

## Marine Microbial Natural Products

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Isolation of diverse chemical compounds from marine organisms implies a promising source of natural products. Oceans cover nearly 70% of the earth's surface and over 90% of the volume of its crust (1). Marine environment contains a variety of species, many of which have no terrestrial counterparts. Recently, trends in search of new drugs emphasize that marine microorganisms could be potential productive sources of novel secondary metabolites (2).

Marine microbial secondary metabolites with chemical diversity and varied bioactivities are gaining wide applications in pharmaceutical and agricultural research (3). Their survival in extreme habitats enables marine microorganisms to develop unique physiological as well as metabolic capabilities, which may not be produced by their terrestrial counterparts. It is reported that the number of bioactive metabolites from marine microorganisms has exponentially increased during the last three decades (4). This diversity has attracted scientists to screen these products to find new medications.

Bioactivity profiles of marine metabolites include neurotoxic, antiviral, antitumor, antimicrobial or cytotoxic properties and are of considerable biotechnological interest. So far, more than 30 compounds are in clinical or preclinical trials. Currently, 16 of 20 marine antitumor compounds under clinical trial are derived from microbial sources (5). A few examples are didemnin B (Aplidine™) and thiocoraline used for the treatment of different cancers (6).

However, despite interest on metabolites from marine derived microorganisms, researchers encounter some problems; for example, in the study of marine bacteria, only 5% of the marine bacteria observed in marine samples were amenable to be cultured with normal microbiological techniques (7). Moreover, taxonomy of marine bacteria is very poorly defined and fermentation yields are very low and may fall in the range of milligrams per liter in some cases. Nevertheless, criteria separating ma-

rine microorganisms from their terrestrial counterparts are not ambiguous; traits that help define some of the more distinct marine microorganisms are their ability to display barophily, halophily and autotrophic growth properties. Moreover, a way essential to distinguish marine and terrestrial microbes is using 16S ribosomal RNA analysis (16S rRNA).

Fortunately, microbiologists developed PCR-based screening assays that may increase the screening efficiency for bioactive compounds. In addition, advancement in the knowledge of genes involved in the biosynthesis of secondary metabolites and the knowledge with different biosynthetic systems, allow completely new approaches, such as combinatorial biosynthesis, to discover novel antibiotics and add another source of data for elucidation of metabolites structure (8). Some novel compounds from marine microorganisms are under investigation in preclinical/clinical trials. It appears that marine microbial natural products are going to be the most promising and endless source of drug development. In addition to the aforementioned methods, other innovative approaches such as ribosome engineering and the one strain and many compounds method (OSMAC), would also strongly support marine microbial natural products development. It is believed that marine microbial natural products can be better understood and discovered in the next decade by a combination of both conventional and innovative approaches (9).

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