antibacterial Properties**[12]**.**

## 2. LITERATURE REVIEW

G. A. Vitale et al. emphasizes on using marine fungus to produce antioxidants. It starts with an overview of existing methods for analyzing antioxidants, then moves on to a discussion of several types of marine fungus antioxidants, as well as their extraction methods. Because they are a rich source of architecturally varied secondary metabolites, fungi play a key role in oceanic bioprospecting. Antibiotics, anticancer, antioxidant, and antiviral drugs are only a few of the bioactive chemicals discovered in aquatic fungus. The quest for natural antioxidant compounds capable of supporting the synthetic antioxidant compounds presently in utilization is a topic that is gaining a lot of interest current days. Furthermore, a look at the future prospects and tendencies of these natural goods within the "blue economy" is provided. Antioxidants can inhibit the emergence of numerous degenerative illnesses, especially cancer, autoimmunity disorders, cardiovascular, and neurodegenerative problems, by inactivating reactive oxygen and nitrogen ions. Furthermore, they are used in a variety of sectors, including food storage, healthcare's, and cosmetic[13].

Saba Hasan et al. highlights several key bioactive compounds found in marine fungus isolates that have antibacterial, anti-tumor, and anti-inflammatory properties. It focuses on the biochemistry and bioactivities of oceanic fungi-derived bioactive alkaloids, polyketides, terpenoids, isoprenoid and non-isoprenoid chemicals, and quinones. Around 16,000 marine natural compounds have been extracted from aquatic creatures, with about 6,800 papers reporting on them, demonstrating that marine microbes are a potential source for the development of new antibiotics, anti-tumor, and anti-inflammatory medicines. Secondary metabolites from aquatic fungus, especially those associated with algal species, sponges, invertebrates, and sediment, prove to be an important resource of antibiotics, antiviral, antifungal, and anti-yeast activity. A few growth stimulating characteristics are also described, which might be beneficial in investigations on tissue regeneration, carcinogenic qualities, and cancer research. Recent research on marine filaments fungus in search of physiologically active secondary metabolites has revealed that they have enormous promise as a source of novel medications[14].

Thomas Willems et al. intends to compile a list of new alkaloids generated by marine fungus that have shown promise as antimicrobials in the last five years. Alkaloids from oceanic fungus offer considerable potential in the ongoing hunt for new antibacterial compounds. Recent investigations of newly acquired alkaloids, on the other hand, are frequently restricted to cytotoxicity studies and fail to address the riddle of their production. However, the latter is frequently a need in order to make things reachable via suitably efficient procedures. A number of discovery techniques are discussed, as well as knowledge gaps in biochemical manufacturing processes. Finally, connections are postulated between architecture of recently found compounds and their action. Considering this encouraging ratio of unique alkaloids effective towards Gram bacteria, the quantity of newly found antimicrobial alkaloids is minimal, owing to the limited range of identification procedures utilized and the fact that recently found alkaloids' antimicrobial characteristics are scarcely described. Finally, this article describes recent results on antimicrobial alkaloid from ocean fungus, demonstrates their possibility as attractive therapeutic possibilities, and offers suggestions on how to maximize this capability [15].

Yitayal S. Anteneh et al. The goal of this study is to look for bioactive compounds in isolated bacteria from sponge. A total of 1234 isolated bacteria were isolated from 12 sponge samples taken from South Australian coastal habitats and cultured on 7 isolated medium using four incubating circumstances. 169 microorganisms were evaluated towards eleven human diseases in conditions optimized for the generation of antibiotic compounds. Seventy microorganisms were shown to be effective against at minimum one test microbial or fungus pathogen, with 37 percent showing action against Staphylococcus aureus, particularly methicillin-resistant strains, and 21 percent producing antifungal activity. A possible new active chemical with antimicrobial action towards S. aureus was isolated. The strains were isolated as Streptomyces sp. using 16S rRNA. The marine sponges of South Australia are a great source of microbes generating compounds with antibacterial activity towards pathogenic bacterial strains and fungus, according to this investigation[16].

K. Kathiresan et al. Ocean actinomycetes have been found to have fungicidal action against plant pathogens. From sediments samples collected from mangrove, estuaries, sand dunes, and commercially contaminated coasts, a total of 160 specimens of ocean actinomycetes were identified. Mangroves sediment were a particularly rich source of maritime actinomycetes. Four phytopathogenic fungi were evaluated against the other strain. Approximately 51% of extracts was determined to be effective, and these isolates seemed to generate strong antifungal chemicals after 120 hours of producing media culture incubation. The optimum carbon and nitrogen supplies were glucose and soya beans, accordingly, while the best salt concentration for maximal antibiotic synthesis was 17.5 parts per million. The cylindrical plate method was shown to be superior than the disc diffusion approach for antifungal testing. The powerful isolates were recognized as species belonging to the genus Streptomyces based on the morphological and cultural features. These variants might be a valuable source for agro-based fungicide separation[17].

## 3. DISCUSSION

Since of their potential as therapeutic drugs, metabolites from marine fungus have taken center stage in drug development. Several metabolites linked to marine fungus have been identified from diverse sources, and they have been shown to have antimicrobial, antiviral, and anticancer activity. Despite the fact that over a thousand oceanic fungi-based compounds have been identified, none have yet made it to marketplace, which might be due to non-comprehensive screening methods and a lack of long-term lead optimization [18]. The locations of these aquatic fungal metabolites have indeed been documented from a variety of sources, including sponges, microalgae, mangrove-derived fungus, and fungi found in ground water. The significance of these natural products stems from their cytotoxicity and associated actions, which are derived from the variety of chemical configurations and chemical bonding found on them. Oceans have become a vast store of a range of biologically active chemicals, which are frequently the consequence of aquatic life's metabolites, in contrast to terrestrial sources. Though the exact reason why marine fungus create such a complex and diverse collection of metabolite is unknown, it is widely thought that they serve important roles in chemical defense and communications. Because the biological synthesis of such metabolites is influenced by environmental, physical, and biological variables, even little alterations in these settings can result in the production of a whole new set of metabolites[11].

## 4. CONCLUSION

The maritime habitat is a great source of chemical and biological variety, with approximately 300,000 known species in the seas, which represents just a small proportion of the total variety of species still to be identified. The oceans cover more than 70% of the Earth's surface, so each droplet collected from them contains 9:1 microbial species that are undiscovered to people. The ocean is a vast source of new substances with tremendous potential as pharmaceuticals, dietary supplements, cosmetics, agrichemicals, and enzymes, all of which have a high potential commercial value. Algae, sponge, coral, and ascidians are just a few examples of marine life that have had their natural ingredients contents examined. Many structurally and pharmaceutically significant compounds with new antibacterial, anticancer, and anti-inflammatory activities have been identified. After receiving little attention from dietary supplement chemists, fungi have come to be regarded as a plausible supply of potentially valuable natural ingredients as emphasis has moved to aquatic microbes.

This review summarizes the current status of biotechnological manufacturing of aquatic fungal antibiotics, medications derived from natural sources, marine fungi, biotechnology for long-term production of new antibiotics, various steps in the production process for creating antibiotics from marine fungi, and structural characteristics of metabolites from marine fungi. Oceans are rich in resources, allowing for a wide range of interdisciplinary research. In conclusion, marine fungi biotechnology can provide a variety of techniques and methodologies for the effective manufacture of antibiotics, and therefore serve as a springboard for the long-term utilization of aquatic life to address societal issues. Process engineers, on the other hand, nevertheless confront a number of challenges. They must be highlighted through designs of approaches for the sustainable growth of aquatic resources and also by the origination of novel generation tools and procedures to allow a better understanding of the oceans and its resources.

**REFERENCES**


[1] R. Agarwal, N. Garg, S. R. Kashyap, and R. P. Chauhan, "Antibacterial finish of textile using papaya peels derived silver nanoparticles," *Indian J. Fibre Text. Res.*, 2015.

[2] Jayanand, M. Gupta, A. Sinha, I. Insa, and D. V. Rai, "Antibacterial potential of Cymbopogon flexuosus oil against Enterobacter aerogenes and Klebsiella pneumoniae," *Biomed.*, 2014.

[3] S. Singh, A. K. Shrivastava, and V. K. Singh, "Arsenic and cadmium are inhibitors of cyanobacterial dinitrogenase reductase (nifH1) gene," *Funct. Integr. Genomics*, 2014, doi: 10.1007/s10142-014-0375-2.

[4] K. Kathiresan, R. Balagurunathan, and M. M. Selvam, "Fungicidal activity of marine actinomycetes against phytopathogenic fungi," *Indian J. Biotechnol.*, 2005.

[5] N. K. Agrawal, R. Agarwal, G. A. Kumar, J. Jain, Y. K. Vijay, and K. C. Swami, "Study of bacterial cell colonization on plasma induced bio-adoptable polymer nanocomposites membranes," 2015. doi: 10.1002/masy.201400186.

[6] N. Jahan, R. Khatoon, S. Ahmad, and A. Shahzad, "Evaluation of antibacterial potential of medicinal plant Spilanthes acmella Murr. And its in vitro raised callus against resistant organisms especially those harbouring bla genes," *J. Appl. Pharm. Sci.*, 2013, doi: 10.7324/JAPS.2013.31021.

[7] *et al.*, "Major bioactive metabolites from marine fungi: A Review," *Bioinformation*, 2015, doi: 10.6026/97320630011176.

[8] M. Daferner, T. Anke, and O. Sterner, "Zopfiellamides A and B, antimicrobial pyrrolidinone derivatives from the marine fungus Zopfiella latipes," *Tetrahedron*, 2002, doi: 10.1016/S0040-4020(02)00942-0.

[9] J. Silber, A. Kramer, A. Labes, and D. Tasdemir, "From discovery to production: Biotechnology of marine fungi for the production of new antibiotics," *Marine Drugs*. 2016. doi: 10.3390/md14070137.

[10] M. N. Jyothi, D. V. Rai, and R. Nagesh babu, "Identification and Characterization of High Temperature Stress Responsive Novel miRNAs in French Bean (Phaseolus vulgaris)," *Appl. Biochem. Biotechnol.*, 2015, doi: 10.1007/s12010-015-1614-2.

[11] N. Skovgaard, "Industrial Microbiology: An Introduction," *Int. J. Food Microbiol.*, 2002, doi: 10.1016/s0168-1605(02)00154-x.

[12] A. L. Demain, "Importance of microbial natural products and the need to revitalize their discovery," *Journal of Industrial Microbiology and Biotechnology*. 2014. doi: 10.1007/s10295-013-1325-z.

[13] N. A. da Silva, W. Garcia Birolli, M. H. Regali Seleghim, and A. L. Meleiro Porto, "Biodegradation of the Organophosphate Pesticide Profenofos by Marine Fungi," in *Applied Bioremediation - Active and Passive Approaches*, 2013. doi: 10.5772/56372.

[14] J. F. Imhoff, "Natural products from marine fungi - Still an underrepresented resource," *Mar. Drugs*, 2016, doi: 10.3390/md14010019.

[15] S. S. Swain, R. N. Padhy, and P. K. Singh, "Anticancer compounds from cyanobacterium Lyngbya species: A review," *Antonie van Leeuwenhoek, International Journal of General and Molecular Microbiology*. 2015. doi: 10.1007/s10482-015-0487-2.

[16] D. Dubey, M. C. Sahu, S. Rath, B. P. Paty, N. K. Debata, and R. N. Padhy, "Antimicrobial activity of medicinal plants used by aborigines of Kalahandi, Orissa, India against multidrug resistant bacteria," *Asian Pac. J. Trop. Biomed.*, 2012, doi: 10.1016/S2221-1691(12)60322-0.

[17] P. Bhadury, B. T. Mohammad, and P. C. Wright, "The current status of natural products from marine fungi and their potential as anti-infective agents," *Journal of Industrial Microbiology and Biotechnology*. 2006. doi: 10.1007/s10295-005-0070-3.

[18] M. Choudhary, Jayanand, and J. C. Padaria, "Transcriptional profiling in pearl millet (Pennisetum glaucum L.R. Br.) for identification of differentially expressed drought responsive genes," *Physiol. Mol. Biol. Plants*, 2015, doi: 10.1007/s12298-015-0287-1.