Marine Polyextremophiles and Their Biotechnological Applications

Bhagwan Rekadwad and Chandrahasya Khobragade

Abstract This chapter describes the versatility of marine microorganisms. They have inherent ability to grow and thrive under polyextremes. The bioactive compounds such as hydrolases, unique pigments, alkaloids, peptides, colored antibiotics, exopolysaccharides, siderophores, ectoine, and proteins produced and released under stressful conditions have potential biotechnological applications especially in agriculture, food, health care, and medicine. We have also discussed the possible applications of polyextremophiles in the treatment of cancer and neurodegenerative diseases.

Keywords Extremophiles • Extremolytes • Microbial diversity • Secondary metabolites

1 Introduction

Marine extremophiles are the organisms that can thrive and reproduce at extremes of salt concentrations (salinity >1.0 M NaCl), pH (>8.0, <5.0), temperature (1–15 °C, >45 °C), and pressure (average 380 atmosphere, >500–1200 atmosphere and beyond), in the presence of high radiations, recalcitrant compounds, heavy metals, and inhibitors. Extremophiles belonging to the *Eubacteria*, *Archaea*, and eukaryotic kingdoms produce extremophilic biomass in ecological niches such as oceans, salt marshes, solar salterns, hypersaline lakes, hot springs, marine hydrothermal vents, and soda lakes. These marine polyextremophiles have great importance and contributed a lot in biotechnological industries. The bioactive compounds such as extremozymes, proteins, and extremolytes are exploited in various bioprocesses and industries. But, it remains to uncover their potential biotechnological applications in health care, food, and agriculture. Very few research groups worldwide are working on molecular mechanisms underlying the potential of such applications (Table 1). The present chapter highlights the applications of marine polyextremophiles.

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Table 1 Polyextremophiles/extremophiles: habitats, survival and defensive strategies, and bioactive compounds and their potential applications in biotechnology

Extremophiles	Habitat/source/ requirement for growth	Survival and defensive strategies	Extremolytes/bioactive compounds	Representative applications	References
Hyperthermophiles	(a) Deep-sea hydrothermal vents (b) Optimum growth at temperatures above 80 °C	Stabilization of enzymes from stress and freeze drying; protection of oxidative protein damage; reduction of VLS in immunotoxin therapy	Superoxide dismutase, DHAP-dependent aldolases	Dismutation or disproportionation of superoxide free radical anions Synthesis of rare sugars and carbohydrates Generation of potable alcohol, solvents, and acetic acid Catalyze lignin degradation in methylotrophs	Valls and de Lorenzo (2002), Mergeay et al. (2003), Gomes and Steiner (2004), Irwin and Baird (2004), Davilla et al. (2008), Radianingtyas and Wright (2003), Zhu et al. (2013), Falcicchio et al. (2014), Niefar et al. (2015), Dalmaso et al. (2015)
Thermophiles	(a) Hot springs, sun-heated soil (b) Artificially heated places such as compost piles, heaps, etc. (c) Grows at temperatures between 45 and 80 °C		Amylases, cellulase, endoglucanase, xylanase, chitinase, glycosidase, mannanase, proteases, lipases, esterase, DNA polymerases, phytase, phosphatase, lichenase Whole microorganism	Starch processing, oligosaccharide synthesis, paper bleaching, food processing, detergents, genetic engineering Ethanol production, bioremediation, and biomineralization	
Halophiles	(a) Oceans, salt marshes, salterns, hypersaline lakes (b) Requires at least 1 M salt for growth	Protection of skin immune cells from UV radiation; enzyme stabilization against heating, freezing, and drying; protection of the skin barrier against water loss and drying out; block of UVA-induced ceramide release in human keratinocytes	Proteases, dehydrogenases, laccases, siderophores, compatible solutes	Peptide synthesis, biocatalysis in organic media, saline water treatment, pharmaceuticals, cosmetic additives	

Acidophiles	(a) Mines, mine drainage, deep-sea hydrothermal vents (b) Optimum pH for growth—below 3	Maintaining a circumneutral intracellular pH; constant pumping of protons in and out of cytoplasm; acidic polymers of the cell membrane; passive regulation of the cytoplasmic pools of polyamines, and low membrane permeability	Amylases, glucoamylases, proteases, cellulase, oxidases	Starch processing, feed component, desulfurization of coal	
Alkaliphiles	(a) Coastal regions, soda lakes (b) Optimum pH for growth—above 8.0		Proteases, cellulase, amylases, lipases, cyclodextrinases	Polymer-degrading agents in detergents, food additives	
Piezophiles (barophiles)	(a) Oceans (b) Grows under high pressure 380 atmosphere (38 MPa) and above	Homeoviscous adaptation, tight packing of their lipid membranes, and increased levels of unsaturated fatty acids; polyunsaturated fatty acids maintain the membrane fluidity; robust DNA repair systems; highly conserved pressure-regulated operons; presence of heat shock proteins	Whole organisms	Food processing and antibiotic production	
Radiophiles (radioresistant)	Tolerance to high doses of radiation	It’s extremely efficient DNA repair mechanism enables it to reassemble the fragmented DNA in a relatively short time	Whole microorganism	Bioremediation of radionuclide-contaminated sites	

(continued)

Table 1 (continued)

Extremophiles	Habitat/source/ requirement for growth	Survival and defensive strategies	Extremolytes/bioactive compounds	Representative applications	References
Metalophiles (metallotolerant)	Tolerance to high levels of heavy metals	Transform certain metal species through oxidation, reduction, methylation, and alkylation. Apart from the enzymatic transformations that lead to metal precipitation and immobilization, other biological reactions that generate less poisonous metal species have been applied to bioremediation	Whole microorganism	Ore bleaching, bioremediation, and biomineralization	
Eurypsychrophiles (psychrotolerant)	(a) Sea and artificial low temperature places (b) Grows at temperatures above 25 °C but also grow below 15 °C	Translation of cold-evolved enzymes; increased flexibility in the portions of protein structure; presence of cold shock proteins and nucleic acid-binding proteins; reduction in the packing of acyl chains in the cell membranes	Proteases, amylases, lipases, dehydrogenases	Polymer-degrading agents in detergents, biosensors	
Stenopsychrophiles (psychrophiles)	(a) Antarctica, deep-sea trenches, and artificial low temperature places (b) Grows at temperatures between 10 and 20 °C	Compared to proteins from mesophiles, psychrophilic proteins show decreased ionic interactions and hydrogen bonds and possess less hydrophobic groups and more charged groups on their			

		surface and longer surface loops. Due to these modifications, at low temperatures, psychrophilic proteins lose their rigidity and gain increased structural flexibility for enhanced catalytic function. As the psychrophilic membranes contain a higher proportion of unsaturated fatty acids, their fluidity and ability to transport nutrients are maintained under very cold conditions. Moreover, the ability to synthesize cold shock or antifreeze proteins as the temperature drops, the more efficient enzyme activity due to alterations in enzyme kinetics, and the stabilization of microtubules enable the psychrophiles to continue their activities			

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Extremophiles	Habitat/source/requirement for growth	Survival and defensive strategies	Extremolytes/bioactive compounds	Representative applications	References
Endolithic	Grows inside rocks	Moisture present within the crusts form saturated NaCl solutions. This could be used by the endolithic microorganisms for primary productivity and growth	?		
Hipolith	Grows on rocks and cold deserts	?	?	?	
Oligotroph	Able to grow in environments of scarce nutrients	?	?	?	
Geophiles	Soil	Mucoidal layer enveloping cell colonies; biofilm formation as stress response to extreme environmental conditions			
Toxitolerant	Polluted sites	Tolerates high concentrations of toxic agents (e.g., organic solvents)	Whole microorganism	Removal and detoxification of organic solvent polluted sites such as industries	
Xerophiles	(a) Desserts (b) Grows in low water availability, resistant to desiccation	Thick layer of cell wall	Whole microorganism	Made available water to the plants. Help in increased crop productivity. Genes can be transferred to other higher taxa	

2 Hydrolases from Marine Microorganisms

The marine polyextremophiles were investigated for the production of hydrolases. These include amylases, cellulases, peptidases, xylanases, chitinases, pullulanases, beta-xylosidase, lipases, and phytases produced by hyperthermophiles, psychrophiles, halophiles, and piezophiles. These marine extremozymes are stable and function in harsh physicochemical conditions. These are useful in food, fodder, biofuel production, medicine, and pharmaceutical and fine chemical industries (Gomes and Steiner 2004; Dalmaso et al. 2015).

3 Bioactive Compound from Marine Microorganisms

Marine microorganisms are always attractive to science. They are capable of producing unique color pigments with broad-ranging pharmacological activities. These have industrial and commercial applications. Microorganisms that produced biologically active and unique compounds include marine *Bacillus*, *Pseudomonas*, *Pseudoalteromonas*, *Streptomyces*, *Vibrio*, and *Cytophaga* isolated from seawater and sediments from sea and coastal region and bacteria associated with marine algae (*Sargassum* and *Codium*). They have produced biotechnologically important products such as alkaloids (prodiginines and tambjamines), indole derivatives (quinines and violacein), macrolides, terpenoids, polyenes, and peptides (Soliev et al. 2011; Soria-Mercado et al. 2012).

Several red, violet, yellow, and red to pink pigments were isolated from marine bacteria. *Serratia marcescens* have produced prodiginines (red-pigmented prodigiosin compounds) as a secondary metabolite. The polyunsaturated hydrocarbon containing 40 carbon molecules is called as carotenes. It exhibits red to pink coloration due to the presence of a wide variety of isoprenoid compounds (β-carotene, lycopene, phytofluene, and phytoene). These carotenoid or carotenoid-like compounds were produced by marine microorganisms related to the *Cytophaga-Flavobacterium-Bacteroides* group. Similarly, *Salinibacter* has contributed a lot in the production of carotenes in salterns. The marine bacterium *Agrobacterium aurantiacum* have carotenoid biosynthesis gene cluster, which has a role in the production of pigment astaxanthin. *Paracoccus haeundaensis* is another astaxanthin producer isolated from the marine environment. Like *Paracoccus haeundaensis*, *Chromobacterium* has the ability to produce the violet pigment indole derivative – violacein. The pigments (prodiginines, carotenes, violacein, phenazine compounds, quinines, glycosylated and pigmented anthracycline antibiotics (fridamycin D, himalomycin A and B), tambjamines, melanins, and other pigmented compounds) produced by marine microorganisms are biologically active compounds. On the other hand, various deep-sea fungi such as *Acremonium*, *Alternaria*, *Aspergillus*, *Chaetomium*, *Cladosporium*, *Exophiala*, *Engyodontium*, *Fusarium*, *Phoma*, *Penicillium*, *Hormonema*, *Rhodosporidium*, *Rhodotorula*, *Schizophyllum*, *Tilletiopsis*, *Tritirachium*, and *Sistotrema* produced polyketide compounds, steroid derivatives, indole derivatives, sesquiterpenoids, alkaloid compounds, aromatic compounds, pyrone analogues, sorbicillin derivative, breviane derivative, compounds containing amino acid structure, novel cyclopentenone, trichoderone, prenylxanthones, depsidone-based analogues, citromycetin analogue, diketopiperazine derivatives, hydroxyphenylacetic acid, and other compounds showing inhibitory activities. These are useful in health care, medicine, pharmaceuticals, and cosmetics as antibacterial, antiviral, antimalarial, antiplasmodial, antiprotozoal antibiotic, algicidal, immunosuppressant, anticancer, anti-inflammatory, antiproliferative, antioxidation, cytotoxic, and protecting agents from UV irradiation (Shieh et al. 2003; Yi et al. 2003; Matz et al. 2004; Lee et al. 2004; Zhang et al. 2005; Nakashima et al. 2005; Kim et al. 2007; Williamson et al. 2007; Feher et al. 2008; Yada et al. 2008; Becker et al. 2009; Mayer et al. 2010; Ahmad et al. 2013; Wang et al. 2015; Simon-Colin et al. 2015).

4 Exopolysaccharides from Marine Bacteria

The diversity of marine microorganisms producing exopolysaccharides (EPSs) is an unexplored area. Its detailed study may lead to the discovery of new molecules and biocatalysts useful in food products, human therapeutics, and pharmaceuticals. The marine EPS producers secrete capsular polymers in their surrounding environment. These secreted EPS polymers remain attached to the cell membrane through the lipopolysaccharides (LPSs) and give a slimy texture to the colonies of producers. This produced slimy LPS may be slowly dispersed into the environment. EPS produced by marine microorganisms combines with other bacterial polysaccharides such as alginate and chitosan which generate resistance to diseases in host. Additionally, it also increases adhesion to the surfaces, exhibits cell integrity, traps nutrients, and protects the host cells from the impact of toxic compounds and adverse freezing-like conditions (Nicolaus et al. 2010; Freitas et al. 2011; Donot et al. 2012; Mehta et al. 2014; Delbarre-ladrat et al. 2014; Finore et al. 2014).

5 Natural Bioactive Products from Marine Hydrothermal Vent Environments

Piezo-acido-hyperthermophiles and piezo-halo-psychrophiles, such as *Streptomyces*, *Micromonospora*, *Rhodococcus marinononascens*, *Bathymodiolus septemdierum*, *Thermococcus* S 557, *Methanococcus jannaschii*, *Bathymodiolus septemdierum*, *Halomonas* LOB-5, *Calyptogena soyoae*, *Thermovibrio ammonificans*, etc., are capable to produce thousands of biologically active neutral compounds. These polyextremophiles have produced microbial metabolites such as

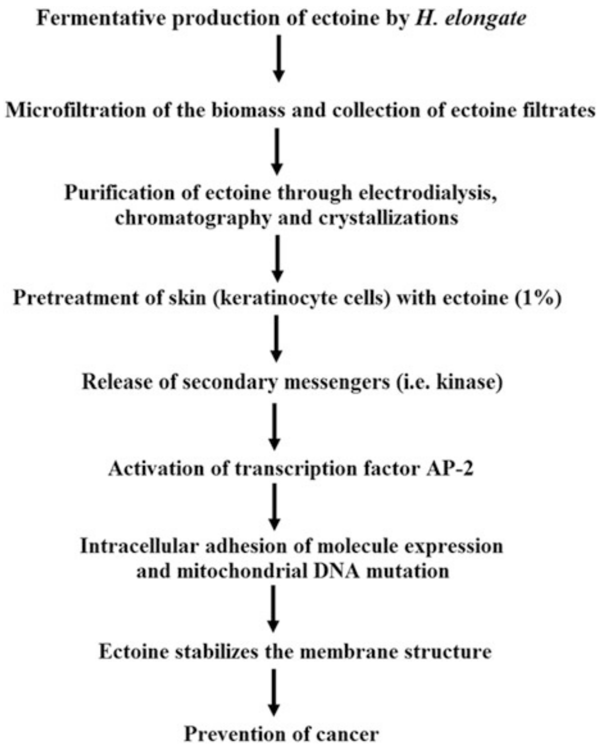

Fig. 1 Proposed hypothetical mechanism mediated by extremolytes in *H. elongata* (adapted and modified from Copeland et al. 2013)

archaeal glycerol ethers, sterols, loihichelins (A–F amphiphilic peptidic siderophores), ammonificins, and amphiphilic siderophores. These produced industrially important microbial metabolites that are useful in the treatment of cancer (Fig. 1), Alzheimer's, Parkinson's, dementia, and other human diseases (Thornburg et al. 2015; Corinaldesi 2015).

6 Future Perspectives

It is vital that marine extremophiles cope and withstand under extreme harsh environmental conditions. They have developed defensive mechanisms to survive in extremes, and their metabolisms play key roles in survival processes. The adaptability of extremophiles arrives from their altered genes and protein, which enables marine extremophiles to produce extremolytes having potential biotechnological applications in the treatment of cancer and degenerative diseases (Alzheimer's, Parkinson's, and dementia) (Calderon et al. 2004; Kanapathipillai et al. 2005; Graf et al. 2008; Kuhlmann et al. 2011; Babu et al. 2015). The produced extremolytes help them to survive and function under harsh physicochemical conditions. Currently, the research is focused on and aiming the polyextremophiles, extremonelles (cell organelles of extremophiles such as mitochondria), and extremolytes' functions in damaging environments. The hypothetical survival mechanisms explain better to understand the survival mechanism of marine extremophiles (Fig. 1).

6.1 Use of Ectoine (5-2-Methyl-1,4,5,6-Tetra-Hydro-Pyridine-4-Carobylic Acid) in Cancer Treatment

Exposure to high level/dosage of radiation leads to alteration of DNA structure. If cellular machinery did not repair the DNA, it will produce cancer. Halophilic bacterium *Halobacter elongate* (*H. elongate*) has a mechanism of ectoine biosynthesis, which neutralizes the impact of high UV radiation exposure/dose. This has a role in cancer treatment (Fig. 1). *H. elongate* produce ectoine from aspartate semialdehyde (ASA). The immune-protective effects of ectoine which treat Langerhans cells and protect DNA from damage (i.e., from cancer) are explained using three-step processes summarized in Sect. 15.6.2 of this chapter.

6.2 Hypothetical Model for Development of Therapeutic Proteins/Products for Treatment of Neurodegenerative Diseases Using Extremophiles/Extremonelles/Extremolytes

The neurodegenerative diseases (Alzheimer's, Parkinson's, and dementia) are the causative for cell death. The cell death occurred due to oxidative stress (as a result, apoptosis and necrosis occur in healthy cells), which leads to the formation of deadly mitochondrial diseases (http://www.projectsmagazine.eu.com/randd_projects/mitochondrial_mechanisms_of_disease_lessons_from_extremophiles). In these types of mitochondrial diseases, the cell walls were ruptured. These lysed products of the cells will be studied for understanding mechanisms of cell death. On the other hand, investigations are in progress on extremophiles, extremonelles, and their stable extremolytes functioning under harsh environmental conditions. Further research is planned to study the ecology and physiology of extremophiles to understand the surviving properties of extremophiles. It is necessary to identify the macromolecules that make the mitochondria and other cellular organs tenacious to damages. The identification will be carried out for critical proteins and enzymes that avoid the cell death. Also, we have planned to focus and perform studies on synthesis of proteins and enzymes, bioassay, and sequencing of mRNA of protein of interest. This will allow developing of drugs that reduce the efficacy of cell death inducer proteins/enzymes/macromolecules. The developed drug will be studied for its efficacy, nontoxicity, and stability using cell lines. After successful trials on cell lines, the experiments will be planned to carry out on experimental animals.

Thus, the ectoine-mediated neutralization and developments of new drugs/macromolecules may reduce or prevent dehydration of skin and skin aging and may be used in treatments of neurodegenerative diseases such as Alzheimer's, Parkinson's, dementia, and Machado-Joseph disease.

Conflicts of Interests Author(s) declares there is no conflict of interests.

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