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## The Sea as a Source of Antibiotics

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## Description

Over the past few decades, there has been a decline in antibiotics development, resulting in fewer new antimicrobial agents approvals. Thus, the era of antibiotics began in the 1920s and 30s with the discovery of penicillin by Alexander Fleming. There are now over 13 classes of antibiotics, some into their fifth generation, consisting on synthetic derivatives from older antibiotics and natural compounds. In the first decades, about 15-20 new antibiotics were developed each decade, but in the last ten years only 6 new drugs have come on the market. In addition to the scarce development of antibiotics, the emergence and increase of multiresistant bacteria to the existent antibiotics used in clinical practice are limiting treatment options for patients.

For these reasons, a need of finding new molecules with antimicrobial activity exists.

Nature is an enormous source of biodiversity that could provide us with new molecules from plants, fungi, and other macro- and microorganisms. In this aspect, seas and oceans are being investigated.

Nowadays, two millions of marine species are known and about 10,000 new species are discovered each year. It is estimated that about 100 millions of species could form part of our seas and oceans.

The potential of the oceans has been discovered by the pharmaceutical/biological research trying to obtain from their habitants some chemical substances, known as active principles that could have effects against pathogenic microorganisms and/or other medical utilities. Nowadays, molecules obtained from marine species have been used against malaria, HIV, or cancer, among others clinical problems.

Among the marine organisms, microalgae are being the focus of the research for new antimicrobial agents.

Microalgae biodiversity is very high, with more than 3,000 known prokaryotic taxons and more than 30,000 eukaryotic species identified among databases [1,2]. This huge biodiversity involves also great ecologic diversities, with microalgae species adapted for growing conditions in all types of waters (salty, brackish, fresh), and temperatures (ranging from polar to tropical and even extremely hot conditions) [3,4]. They are also adapted to diverse light intensities (surface waters, symbiosis inside animals and deep waters) [5], and are able to survive at large pH ranges [6]. Microalgae metabolism can be autotrophic, heterotrophic or even mixotrophic [7,8]. All metabolic possibilities are consequently associated to these taxonomic and ecologic diversities. All these genetic copiousness is also responsible for the existence, in most microalgae, of complex biosynthetic pathways. These pathways give rise to a vast array of enzymes and metabolites that have attracted industry attention [9].

As other photosynthetic cells, microalgae produce a diverse array of profitable, often unexplored products, with applications in the pharmacy, food, feed, cosmetic and chemistry sectors. Some of these compounds already possess a market price that makes their production at industrial scale highly profitable.

Some important examples of these products from microalgae are polyunsaturated fatty acids (PUFAs as  $\omega$ -3 and  $\omega$ -6) with cardioprotective and anti-inflammatory effects against different types of cancers (in the case of  $\omega$ -3). Vitamins (E, C) are important antioxidants in animal nutrition, protecting different tissues and organs from damage caused by reactive oxygen species (ROS) as in atherosclerosis or neuron damage [10-12]. Bio-colorants as phycocyanin, beta-carotene, astaxanthin and lutein are used as natural colorants in food or feed, with an important antioxidant effect on prevention of diseases (vitamin A blindness, macular degeneration) [13,14]. Immunostimulants and hypolipidemic-glucides as  $\beta$ -1,3glucan are polysaccharides showing antitumor activity and antiatherosclerosis effects [15,16]. Cell extracts from several microalgae species have demonstrated in vitro antimicrobial activity against several bacterial and fungal pathogens and an inhibitory effect on the growth of various human tumor cell lines [17]. Aquaculture feed is used in the intensive farms of salmon, shrimps, bivalves, etc., where some microalgae species provide a high protein and/or a ω-3 fatty acids content [18]. Cosmetic ingredients exert an intense antioxidant activity and a diverse array of functions on epithelial cellular processes (lipases inhibition, aquaporins induction) [19,20]. Industrial enzymes (lipases, cellulases or proteases) sometimes are used under high temperatures or extreme pH conditions, where conventional enzymes cannot work.

Algae, sponges, corals, jellyfish, echinoderms, sea squirts, sea snails, cephalopods, crustaceans, amphibians, are other marine organisms of which biomolecules with clinical activity have been obtained.

Despite the successes achieved so far, from each 10,000 substances extracted from marine creatures only 100 are bioactive and could be used in clinical.

Although it is well known that seas and oceans are sources of possible molecules with antibacterial activity, further research are needed to find them.

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