MARINE BIOTECHNOLOGY

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Keywords: Marine bacteria, corals, sponges, biomedicals, enzymes, biopolymers, aquaculture.

Contents

Summary

The marine environment is rich in biodiversity with novel species of micro-organisms and macro-organisms, which could serve as a source for a variety of novel products and processes. Some biomedical products based on marine biotechnology have already been commercialized. Enzymes obtained from marine organisms are already in use in molecular biology research and food processing (see also *Marine Microbial Enzymes*). Polysaccharides with application in the food and chemical industries are already being obtained from marine organisms. However, very little is known about marine organisms, and the potential to exploit these organisms for biomedical products, biopolymers, biocatalysts, bioremediation, food production and processing is almost unlimited.

1. Scope of Marine Biotechnology

Marine Biotechnology can be broadly defined as the technology that uses living marine organisms, or their parts, to make or modify products. Oceans cover 75 percent of the Earth's surface and the marine biosphere is one of the richest of Earth's habitats. Marine biodiversity is extremely high and this is the direct consequence of the extraordinary variability of the biosphere that encompasses a huge thermal range (from -1.5°C in Antarctic waters to 350°C in deep hydrothermal vents), with pressures ranging from 1 to over 1000 atmospheres, nutrient variations ranging from oligotrophic to eutrophic and highly photic to non-photic zones. This variability has led to an extensive specialization at all levels from micro-organisms to mammals. Novel species of micro-organisms and macro-organisms are being discovered in the marine biosphere. For example, novel species of mussels, clams, polychaetes, tube worms, anemones and crabs have been discovered in hydrothermal vents. Microbial diversity in the marine environment is not well understood, mainly because less than 1 percent of the marine microorganisms can be cultured by conventional microbiological methods (see also *Viable but Nonculturable Bacteria in the Marine Environment and the Biotechnological Tools to Detect Them*). However, recently, direct analysis of the sequence of ribonucleic acid found in the ribosomes (rRNA) is being used to study microbial diversity, and such studies have shown that marine coastal, surface and subsurface waters contain very large populations of microbial picoplankton with a high abundance of archaeal species (see also BG6.58.8.8). Archaeal species have been shown to constitute up to 34 percent of the total prokaryotic biomass in the vast volumes of cold Antarctic oceans.

The biological diversity of the marine biosphere offers enormous scope for the discovery of novel products and processes which have application in biomass and food production (for example, aquaculture and fisheries); production of polymers, biocatalysts, biomedical products, and organics; bioremediation and biomining etc. New products and processes are a key to future developments in biotechnology, and are dependent on new sources of biomaterials. Therefore, the greater the biodiversity, the greater the opportunity for discoveries that may lead to valuable biotechnologies. Sixty percent of the ocean area is covered by water more than 200 m deep.

Until recently, the deep sea was considered a biological desert, but it is now realized that the species diversity in the deep sea could exceed 10 million. From the biotechnological point of view, the marine environment facilitates the selection of novel products and processes illustrated in Table 1. Several products based on marine biotechnology have already reached the market and much more is in the pipeline. It has been predicted that in the coming decades, marine biotechnology will have a major share in the products coming from the area of Biotechnology.

Defining conditions	**Habitat**	**Products/Processes of biotechnological interest**
Anaerobic	Deep seafloor sediments	Anaerobic biotransformation and biodegradation
Low temperature	Deep sea, polar seas	Cold-active enzymes, antifreeze compounds, surfactants, biodegradation at low temperature and bioremediation
Low nutrient levels	off shore waters	High-affinity catalysts and ligands
High nutrient levels, symbiotic and commensal	Near shore sediments, epibionts and symbionts on fauna and flora	Consortia for enhanced turnover rates, novel bioactive chemicals, sensing signalling defence chemicals
High pressure	Deep sea	Novel and improved biocatalysts

High temperature, metals	Hydrothermal vents	Thermostable and solvent stable biocatalysts, Biohydrometallurgy.
High salinity	Saturated brines	Novel metabolites, halotolerant biocatalysts
Hydrocarbons	Hydrocarbon seeps	Bioremediation, biotransformation

Table 1. Conditions in marine environment and consequent biotechnological potential.

2. Industries Based on Marine Biotechnology

2.1. Biomedicals

During the last decade, marine biotechnology has already shown signs of fulfilling the promise of delivering products that would contribute to health care, food and chemical production. Table 2 gives examples of pharmaceuticals based on marine biotechnology that have already been commercialized. Until four decades ago, the major impediment to the search for marine natural products was the inaccessibility of the organisms. Early studies were carried out only with intertidal and shallow subtidal environments. However, with advances in diving technology, the availability of remotely controlled vehicles and submersibles, samples from depths of over 1000 m can be collected and examined.

Drug	Source	Indication
Acyclovir (Glaxo, Wellcome) Zovirax (Mylan) (ara-A)	Based on spongouridine and spongothymidine originally isolated from the sponge *Cryptotheca crypta*	Antiviral: herpes simplex virus types 1 and 2, Varicella zoster virus
Cytarbine (cytosar-U) (cytosine arabinoside; arc-C) (Pharmacia & Upjon)	Based on spongouridine and spongothymidine originally isolated from sponge *Cryptotheca crypta*	Acute non lymphocytic leukemia, acute lymphocytic leukemia chronic myelocytic leukemia, meningeal leukemia
Cepholosporins (many manufacturers)	Discovered from pseudo-marine fungus *Cephalosporium crumonium*	Brood spectrum antibiotic
Resilience skin care product (Estee Lauder)	Based on pseudopterosins, a series of diterpenoid Isolated from sea whip *Pseudopterogonia elizebethae*	Anti-inflammatory compound

Table 2. Drugs already developed through marine biotechnology.

Sponges and corals have proved to be a very potent source of bioactive compounds. About four decades ago, a series of arabinosyl nucleosides were isolated from the Caribbean sponge, *Cryptotethia crypta,* of which spongouridine was found to be a potent tumor inhibitor. Based on this, the analogs ara-A and ara-C have been synthesized and commercialized for treatment of viral infections and also in different types of leukemia (Table 3). Pseudopterosins, a series of diterpenoid glycosides isolated from the Caribbean sea whip, *Pseudopterogorgia elizabethae,* show anti-inflammatory properties, and the natural extract from this sea whip is used by Estee Lauder in their Resilience line of skin care products.

There are a number of products from marine biotechnology that are undergoing clinical trials under the auspices of the US National Cancer Research Institute (NCI). These include ecteinascidin 743, a novel alkaloid isolated from the marine ascidian, *Ecteinascidia turbinata,* that shows anti-tumor activity; bryostatin - I, a macrolide anti-tumor agent isolated from the common fouling bryozoan, *Bugula neritina*; dolostatin-10, a linear peptide found in the sea hare, *Dolabella auricularia,* and halichondrin B, an anti-cancer agent found in the sponge *Halichondria okadai.*

Compound	**Source**	**Activity**
Discodermolide	Sponge, *Discodermia dissoluta*	Anti-cancer
Isogranulatimide	Tunicate from Brazil	Anti-tumor
Debromohymenialdisine	*Stylotella aurantium*	Osteoarthritis
Bryostatin-1	Bryozoan *Bugula neritina*	Anti-cancer
Ecteinascidin 743	Ascidian *Ecteinascidia turbinata*	Anti-cancer
Dolostatin-10	Sea hare *Dolabella auricularia*	Anticancer
Halichondrin B	Sponge *Halichondria okadai*	Anti-cancer
Curacin A	Cyanobacterium *Lyngbia majuscula*	Anti-cancer

Table 3. Drugs, from marine sources, under development.

There are also a few compounds that are being evaluated in pre-clinical trials. Discodermolide, a novel polyhydroxylated lactone from the deep-water sponge, *Discodermia dissoluta,* shows higher immunosuppressive activity compared to clinically useful immunosuppressive agents such as cyclosporin A and FK 506. Curacin A, isolated from the marine cyanobacterium, *Lyngbya majuscula,* shows potent anti-proliferative activity and some selectivity for colon, renal and breast cancer derived cell lines. This compound inhibits polymerization of purified tubulin, a mechanism of action shared by clinically useful anticancer drugs such as Taxol.

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Biographical Sketch

Dr. (Mrs.) Indrani Karunasagar is presently the Director of the UNESCO Microbial Resources Centre (MIRCEN) for Marine Biotechnology at the College of Fisheries, Mangalore. She took her M.Sc. degree in Microbiology from Mysore University and Ph.D. degree in Microbiology from Mangalore University. She has postdoctoral experience at the Institute of Aquaculture, University of Stirling, UK and University of Maryland, Centre for Marine Biotechnology, USA. Her main research interests are diseases in aquaculture and their diagnosis by molecular methods, applications of probiotics, vaccines and immunostimulants in aquaculture and marine toxins. She has served as an Expert Member of committees of the Food & Agriculture Organisation (FAO) and as a Scientific Advisor to the International Foundation for Science (IFS), Sweden.