Extremophiles: Applications and Adaptive Strategies

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***Abstract*: Limits of life on earth is still an expanding topic and extensive research is being carried out throughout the world. These limits are the nether and higher boundaries of various parameters like atmospheric, geochemical, temperature and water/nutrient availability. By the means of evolution many microorganisms have evolved and adapted to harsh extreme conditions whose study can give us insight into their defense mechanisms and adaptive strategies. The secondary metabolites as well as enzymes which are stable over a broad range of conditions can be extracted and put forward for the betterment of the environment and humankind. This review focuses on extremophiles living in the extreme environmental conditions of temperature, radiation, desiccation, salinity and pH.**

***Index Terms*: Extremophiles, Thermophiles, Xerophiles, Psychrophiles, Acidophiles, Alkaliphiles**

I. INTRODUCTION

In the recent decades many studies have emphasized on exploring the capabilities of living things to survive in extreme conditions. These extreme conditions refer to the upper and lower boundaries of various parameters including pH, temperature, salinity, desiccation, radiation, pressure and nutrient availability [1]. Microorganisms that are capable of growing in such extreme conditions are known as extremophiles (extreme-loving). However one should not confuse extremotolerants with extremophiles. Extremotolerant are those organisms which can withstand the extreme conditions upto a certain extent [2]. Microorganisms that can grow in two or more extreme conditions are called polyextremophiles [3]. This shows us that life can acclimatize to extensive parameters and thus by understanding the extremes in which life can sustain, we can advance our knowledge and search for life elsewhere in the universe. This review focuses on different extreme conditions and the strategies employed by microorganisms to survive in these harsh conditions. Review also gives insights on applications of enzymes and secondary metabolites obtained from these extremophiles.

II. EXTREMOPHILES

1. Temperature:

Temperature on earth ranges from -98℃ to 495℃ which was recorded at East Antarctica and Beebe deep hydrothermal vent [4][5]. Depending on the temperatures in which microorganisms can survive, they can be divided into three categories namely psychrophiles, mesophiles and thermophiles. Psychrophilic microorganisms grow optimally at temperatures below 15-20℃ [6]. Mesophiles are the microorganisms that grow optimally between 20-45℃ [7]. Microorganisms growing optimally at temperatures above 45℃ are called Thermophiles [8]. Out of these three categories, psychrophiles and thermophiles are regarded as extremophiles.

A. Psychrophiles:

The term psychrophiles originate from two Greek words “Psukhros” which means cold and “Philein” meaning love [9]. Psychrophiles belonging to different phyla have been reported including *Actinobacteria, Ascomycota, Basidiomycota, Chlamydiae, Chloroflexi, Cyanobacteria, Firmicutes, Euryarchaeto, Gemmatimonadetes, Nitrospirae, Mucoromycota, Planctomycetes, Proteobacteria, Thaumarchaeota, Verrucomicrobia, Flavobacterium, Shewanella Clostridium* and many more [10][11][12][13][14].

Psychrophiles and their products have a wide spectra of applications. Pigments such as carotenoid, due to their low toxicity and high stability have applications in fields like food, cosmetology and pharmaceuticals as coloring agent [15]; Indolic biochromes have multiple properties such as antitumour, antiviral, antiparasitic, antibacterial, antiprotozoal, and antioxidant activities [16][17]; Ubiquinone Q-10 is used in treatment of various diseases like Parkinson’s, Alzheimer’s and cardiovascular diseases [18]. Cold-active enzymes extracted from psychrophiles are important from an industrial point of view. B-glycosidase extracted from *Exiguobacterium oxidotolerans*, a deep sea sediment dwelling bacteria, which at 10℃ retains 61% of its utmost activity within pH 6.6-9.0 [19]; *Zunongwangia profunda* and *Flammeovirga pacifica* living in deep sea, produces cold adapted xylanases which are used in bakery industry [20][21]. Cold adapted α-amylase isolated from a deep sea resident of *Bacillus* spp. has its application in detergent as well as textile and food industries [22]. Exopolysaccharides (EPSs) isolated from psychrophilic marine bacteria *Colwellia psychrerythraea* show antifreeze properties [23]. EPSs are also used as thickeners, gelling agents, stabilizers as well as prebiotic, antioxidant and antitumoral [24].

Psychrophilic microorganisms employ various strategies to adapt themselves to lower temperatures including structural adaptations and enzyme adaptations. Genes responsible for long chain fatty acid production are upregulated and thus change the lipid bilayer composition of cell membrane [25]. This fatty acids are highly branched, long chained having cis-isomerisation (KAS-II and KAS-III) which help in preventing formation of ice crystals of fluids in cell membrane [26][27]. Long Chain Polyunsaturated Fatty acids (LC-PUFAs) like eicosapentaenoic (EPA, 20:5ω3), docosahexaenoic (DHA, 22:6ω3) and arachidonic (ARA, 20:4ω6c) acid play vital role in maintaining cell membrane fluidity in marine organisms as well as LC-PUFAs act as antioxidants against ROS like H_2O_2 which is present in high levels in deep sea [28][29][30][31]. Membrane pigments such as carotenoids play a vital role in membrane stabilization by acting against the fluidizing effects of LC-PUFAs [32]. These pigments also contribute in protecting organisms from freeze-thaw cycles [33]. Some psychrophilic organisms show hydrophobic encrustations made up of choline, peptidoglycan and calcium carbonate outside cell wall [34]. Modification in LPS structure is also seen in some Gram negative organisms in which shortened length LPS is produced without a specific O-chain component [35]. Psychrophilic organisms produce compatible solutes which are non-toxic, organic, low molecular mass osmolytes in high amounts [36]. These osmolytes help in maintaining the osmotic pressure and thus prevent loss of water and cell shrinkage as well as reduce intracellular glass transition temperature [37]. Another strategy to survive in the cold is by production of Antifreeze Proteins (AFPs). AFPs help the organism in maintaining inner cell fluidity via two processes; thermal hysteresis (TH) and ice recrystallization inhibition (IRI). In TH, AFPs lower the freezing temperature without affecting melting temperature of a solution whereas in IRI, AFPs inhibit growth of ice crystals [38][39]. On the contrary are the ice nucleating proteins (INPs) that are released in extracellular space which initiates ice nucleation/formation and help them damage plants and get access to nutrients [40]. Secretion of exopolysaccharides (EPSs) act as a barrier for ice formation around the cell as well as provide a habitable semi liquid environment [41]. Genomic and protein stability is conferred by DNA/RNA chaperone and protein chaperones whose production is upregulated and is continuously overexpressed in psychrophilic organisms [42]. Several studies have shown the capability of various psychrophilic organisms to accumulate and/or degrade polyhydroxyalkanoate (PHA) and/or cyanophycin like compounds which can act as carbon and nitrogen reservoirs [43].

Apart from above mentioned strategies there are many more minor yet important adaptations that help microorganisms to survive in harsh cold environments.

B. Thermophiles:

The term thermophiles is derived from Greek words; “thermotita” meaning heat and “philia” which means love. Thermophilic organisms include wide range of archaea and bacteria genre like *Moorella, Gelria, Pseudomonas, Geobacillus, Bacillus, Thermococcus, Thermus, Mycobacterium, Thermotoga, Gallionella, Crenothrix, Sphaerotilus, Leptothrix, Lieskeella, Pyrococcus, Sulfolobus, Metallosphaera, Caldicellulosiruptor, Thermoanaerobacter*, etc [44][45].

Enzymes isolated from thermophiles have significant biotechnological applications. Lipases isolated from thermophiles are used in detergents, in pharmaceutical formulations as esterification agent, they are also used in pulp and paper industries to remove hydrophobic components [46][47][48]. Thermolysin is used in synthesis of DNA processing enzymes, dipeptides and pretaq [49]. Prolidase isolated from *Pyrococcus furiosus* is the most stable prolidase which shows no loss of activity even after 12hrs at temperatures above 100℃ [50]. Novel pH stable and thermostable β-agarase AgaP4383 isolated from *Flammeovirga pacifica* WPAGA1 showed endolytic activity against agar at temperature 50°C without any loss for 10hrs, this activity can be useful in successfully extracting DNA from agarose gel [51][52]. *Taq* DNA Polymerase isolated from *Thermus aquaticus* set a benchmark by proving its application in Polymerase Chain reaction [53]. Chen, G., et al. reported detoxifying activity of thermophilic bacteria *Anoxybacillus* sp. PDR2 against azo dye Direct Black G, thus implying importance of thermophilic organisms in bioremediation [54]. Laccase-like multicopper oxidase isolated from Thermothelomyces thermophila carries out oxidative cyclization of 2’,3,4-trihydroxychalcone; other than that lacasses can be used in bioremediation, bio sensor, dye decolorization, etc [55].

Similar to psychrophiles, thermophilic organisms also need to modify their cell membrane, protein folding and packaging strategies, metabolic pathways, as well as produce heat shock proteins in order to survive in higher temperatures. Membrane phospholipids has been instrumental in protecting cell internals from its harsh surroundings. In thermophilic bacteria, length of lipid acyl chains is increased along with iso/anteiso ratio of branching and degree of saturation [56][57]. Thermophilic archaea contain lipid monolayers formed from glycerol dialkyl glycerol tetraethers (GDGTs) which are isoprenoidal tetraether lipids which lower the permeability of membrane for the solutes [58]. In *Thermoplasma* and *Sulfolobus* strains, C_{40} isoprenoid cyclisation was increased when grown at high temperatures, which resulted in tight packaging of lipids and thus lowering the fluidity of cell membrane [59]. Other than changes in cell membrane, thermostable proteins and enzymes play a significant role in allowing organisms to tackle adverse effects of high temperature. In thermostable proteins it was observed that there was reduction of thermolabile amino acids like threonine, histamine and glutamine as well as increase in frequency of charged residues like positively charged lysine and arginine and negatively charged glutamic acid implying that ionic bonds may help stabilize the proteins at higher temperature [60][61][62]. Increase in the number of intra helical salt bridges may also contribute to protein stability at high temperatures [63]. Chaperones has an important role to play in protein folding and refolding as well as unfolding and refolding of misfolded proteins. Chaperones are also designated as heat shock proteins as their synthesis is upshifted by increase in temperature [64]. There are five major conserved classes of heat-shock chaperones namely- Hsp100s, Hsp90s, Hsp70s, Hsp60s and sHsps [65]. In the organism *Pyrodictium occultum*, overproduction of 16-subunit chaperone was observed at 108°C [66]. Archaea like *Thermoplasma acidophilum* and *Methanobacterium thermoautotrophicum* showed the presence of Hsp70 also known as DnaK [67]. Similar to psychrophilic organisms, thermophiles also produce and accumulate compatible solutes in order to overcome stress like high temperature and desiccation. One such compatible solute called Cyclic 2,3-Diphosphoglycerate (cDPG) was detected for the first time in thermophile *Methanobacterium thermoautotrophicum* [68]. 0.5 *M* concentration of potassium-cDPG was able to prevent rapid inactivation of enzyme formyltransferase at 90°C in *Methanopyrus kandleri* [69]. cDPG also serve as a storage compound for phosphate and energy as well as it also protects plasmid DNA from hydroxyl radical’s oxidative damage [70]. Another such compatible solute is Diglycerol Phosphate (DGP). Only 15% drop in activity of glutamate dehydrogenase was observed with 100 *mM* DGP rather than 80% drop observed without DGP in *Thermococcus litoralis* when incubated at 90°C for 80 minutes [71]. Many other extremolytes like ectoin, proline, mannitol, mannosyl-glyceramide, glucosyl-glycerate and di-myo-inositol 1,1-phosphate have been reported to confer thermostability [72]. Studies have shown presence of high G+C content at the stem region of structural RNAs imparting thermostability [73]. Aslo, polyadenine tracts present in mRNA impart thermostability in single stranded RNA [74]. Studies carried out by Deeya Saha and team sheds light on overlapping genes as a new strategy to overcome thermophilic stress [75]. Role of G+C content in thermostability of DNA stills remains a point of debate.

2. Radiation:

Lower Earth Orbit (LEO) and space beyond LEO consist of various radiations like GCR, SEP and UV. We have seen how this radiation interacts with cells at DNA level and how it can alter it. However, studies have reported resistance in microorganisms against these radiations. Microorganisms employ various strategies like upregulation of DNA repair proteins, increased ability to counteract oxygen-free radicals, genomic rearrangements, upregulation of certain enzymes, pigment formation, etc [76].

Various studies have reported radiation resistant microorganisms. Gram negative bacterium *Acinetobacter radioresistens* 50v1 showed resistance to high UV radiation along with vapor and plasma H_2O_2 [77]. *Deinococcus radiodurans* can withstand with no loss in viability, high IR radiation dose of 5000-15000 Gy [78]. *Cryomyces antarcticus* a black fungus found in Antarctica permafrost has been reported to resist high UV doses for prolonged duration as well as it also remained viable at 6.66 kGy of gamma radiation [79]. *Bacillus pumilus* SAFR-032 showed survivability of 85-100% as well as its spores showed survivability of 10-40% when exposed to EXPOSE facility for 18 months [80]. Desert cyanobacteria *Chroococcidiopsis* was reported to withstand high UVC radiation in BOSS and BIOMEX experiments [81]. *Caenorhabditis elegans* a nematode was reported to withstand high LET gamma ray exposure with no effect on chemotaxis as well as locomotion [82]. *Xanthoria elegans* showed not only resistance but increased viability as well as higher photosynthetic activity when exposed to 208-215 mGy [83]. Musilova, M. et al. isolated radiation resistant *Halomonads* from Antarctic dry valleys and also established the correlation between desiccation resistance and radiation resistance [84].

Biotechnological applications of radiation resistant organisms include bioremediation, biomining and disposal of radioactive waste. Biomineralization of uranium by phosphatases released by various organisms like *D.radiodurans, Sphingomonas, C.crescentus*, *Bacillus*, *H.noricense* etc [85]. Mycosporine-like amino-acids (MAA) can absorb UV radiation as well as antioxidants and thus can be used in sunscreens [86]. Bacterioruberin produced by *Rubrobacter radiotolerans* can prevent screen cancer by repairing DNA strands damaged by ionizing radiation [87]. *C.cellulans* and *B.pumilus* were able to degrade cellulose at high rate [88]. *Shewanella putrefaciens* and *Geobacter sulfurreducens* have been proclaimed to convert soluble uranium into insoluble uranium [89].

Radiation affects mostly DNA and RNA, thus, various strategies are employed at genomic and proteomic levels to resist radiation. Adaptation strategies against radiation are widely studied in *Deinococcus radiodurans* as it is highly radiation resistant bacteria plus a polyextremophile. The cell envelope of D.radiodurans is different from other Gram negative bacteria. Electron microscopic study of its envelope has revealed that it has six layers with innermost layer being plasma layer and outermost being the S-layer. Second layer is a porous cell wall containing peptidoglycan. Third layer is made up of fine compartments whereas the fourth layer is an outer membrane. The fifth layer emits light under the influence of electrons in an electron microscope [90][91][92]. Before DNA repair, it is important to get rid of products formed by detrimental effects of radiation, one of the processes to achieve this is cellular cleansing. In this process, the organism eliminates damaged fragments of DNA thus preventing integration of disrupted bases during DNA synthesis and thereby avoiding higher levels of mutagenesis [93]. Other remaining mutagens present within the cell are removed using enzyme MutT which belongs to the pyrophosphohydrolase family [94]. Superoxide dismutases like SodA and catalases like KatA help in enzymatic removal of reactive oxygen species as well as dienoxanthin and pyrroloquinoline-quinone (PQQ) act as antioxidants and impart gamma radiation resistance in *D.radiodurans*. [95][96]. Various pathways are proposed for DNA repair in *D.radiodurans*. UV endonuclease-beta enzyme is isolated from *D.radiodurans* which recognize and cut out pyrimidine cyclobutane dimers formed by UV irradiation [97]. Other enzymes that play a role in DNA repair are thymine glycol glycosylase, uracil DNA glycosylase and deoxyribophosphodiestrase [98]. PprA and DrRecA are ascertained to be crucial in gamma radiation resistance in *D.radiodurans*. Pleiotropic protein promoting DNA repair protein activates NAD and ATP-dependent RNA ligases which inhibit exonucleolytic degradation and protect DNA ends [99]. DrRecA plays a crucial role in extended synthesis-dependent strand annealing (ESDSA). Irradiation leads to formation of overhangs in double stranded DNA fragments. DrRecA binds to these overhangs and undergoes homologous recombination to form an intact genome [100]. Another type of DNA damage induced by UVC radiation is formation of bipyrimidine photoproducts (BPPs). These BPPs are removed via two separate nucleotide excision repair pathways. These pathways rely on different proteins like UV DNA damage endonuclease, DNA polymerase I and Protein A of the UvrABC system [101]. Secondary structures of DNA/RNA called Guanine quadruplex (G4) play an important role in imparting radioresistance in *D.radiodurans*. *D.radiodurans* was exposed to G4 stabilizing drug called N-Methyl mesoporphyrin (NMM) prior to irradiation. Hampered DNA metabolism as well as sensitivity towards irradiation was observed [102]. Studies on IR resistant *Rubrobacter radiotolerans* and *Rubrobacter xylanophilus* showed that Mn^{2+} along with higher intracellular concentration of compatible solute trehalose play an important role in scavenging reactive oxygen species and thus eliminating the ROS formed due to irradiation [103]. *Thermococcus gammatolerans* is the most radioresistant archea reported [104]. Oxidative damage in DNA of *Thermococcus gammatolerans* after exposure to 5 kGy of gamma radiation was observed. Post exposure study revealed that it was repaired by two base excision repair enzymes called endonuclease III (TGAM_1277) and DNA lyase (TGAM_1653) whose transcription was upregulated after irradiation. These enzymes had β-elimination cleavage activity by which TGAM_1277 was able to remove affected pyrimidines whereas TGAM_1653 was able to eliminate oxidized guanine [105]. Various proteins like thioredoxin reductase, peroxiredoxin, and superoxide reductase capable of dealing with oxidative stress have been reported in the archaea [106].

3. Desiccation:

Life as we know requires liquid water to carry out its function and sustain. Desiccation is defined as removal of water from a body. Complete desiccation refers to water content below 0.1 g water per gram of dry mass [107][108]. Water activity (a_w) can be defined as pressure of water vapor in a material divided by vapor pressure of pure water at the same temperature [109].

Desiccation tolerance can be observed in a variety of living organisms starting from bacteria, fungi to plants. Organisms that can prevail in dessication are called xerophiles. *Bradyrhizobium japonicum*, *Rhodococcus jostii* RHA1, *Mycobacterium*, *Chloroflexus aurantiacus*, *Staphylococcus aureus*, *Methanothermobacter thermautotrophicus*, *Sulfolobus metallicus*, *Thermoproteus tenax*, *Hydrogenothermus marinus*, *Aquifex aeolicus*, *Archaeoglobus fulgidus*, etc. have been described as xerophiles [110][111][112][113][114].

Desiccation tolerant bacteria *Sphingomonas sp.* OF178, *Azospirillum brasilense* Sp7 and *Acinetobacter sp.* EMM02 has been reported to improve maize plant growth [115]. *Pseudomonas fluorescens*, *Pseudomonas migulae* and *Enterobacter hormaechei* were isolated from a drought tolerant crop called oxtail millet, were found to be xerophiles and improved soil/root ratio as well as moisture in soil around roots thus enhancing plant growth [116]. Organisms like *Acidithiobacillus ferrooxidans* strain Wenelen DSM 16786 and *Acidithiobacillus thiooxidans* strain Licanantay DSM 17318 have been isolated from Atacama Desert and have been patented for bioleaching of copper [117]. *Lechevalieria* and *Amycolatopsis* species have been isolated from Atacama Desert and have been shown positive for nonribosomal peptide synthase gene clusters which are responsible for production of antitumoral agents [118]. Drought resistant, phosphorus solubilizing microbes have been stated to improve plant growth [119]. Thus, studies are being conducted to analyze the potential of these xerophiles to establish and help sustain life in dry conditions as well as examine their other biotechnological applications.

Survival strategies employed by xerophiles include biofilm formation, increased secretion of EPS as well as extracellular DNA (eDNA), increased intracellular Mn(II), import and synthesis of compatible solutes or osmolytes, formation of HSP, and protein aggregation [120]. Various organisms such as *Klebsiella* spp., *Salmonella* spp., and some mucoid strains of *E.coli* produce a capsular polysaccharide called Colanic acid. Ophir and Gutnick isolated strains of *E.coli* K-12 which were able to produce colanic acid as EPS. The ability to produce EPS imparted resistance against desiccation which resulted in upto 35% survival as compared to their non-mucoid variants which showed 0.7 to 5% survival [121]. *Methanosarcina barkeri* produces EPS called Methanochondroitin which imparts desiccation resistance by retaining the water at critical level inside the cell [122]. Along with EPS production, accumulation of compatible solutes or osmoprotectants plays an important role in desiccation resistance by enabling vetrification of cytoplasmic matrix.. Anhydrobiotic cyanobacteria called *Chroococcidiopsis* showed presence of genes encoding for enzymes responsible for biosynthesis of trehalose and sucrose which were upregulated by 8 to 9 folds after 60 minutes of desiccation [123]. A nosocomial pathogen *Acinetobacter baumannii* has been reported to accumulate exogenous trehalose in response to desiccation [124]. Amassing of compatible solutes like K^+ ions, betaine, trehalose and sucrose was observed in *Rhizobia* when exposed to desiccation using NaCl [125]. Accumulation of Mn^{2+} was observed in *Deinococcus radiodurans* when it was subjected to desiccation stress thus protecting the proteins from oxidative stress resulting from desiccation [126]. Lack of water due to desiccation can lead to protein misfolding and agglomeration resulting in death of microbes. However in some organisms this protein aggregation provides resistance against desiccation via mechanisms yet to be discovered. Aggregation of proteins was observed in *Acinetobacter baumannii* during desiccation, which in turn protected functional proteins from desiccation [127]. Reversible aggregation of pyruvate kinase was observed in yeast exposed to desiccation, which prevented degeneration of protein and ensured the proper restart of cell cycle post stress [128]. HSPs form hydrogen bonds with other molecules and compensate for loss of water. The upregulation of heat shock proteins (HSPs) in response to desiccation was observed in cyanobacterium *Anabaena* sp. 7120 as well as of Hsp20 in *D.radiodurans* [129].

4. Salinity:

Salinity can be defined as concentration of salts dissolved in seawater and is expressed as parts per thousand or salt in grams per kilogram of seawater [130]. The salinity of the seawater is around 35 ppt or 3.5% [131]. The organisms capable of reproducing and surviving in high salt concentration niches are called Halophiles and depending on their ability to tolerate different concentrations of salt they are classified as slight, moderate, borderline extreme and extreme halophiles [132].

Halophiles can be isolated from brackish or hypersaline environments and comprises organisms from genus like *Bacillus*, *Brevibacterium*, *Dunaliella* (Algae), *Dactylococcopsis* (Cyanobacteria) *Halobacillus*, *Halococcus*, *Haloferax*, *Halogeometricum*, *Halomonas*, *Haloterrigena*, *Marinococcus*, *Natrialba*, *Natrinema*, *Salinibacter*, *Salinicoccus*, *Salinivibrio*, *Virgibacillus*, etc. [133][134][135].

Halophilic archaea, bacteria and fungi are known to produce carotenoids, hydrolytic enzymes, retinal proteins, macromolecule stabilizers, biofertilizers, and bioplastics, anticancer and antimicrobial compounds [136]. β - Carotene is mainly produced by halophilic algae called *Dunaliella salina*. It has potential applications in medicine as it exhibits antiviral, anti-inflammatory, anti-cancerous, and anti-allergic activity. Another carotenoid pigment produced by halophiles is Bacteriorhodopsin. It is found in cell membrane also called as purple membrane of halophilic archaea such as *Halobacterium salinarium*, *Haloferax larsenii*, *Haloarcula japonica*, *Halorubrum sodomense*, *Halostagnicola larsenii*, *Haloferax mucosum*, etc. The light driven proton pump activity changed the course of bioelectronics. It is used to produce holographic associative processors, optical volumetric memories, motion biosensors, photovoltaic cells, x-ray sensors, photoelectric immunosensors, artificial retinas, and so on. Bacterioruberin, a carotenoid pigment, synthesized by halophiles act as antioxidant and research is being conducted on its application in optoelectronics and photovoltaics [137][138][139][140][141]. Das, D. et al. isolated α-amylase producing halophiles belonging to genus *Halococcus*, *Halorubrum*, *Haloarcula* and *Halogeometricum*. α-amylase has potential application in food, brewing, laundry, textile and pharmaceutical industry. They also isolated protease, lipase, and esterase producing organisms and reported more than one hydrolytic activity in organisms. Industries like leather, detergent, textile, paper, cosmetic and pharmaceuticals make use of lipases and esterases [142][143]. Halophiles also play a crucial role in bioremediation in sea water where saline concentration is high. Waghmode, S. et al. reported biosurfactant producing halophilic organism *Planococcus maritimus* which was able to tolerate 2.7 *M* NaCl [144]. Gomes, M. B. et al. reported reported halophilic organisms belonging to genus *Bacillus*, *Brevibacterium*, *Halomonas*, *Idiomarina*, *Marinobacter*, *Modicisalibacter*, *Nitratireductor*, capable to degrading different hydrocarbons including benzopyrene, hexadecane, naphthalene, phenol, phenanthrene and pyrene [145]. Eslami, M. et al. reported azo dye degradation using halophilic bacterium *Halomonas elongata* [146]. Yadav and Saxena have reviewed the use of halophilic organisms for sustainable agriculture [147]. Halophilic organisms such as *Bacillus*, *Halobacillus*, *Dietzia*, *Halomonas*, *Marinobacter*, *Idiomarina*, *Paenibacillus*, *Rhodococcus*, *Planococcus*, *Stapia*, *Vibrio* and *Pseudomonas* are able to produce enzymes, L-arginase, L-asparaginase and L-glutaminase which manifest anticancer activity [148]. Production of bioplastics like polyhydroxyalkanoate (PHA), polyhydroxybutyrate (PHB) and polyhydroxyvalerate (PHV) have been reported in halophiles like *Halococcus*, *Halorubrum*, *Haloferax*, *Halobacterium*, *Halopiger*, *Natronobacterium*, *Haloarcula* and *Natranococcus* [149].

As we all know that higher concentration of salt outside cells leads to release of water from cells by a phenomenon called osmosis. Thus cellular membranes exhibit a key role in maintaining osmotic balance in halophilic organisms. It has been well established that the membrane proteins of halophilic organisms have more acidic and polar amino acid composition as compared to non-halophiles. The tetraethers responsible for locking the two halves of bilayer are absent in halophiles thus maintaining the fluidity of membranes in high salinity. Phosphatidylglycerol phosphate is the major component of lipid bilayer, with some amount of usual phosphatidyl glycerol. In some halobacterium species phosphate is substituted by sulfate. Thus, existence of high concentration of negative charge is an adaptive mechanism to cope up with extracellular high Na^{+} concentrations along with internal K^{+} concentration [150]. DasSarma et al. studied amino acid sequences of cold adapted proteins in halophilic archaea *Halorubrum lacusprofundi* from Antarctica. They found that amino acids found in mesophilic variants were replaced by acidic and polar amino acids. Also bigger amino acids were substituted with smaller ones resulting in misfolding of protein and thus imparting flexibility required to work under stress conditions [151]. Halophilic microorganisms maintain osmotic pressure within their cytoplasm by employing two strategies called salt-in cytoplasm and organic-osmolyte strategy. In the salt-in cytoplasm strategy, halophiles accumulate K^{+} ions along with Cl^{-} ions as counter ions within cytoplasm in molar concentrations which are later on replaced with Na^{+} ions in the stationary phase. To make enzymes adaptive to these high ionic environments, they are composed of acidic charged amino acids. Thus this mechanism maintains the hydration within the cell. In the later strategy, organisms either produce or take up organic compatible solutes from the environment and thus maintain osmotic balance. These organic solutes can be sugars, amino acids and/or their derivatives, polyols. Other than maintaining osmotic balance, these organic solutes also stabilize proteins and cells [152].

Apart from these main strategies, various other mechanisms such as upregulation of heat shock proteins, stress proteins, DNA repair proteins like Uvr system, proteasome subunits and formation of biofilm, are observed within halophiles to deal with stress caused due to high salinity [153].

5. pH:

Depending on the pH, extremophiles are characterized into two categories namely, acidophiles and alkaliphiles. Acidophiles are those organisms whose optimal pH requirement lies between 1 and 5 whereas alkaliphiles are those who grow when pH is above 9 [154].

A. Acidophiles:

Acidophiles are organisms that can continue to exist in highly acidic environments (pH 3–4**).** Diverse group of archaea and bacteria can thrive in an acidic environment such as *Euryarchaeota, Ferroplasma, Acidobacter, Acidohalobacteria, Leptospirillum, Sulfobacillus, Acidibacillus, Desulfurococcus, Metallosphaera, Pyrococcus, Acidianus, Sulfolobus, picrophilus*. They are found in natural environments such as marine volcanic vents, acidic sulfur spring, solfataric fields, sulfuric pools, and geysers, acid mine drainage, acid rock drainage as well as artificial environments such as areas associated with human activities like metal ores and coal mining [155][156].

Acidophiles play a critical function in biomining of metals from the low-grade ores and the enzymes such as amylase, pectinase, cellulase, xylanase yielded by them have found several applications in the food and feed industry. α-amylase from *Pyrococcus furiosus* (pH5.5), *Alicyclobacillus* (pH3.0), *Bacillus acidicola* (pH-4.0), *Bacillus* sp. DR90 (pH-4.0) is used in the starch industry [157][158]. Pectinase from *Scleritium rolfsii* (pH-3.5), *Mucor pusillus* (pH-5.0), *Rhizoctonia solani* (pH-4.8), *Penicillium frequentans* (pH-4.5) for fruit juice clarification [159]. Xylanase from *Aspergillus foetidus* (pH-5.3), *Aspergillus Awamori* (pH-5.0) *and phytase from Aspergillus niger* (pH-5.0) is used in baking industry and animal feed [160][161][162]. *Acidithiobacillus and Ferroplasma* species are used for biological electricity production where as *Acidiphilium rubrum* is capable of removing contaminants from polluted extreme environments [159]**.** Chemolithotrophic bacterial strains *L. ferrooxidans* and *At. ferrooxidans* are used to detect organic molecules on Mars as chemolithoautotrophic acidophiles provide a link to early Earth when oxygen was unavailable. Tinto River (Spain) and Eagle plains (Canada), are also considered to be important terrestrial analogs of mars as they are inhabited by acidophilic microorganisms [163].

Microorganisms usually require a neutral intracellular pH, however the mechanism of acidophile homeostasis is unknown. The impenetrability of the cell membrane, which limits the inflow of protons into the cytoplasm, is one of the adaptations that helps acidophiles maintain their internal pH. There's a link between the existence of tetraether lipids in the cell membrane and acid pH tolerance in archaea. Another strategy for maintaining pH homeostasis and preventing protons from entering cells has been proposed: reducing the pore size of membrane channels. *At. ferrooxidans* outer membrane porin Omp40 has a bigger exterior loop that may be responsible for modulating the size of the pores in the cells as well as ion selectivity, as result in pH shift from pH3.5 to 1.5 they are expressed [163]. According to Baker-Austin, C., et al., the production of inside positive $\Delta\psi$ that is formed by Donnan potential of positively charged ions is the second major strategy for the active mechanism used by acidophiles to minimize the influx of protons. A positive inside transmembrane potential is due to a reversed $\Delta\psi$ that could prevent protons from leakage into the cells. Acidophiles, in particular Na+/K+ transporters, may use similar techniques to generate a reversed membrane potential to oppose the inward flow of protons. Although raising the expression of secondary transporters and improving proton efflux and consumption are common strategies, the most effective technique is to minimize the proton permeability of the cell membrane. To respond to proton attack, acidophiles can produce a very impermeable membrane. When protons reach the cytoplasm, acidophiles use their buffering capacity to trap and release protons as one of their defense mechanisms. Buffer molecules containing basic amino acids like lysine, histidine, and arginine are found in the cells and aid in proton sequestration [164][165][163]. Metal tolerance is seen in acidophiles through both passive and active mechanisms. The metal efflux proteins transport metals out of the cytoplasm, and the metal is converted to a less harmful form by active processes. The creation of metal sulfate complexes reduces the concentration of the free metal ion, and an internal positive membrane potential provides a chemiosmotic gradient against which metal cations must flow in the passive process. These bacteria also resist high levels of metals by using active efflux or trapping of the metal ions by metal chaperones [166][167].

B. Alkaliphiles:

Alkaliphilic microorganisms, often known as "alkaliphiles," are microorganisms that thrive at pH levels higher than 9, typically in the 10–13 range. Obligate alkaliphiles grow only at pH values of ~pH 9 and higher, while facultative alkaliphiles are strains that grow ideally under severe alkaline conditions but are still capable of thriving near neutral pH. Haloalkaliphiles require a high salinity (up to 33% (w/v) NaCl) as well as an alkaline pH (>pH 9)**.** *Bacillus pseudofirmus and Bacillus halodurans, Alkalibacterium strains Alkaliphilus metalliredigens, Thioalkalivibrio, and Pseudomonas alcaliphila, Natranaerobius thermophilus* were isolated from soda lakes, hydrothermal vents, and carbonate-rich soil [168]**.**

Alkaliphiles are widely used in industry, particularly in the detergent and textile industries. Alkaliphile enzymes have a wide range of industrial applications. Many products such as antibiotics and carotenoids have also been reported. Apart from that, they play a vital role in biogeocycling. Several reports suggested that they are also able to break down xenobiotic compounds [169]. Detergents, the food industry, and the tanning of leather all require alkaline proteases several bacillus strains such as *Bacillus cohnii D-6, Bacillus LP-Ya, Bacillus KSM-9860, Bacillus NP-1* were reported for the production of alkaline protease [170]. A high amount of an extracellular and thermostable xylanase enzyme has also been developed from *Bacillus pumilus ASH* [171]. Al-Johani, N. B., *et al.*, 2017 reported the development of alkaline amylase from *Bacillus subtilis* [172]. The antibiotic Naphthospironone A was isolated from alkalophilic *Nocardiopsis* species and showed cytotoxic and antibiotic action [173]. Carotenoids were produced using alkaliphilic *Microbacterium arborescens-AGSB, Paracoccus bogoriensis BOG6, and Roseinatronobacter thiooxidans ALG1* [169]**.**

All alkaliphiles have an intracellular pH homeostasis; alkaliphiles maintain a lower cytoplasmic pH than their external environment [174]. Alkaliphiles keep the intracellular pH below that of the surrounding environment. Metabolic energy is required to maintain the reversed pH gradient. Alkaliphiles have to take solutes from the environment. Aerobic alkaliphiles regulate their intracellular pH via a Na+/H+ antiporter in conjunction with H+ coupled respiration. [175]. The Mrp antiporter is a cation/proton antiporter which is most dominantly present in alkaliphiles [176]. Alkaliphiles are rich with negatively charged residues in their cell walls. The alkaliphilic's principal cell wall component is glutamic and glucuronic acids, which are negatively charged residues. This highly negatively charged cell wall structure interacts with cations such as H+, delaying the rapid loss of H+ from the cell surface due to the equilibration action of the alkaline bulk phase in the environment, which contributes considerably to alkaliphile pH homeostasis and bioenergetics [177]**.** One of the most essential difficulties for living in alkaline environments is bioenergetics. Alkaliphiles are thought to have mechanisms that compensate for the negative element, namely, a lack of H+, in energy production [178]. It has been studied that the isoelectric point of alkaliphilic proteins is much lower than its homologues found in other prokaryotic organisms. Such proteins have a reduced number of basic amino acids like arginine and lysine, and an increased number of acidic amino acids like glutamate and aspartate. Examples include, SecY protein present in *B.halodurans* C-125, c-binding domain of cytochrome oxidase subunit II found in *B.pseudofirmus* OF4 [179]. Many of the alkaliphiles are also thermophilic or halophilic in nature and thus the survival strategies other than those explained above remain the same.

III. CONCLUSION

Pigments, exopolysaccharides, various enzymes, and secondary metabolites extracted from extremophilic organisms have a wide range of applications. They can be used in various industries like detergents, textiles, pharmaceuticals, and the biotechnological industry. They show antitumor, antibacterial as well as antiviral activity and thus can be extensively used in medicinal treatments. Extremophiles can be employed in bioremediation strategies as they are adapted to harsh conditions and can still perform efficiently. Condition specific adaptive and defense strategies are exhibited by microorganisms. Archaea are the most robust and extremophilic class of microorganisms. Many different adaptation strategies have been discovered yet a lot is to be known and thus extensive research in the field of extremophiles is required.

REFERENCES

[1] Rothschild, L. J., & Mancinelli, R. L. (2001). Life in extreme environments. *Nature*, *409*(6823), 1092-1101.

[2] Buzzini, P., Turchetti, B., & Yurkov, A. (2018). Extremophilic yeasts: the toughest yeasts around?. *Yeast*, *35*(8), 487-497.

[3] Scoma, A., Garrido-Amador, P., Nielsen, S. D., Røy, H., & Kjeldsen, K. U. (2019). The polyextremophilic bacterium Clostridium paradoxum attains piezophilic traits by modulating its energy metabolism and cell membrane composition. *Applied and environmental microbiology*, *85*(15), e00802-19.

[4] Scambos, T. A., Campbell, G. G., Pope, A., Haran, T., Muto, A., Lazzara, M., ... & Van den Broeke, M. R. (2018). Ultralow surface temperatures in East Antarctica from satellite thermal infrared mapping: the coldest places on Earth. *Geophysical research letters*, *45*(12), 6124-6133.

[5] McDermott, J. M., Sylva, S. P., Ono, S., German, C. R., & Seewald, J. S. (2018). Geochemistry of fluids from Earth's deepest ridge-crest hot-springs: Piccard hydrothermal field, Mid-Cayman Rise. *Geochimica et Cosmochimica Acta*, 228, 95-118.

[6] Turchetti, B., Marconi, G., Sannino, C., Buzzini, P., & Albertini, E. (2020). DNA methylation changes induced by cold in psychrophilic and psychrotolerant Naganishia yeast species. *Microorganisms*, *8*(2), 296.

[7] Foltys, V., & Kirchnerová, K. (2006). Mesophilic and psychrotrophic aerobe sporulating microorganisms in raw cow's milk. *Central European Journal of Biology*, *1*(4), 545-560.

[8] Kushkevych, I., Cejnar, J., Vítězová, M., Vítěz, T., Dordević, D., & Bomble, Y. J. (2020). Occurrence of thermophilic microorganisms in different full scale biogas plants. *International journal of molecular sciences*, *21*(1), 283.

[9] Feller, G., & Gerday, C. (2003). Psychrophilic enzymes: hot topics in cold adaptation. *Nature reviews microbiology, 1*(3), 200-208.

[10] Sinclair, N. A., & Stokes, J. L. (1964). Isolation of obligately anaerobic psychrophilic bacteria. *Journal of Bacteriology, 87*(3), 562-565.

[11] Kishore, K. H., Begum, Z., Pathan, A. A. K., & Shivaji, S. (2010). Paenibacillus glacialis sp. nov., isolated from the Kafni glacier of the Himalayas, India. *International journal of systematic and evolutionary microbiology*, *60*(8), 1909-1913.

[12] Yadav, A. N., Kumar, V., Dhaliwal, H. S., Prasad, R., & Saxena, A. K. (2018). Microbiome in crops: diversity, distribution, and potential role in crop improvement. In *Crop improvement through microbial biotechnology* (pp. 305-332). Elsevier.

[13] Chaudhary, D. K., Kim, D. U., Kim, D., & Kim, J. (2019). Flavobacterium petrolei sp. nov., a novel psychrophilic, diesel-degrading bacterium isolated from oil-contaminated Arctic soil. *Scientific reports*, *9*(1), 1-9.

[14] Govarthanan, M., Ameen, F., Kamala-Kannan, S., Selvankumar, T., Almansob, A., Alwakeel, S. S., & Kim, W. (2020). Rapid biodegradation of chlorpyrifos by plant growth-promoting psychrophilic Shewanella sp. BT05: An eco-friendly approach to clean up pesticide-contaminated environment. *Chemosphere*, *247*, 125948.

[15] Hari, R. K., Patel, T. R., & Martin, A. M. (1994). An overview of pigment production in biological systems: functions, biosynthesis, and applications in food industry. *Food Reviews International*, *10*(1), 49-70.

[16] Nakamura, Y., Sawada, T., Morita, Y., & Tamiya, E. (2002). Isolation of a psychrotrophic bacterium from the organic residue of a water tank keeping rainbow trout and antibacterial effect of violet pigment produced from the strain. *Biochemical Engineering Journal*, *12*(1), 79-86.

[17] Durán, N., Justo, G. Z., Ferreira, C. V., Melo, P. S., Cordi, L., & Martins, D. (2007). Violacein: properties and biological activities. *Biotechnology and applied biochemistry*, *48*(3), 127-133.

[18] Kawamukai, M. (2018). Biosynthesis and applications of prenylquinones. *Bioscience, biotechnology, and biochemistry*, *82*(6), 963-977.

[19] Chen, S., Hong, Y., Shao, Z., & Liu, Z. (2010). A cold-active β-glucosidase (Bgl1C) from a sea bacteria Exiguobacterium oxidotolerans A011. *World Journal of Microbiology and Biotechnology, 26*(8), 1427-1435.

[20] Liu, X., Huang, Z., Zhang, X., Shao, Z., & Liu, Z. (2014). Cloning, expression and characterization of a novel cold-active and halophilic xylanase from Zunongwangia profunda. *Extremophiles*, *18*(2), 441-450.

[21] Cai, Z. W., Ge, H. H., Yi, Z. W., Zeng, R. Y., & Zhang, G. Y. (2018). Characterization of a novel psychrophilic and halophilic β-1, 3-xylanase from deep-sea bacterium, Flammeovirga pacifica strain WPAGA1. *International journal of biological macromolecules, 118*, 2176-2184.

[22] Dou, S., Chi, N., Zhou, X., Zhang, Q., Pang, F., & Xiu, Z. (2018). Molecular cloning, expression, and biochemical characterization of a novel cold-active α-amylase from Bacillus sp. dsh19-1. *Extremophiles*, *22*(5), 739-749.

[23] Carillo, S., Casillo, A., Pieretti, G., Parrilli, E., Sannino, F., Bayer-Giraldi, M., ... & Corsaro, M. M. (2015). A unique capsular polysaccharide structure from the psychrophilic marine bacterium Colwellia psychrerythraea 34H that mimics antifreeze (glyco) proteins. *Journal of the American Chemical Society*, *137*(1), 179-189.

[24] Liu, C., Lu, J., Lu, L., Liu, Y., Wang, F., & Xiao, M. (2010). Isolation, structural characterization and immunological activity of an exopolysaccharide produced by Bacillus licheniformis 8-37-0-1. *Bioresource technology*, *101*(14), 5528-5533.

[25] D'Amico, S., Claverie, P., Collins, T., Feller, G., Georlette, D., Gratia, E., ... & Gerday, C. (2001). Cold-adapted enzymes: an unachieved symphony. In *Cell and Molecular Response to Stress* (Vol. 2, pp. 31-42). Elsevier.

[26] Goordial, J., Raymond-Bouchard, I., Zolotarov, Y., de Bethencourt, L., Ronholm, J., Shapiro, N., ... & Whyte, L. (2016). Cold adaptive traits revealed by comparative genomic analysis of the eurypsychrophile Rhodococcus sp. JG3 isolated from high elevation McMurdo Dry Valley permafrost, Antarctica. *FEMS microbiology ecology*, *92*(2).

[27] He, J., Yang, Z., Hu, B., Ji, X., Wei, Y., Lin, L., & Zhang, Q. (2015). Correlation of polyunsaturated fatty acids with the cold adaptation of Rhodotorula glutinis. *Yeast*, *32*(11), 683-690.

[28] Nishida, T., Morita, N., Yano, Y., Orikasa, Y., & Okuyama, H. (2007). The antioxidative function of eicosapentaenoic acid in a marine bacterium, Shewanella marinintestina IK-1. *FEBS letters*, *581*(22), 4212-4216.

[29] Okuyama, H., Orikasa, Y., & Nishida, T. (2008). Significance of antioxidative functions of eicosapentaenoic and docosahexaenoic acids in marine microorganisms. *Applied and Environmental Microbiology*, *74*(3), 570-574.

[30] Feng, S., Powell, S. M., Wilson, R., & Bowman, J. P. (2014). Extensive gene acquisition in the extremely psychrophilic bacterial species Psychroflexus torquis and the link to sea-ice ecosystem specialism. *Genome biology and evolution*, *6*(1), 133-148.

[31] Yoshida, K., Hashimoto, M., Hori, R., Adachi, T., Okuyama, H., Orikasa, Y., ... & Morita, N. (2016). Bacterial long-chain polyunsaturated fatty acids: their biosynthetic genes, functions, and practical use. *Marine drugs*, *14*(5), 94.

[32] Jagannadham, M. V., Chattopadhyay, M. K., Subbalakshmi, C., Vairamani, M., Narayanan, K., Mohan Rao, C., & Shivaji, S. (2000). Carotenoids of an Antarctic psychrotolerant bacterium, Sphingobacterium antarcticus, and a mesophilic bacterium, Sphingobacterium multivorum. *Archives of microbiology*, *173*(5), 418-424.

[33] Dieser, M., Greenwood, M., & Foreman, C. M. (2010). Carotenoid pigmentation in Antarctic heterotrophic bacteria as a strategy to withstand environmental stresses. *Arctic, Antarctic, and Alpine Research*, *42*(4), 396-405.

[34] Mykytczuk, N., Foote, S. J., Omelon, C. R., Southam, G., Greer, C. W., & Whyte, L. G. (2013). Bacterial growth at− 15 C; molecular insights from the permafrost bacterium Planococcus halocryophilus Or1. *The ISME journal*, *7*(6), 1211-1226.

[35] Corsaro, M. M., Casillo, A., Parrilli, E., & Tutino, M. L. (2017). Molecular structure of lipopolysaccharides of cold-adapted bacteria. In *Psychrophiles: from biodiversity to biotechnology* (pp. 285-303). Springer, Cham.

[36] Ghobakhlou, A. F., Johnston, A., Harris, L., Antoun, H., & Laberge, S. (2015). Microarray transcriptional profiling of Arctic Mesorhizobium strain N33 at low temperature provides insights into cold adaption strategies. *BMC genomics*, *16*(1), 1-14.

[37] Fonseca, F., Meneghel, J., Cenard, S., Passot, S., & Morris, G. J. (2016). Determination of intracellular vitrification temperatures for unicellular microorganisms under conditions relevant for cryopreservation. *PLoS One*, *11*(4), e0152939.

[38] Kim, H. J., Lee, J. H., Hur, Y. B., Lee, C. W., Park, S. H., & Koo, B. W. (2017). Marine antifreeze proteins: structure, function, and application to cryopreservation as a potential cryoprotectant. *Marine drugs*, *15*(2), 27.

[39] Kawahara, H. (2013). Characterizations of functions of biological materials having controlling-ability against ice crystal growth. In *Advanced Topics on Crystal Growth* (pp. 119-143). Rijeka, Croatia: InTech.

[40] Tendulkar, S., Hattiholi, A., Chavadar, M., & Dodamani, S. (2021). Psychrophiles: A journey of hope. *Journal of biosciences*, *46*(3), 1-15.

[41] Garcia-Lopez, E., Alcazar, P., & Cid, C. (2021). Identification of Biomolecules Involved in the Adaptation to the Environment of Cold-Loving Microorganisms and Metabolic Pathways for Their Production. *Biomolecules*, *11*(8), 1155.

[42] Lim, J., Thomas, T., & Cavicchioli, R. (2000). Low temperature regulated DEAD-box RNA helicase from the Antarctic archaeon, Methanococcoides burtonii. *Journal of molecular biology*, *297*(3), 553-567.

[43] Tribelli, P. M., & López, N. I. (2018). Reporting key features in cold-adapted bacteria. *Life*, *8*(1), 8.

[44] Zeldes, B. M., Keller, M. W., Loder, A. J., Straub, C. T., Adams, M. W., & Kelly, R. M. (2015). Extremely thermophilic microorganisms as metabolic engineering platforms for production of fuels and industrial chemicals. *Frontiers in microbiology*, *6*, 1209.

[45] Elumalai, P., Parthipan, P., Narenkumar, J., Anandakumar, B., Madhavan, J., Oh, B. T., & Rajasekar, A. (2019). Role of thermophilic bacteria (Bacillus and Geobacillus) on crude oil degradation and biocorrosion in oil reservoir environment. *3 Biotech*, *9*(3), 1-11.

[46] Naganthran, A., Masomian, M., Rahman, R. N. Z. R. A., Ali, M. S. M., & Nooh, H. M. (2017). Improving the efficiency of new automatic dishwashing detergent formulation by addition of thermostable lipase, protease and amylase. *Molecules*, *22*(9), 1577.

[47] Kin, M. G., & Lee, S. B. (1996). Enzymatic resolution of racemic ibuprofen by lipase-catalyzed esterification reaction: Effects of water content and solid supports. *Journal of fermentation and bioengineering*, *81*(3), 269-271.

[48] Ramnath, L., Sithole, B., & Govinden, R. (2017). Classification of lipolytic enzymes and their biotechnological applications in the pulping industry. *Canadian journal of microbiology*, *63*(3), 179-192.

[49] Bruins, M. E., Janssen, A. E., & Boom, R. M. (2001). Thermozymes and their applications. *Applied biochemistry and biotechnology*, *90*(2), 155-186.

[50] Ghosh, M., Grunden, A. M., Dunn, D. M., Weiss, R., & Adams, M. W. (1998). Characterization of native and recombinant forms of an unusual cobalt-dependent proline dipeptidase (prolidase) from the hyperthermophilic archaeon Pyrococcus furiosus. *Journal of bacteriology*, *180*(18), 4781-4789.

[51] Hou, Y., Chen, X., Chan, Z., & Zeng, R. (2015). Expression and characterization of a thermostable and pH-stable β-agarase encoded by a new gene from Flammeovirga pacifica WPAGA1. *Process Biochemistry*, *50*(7), 1068-1075.

[52] Fu, X. T., & Kim, S. M. (2010). Agarase: review of major sources, categories, purification method, enzyme characteristics and applications. *Marine drugs*, *8*(1), 200-218.

[53] Saiki, R. K., Scharf, S., Faloona, F., Mullis, K. B., Horn, G. T., Erlich, H. A., & Arnheim, N. (1985). Enzymatic amplification of β-globin genomic sequences and restriction site analysis for diagnosis of sickle cell anemia. *Science*, *230*(4732), 1350-1354.

[54] Chen, G., An, X., Li, H., Lai, F., Yuan, E., Xia, X., & Zhang, Q. (2021). Detoxification of azo dye Direct Black G by thermophilic Anoxybacillus sp. PDR2 and its application potential in bioremediation. *Ecotoxicology and Environmental Safety*, *214*, 112084.

[55] Zerva, A., Koutroufini, E., Kostopoulou, I., Detsi, A., & Topakas, E. (2019). A novel thermophilic laccase-like multicopper oxidase from Thermothelomyces thermophila and its application in the oxidative cyclization of 2′, 3, 4-trihydroxychalcone. *New biotechnology*, *49*, 10-18.

[56] Reizer, J., Grossowicz, N., & Barenholz, Y. (1985). The effect of growth temperature on the thermotropic behavior of the membranes of a thermophilic Bacillus. Composition-structure-function relationships. *Biochimica et Biophysica Acta (BBA)-Biomembranes*, *815*(2), 268-280.

[57] Svobodová, J., & Svoboda, P. (1988). Membrane fluidity inBacillus subtilis. Physical change and biological adaptation. *Folia microbiologica*, *33*(3), 161-169.

[58] Sahonero-Canavesi, D. X., Villanueva, L., Bale, N. J., Bosviel, J., Koenen, M., Hopmans, E. C., & Sinninghe Damsté, J. S. (2021). Changes in the distribution of membrane lipids during growth of Thermotoga maritima at different temperatures: Indications for the potential mechanism of biosynthesis of ether-bound diabolic acid (membrane-spanning) lipids. *Applied and Environmental Microbiology*, AEM-01763.

[59] De Rosa, M. (1988). De Rosa, M.; Gambacorta, A. The lipids of Archaebacteria. *Prog. Lipid Res*, *27*, 153-175.

[60] Singer, G. A., & Hickey, D. A. (2003). Thermophilic prokaryotes have characteristic patterns of codon usage, amino acid composition and nucleotide content. *Gene*, *317*, 39-47.

[61] Tekaia, F., Yeramian, E., & Dujon, B. (2002). Amino acid composition of genomes, lifestyles of organisms, and evolutionary trends: a global picture with correspondence analysis. *Gene*, *297*(1-2), 51-60.

[62] Friedman, R., Drake, J. W., & Hughes, A. L. (2004). Genome-wide patterns of nucleotide substitution reveal stringent functional constraints on the protein sequences of thermophiles. *Genetics*, *167*(3), 1507-1512.
[63] Kumar, S., & Nussinov, R. (2001). Fluctuations in ion pairs and their stabilities in proteins. *Proteins: Structure, Function, and Bioinformatics*, *43*(4), 433-454.
[64] Netzer, W. J., & Hartl, F. U. (1998). Protein folding in the cytosol: chaperonin-dependent and-independent mechanisms. *Trends in biochemical sciences*, *23*(2), 68-73.
[65] Kumsta, C., & Jakob, U. (2009). Redox-regulated chaperones. *Biochemistry*, *48*(22), 4666-4676.
[66] Phipps, B. M., Typke, D., Hegerl, R., Volker, S., Hoffmann, A., Stetter, K. O., & Baumeister, W. (1993). Structure of a molecular chaperone from a thermophilic archaebacterium. *Nature*, *361*(6411), 475-477.
[67] Macario, A. J., Lange, M., Ahring, B. K., & De Macario, E. C. (1999). Stress genes and proteins in the archaea. *Microbiology and Molecular Biology Reviews*, *63*(4), 923-967.
[68] Kanodia, S., & Roberts, M. F. (1983). Methanophosphagen: unique cyclic pyrophosphate isolated from Methanobacterium thermoautotrophicum. *Proceedings of the National Academy of Sciences*, *80*(17), 5217-5221.
[69] Shima, S., Hérault, D. A., Berkessel, A., & Thauer, R. K. (1998). Activation and thermostabilization effects of cyclic 2, 3-diphosphoglycerate on enzymes from the hyperthermophilic Methanopyrus kandleri. *Archives of microbiology*, *170*(6), 469-472.
[70] Lentzen, G., & Schwarz, T. (2006). Extremolytes: natural compounds from extremophiles for versatile applications. *Applied microbiology and biotechnology*, *72*(4), 623-634.
[71] Lamosa, P., Burke, A., Peist, R., Huber, R., Liu, M. Y., Silva, G., ... & Santos, H. (2000). Thermostabilization of proteins by diglycerol phosphate, a new compatible solute from the hyperthermophile Archaeoglobus fulgidus. *Applied and Environmental Microbiology*, *66*(5), 1974-1979.
[72] Becker, J., & Wittmann, C. (2020). Microbial production of extremolytes—high-value active ingredients for nutrition, health care, and well-being. *Current opinion in biotechnology*, *65*, 118-128.
[73] Galtier, N., & Lobry, J. R. (1997). Relationships between genomic G+ C content, RNA secondary structures, and optimal growth temperature in prokaryotes. *Journal of molecular evolution*, *44*(6), 632-636.
[74] Paz, A., Mester, D., Baca, I., Nevo, E., & Korol, A. (2004). Adaptive role of increased frequency of polypurine tracts in mRNA sequences of thermophilic prokaryotes. *Proceedings of the National Academy of Sciences*, *101*(9), 2951-2956.
[75] Saha, D., Panda, A., Podder, S., & Ghosh, T. C. (2015). Overlapping genes: a new strategy of thermophilic stress tolerance in prokaryotes. *Extremophiles*, *19*(2), 345-353.
[76] Senatore, G., Mastroleo, F., Leys, N., & Mauriello, G. (2018). Effect of microgravity & space radiation on microbes. *Future Microbiology*, *13*(07), 831-847.
[77] McCoy, K. B., Derecho, I., Wong, T., Tran, H. M., Huynh, T. D., La Duc, M. T., ... & Mogul, R. (2012). Insights into the extremotolerance of Acinetobacter radioresistens 50v1, a gram-negative bacterium isolated from the Mars Odyssey spacecraft. *Astrobiology*, *12*(9), 854-862.
[78] Minton, K. W. (1996). Repair of ionizing-radiation damage in the radiation resistant bacterium Deinococcus radiodurans. *Mutation Research/DNA Repair*, *363*(1), 1-7.
[79] Selbmann, L., Pacelli, C., Zucconi, L., Dadachova, E., Moeller, R., de Vera, J. P., & Onofri, S. (2018). Resistance of an Antarctic cryptoendolithic black fungus to radiation gives new insights of astrobiological relevance. *Fungal biology*, *122*(6), 546-554.
[80] Vaishampayan, P. A., Rabbow, E., Horneck, G., & Venkateswaran, K. J. (2012). Survival of Bacillus pumilus spores for a prolonged period of time in real space conditions. *Astrobiology*, *12*(5), 487-497.
[81] Baqué, M., de Vera, J. P., Rettberg, P., & Billi, D. (2013). The BOSS and BIOMEX space experiments on the EXPOSE-R2 mission: Endurance of the desert cyanobacterium Chroococcidiopsis under simulated space vacuum, Martian atmosphere, UVC radiation and temperature extremes. *Acta Astronautica*, *91*, 180-186.
[82] Sakashita, T., Suzuki, M., Hamada, N., Shimozawa, Y., Shirai-Fukamoto, K., Yokota, Y., ... & Kobayashi, Y. (2012). Behavioral resistance of Caenorhabditis elegans against high-LET radiation exposure. *Biological Sciences in Space*, 26, 7-11.
[83] Brandt, A., de Vera, J. P., Onofri, S., & Ott, S. (2015). Viability of the lichen Xanthoria elegans and its symbionts after 18 months of space exposure and simulated Mars conditions on the ISS. *International Journal of Astrobiology*, *14*(3), 411-425.
[84] Musilova, M., Wright, G., Ward, J. M., & Dartnell, L. R. (2015). Isolation of radiation-resistant bacteria from Mars analog Antarctic Dry Valleys by preselection, and the correlation between radiation and desiccation resistance. *Astrobiology*, *15*(12), 1076-1090.
[85] Lopez-Fernandez, M., Jroundi, F., Ruiz-Fresneda, M. A., & Merroun, M. L. (2021). Microbial interaction with and tolerance of radionuclides: underlying mechanisms and biotechnological applications. *Microbial Biotechnology*, *14*(3), 810-828.
[86] De la Coba, F., Aguilera, J., De Galvez, M. V., Alvarez, M., Gallego, E., Figueroa, F. L., & Herrera, E. (2009). Prevention of the ultraviolet effects on clinical and histopathological changes, as well as the heat shock protein-70 expression in mouse skin by topical application of algal UV-absorbing compounds. *Journal of dermatological science*, *55*(3), 161-169.
[87] Asgarani, E., Terato, H., Asagoshi, K., Shahmohammadi, H. R., Ohyama, Y., Saito, T., ... & Ide, H. (2000). Purification and characterization of a novel DNA repair enzyme from the extremely radioresistant bacterium Rubrobacter radiotolerans. *Journal of radiation research*, *41*(1), 19-34.

[88] Gabani, P., Copeland, E., Chandel, A. K., & Singh, O. V. (2012). Ultraviolet-radiation-resistant isolates revealed cellulose-degrading species of Cellulosimicrobium cellulans (UVP 1) and Bacillus pumilus (UVP 4). *Biotechnology and applied biochemistry*, *59*(5), 395-404.
[89] Lloyd, J. R., Leang, C., Myerson, A. L. H., Coppi, M. V., Cuifo, S., Methe, B., ... & Lovley, D. R. (2003). Biochemical and genetic characterization of PpcA, a periplasmic c-type cytochrome in Geobacter sulfurreducens. *Biochemical Journal*, *369*(1), 153-161.
[90] Baumeister, W., Kübler, O., & Zingsheim, H. P. (1981). The structure of the cell envelope of Micrococcus radiodurans as revealed by metal shadowing and decoration. *Journal of ultrastructure research*, *75*(1), 60-71.
[91] Thompson, B. G., Murray, R. G. E., & Boyce, J. F. (1982). The association of the surface array and the outer membrane of Deinococcus radiodurans. *Canadian Journal of Microbiology*, *28*(9), 1081-1088.
[92] Kübler, O., & Baumeister, W. (1978). The structure of a periodic cell wall component (HPI-layer of Micrococcus radiodurans). *Cytobiologie*, *17*(1), 1-9.
[93] Battista, J. R. (1997). Against all odds: the survival strategies of Deinococcus radiodurans. *Annual review of microbiology*, *51*(1), 203-224.
[94] Slade, D., & Radman, M. (2011). Oxidative stress resistance in Deinococcus radiodurans. *Microbiology and molecular biology reviews*, *75*(1), 133-191.
[95] Markillie, L. M., Varnum, S. M., Hradecky, P., & Wong, K. K. (1999). Targeted mutagenesis by duplication insertion in the radioresistant bacterium Deinococcus radiodurans: radiation sensitivities of catalase (katA) and superoxide dismutase (sodA) mutants. *Journal of Bacteriology*, *181*(2), 666-669.
[96] Jung, K. W., Lim, S., & Bahn, Y. S. (2017). Microbial radiation-resistance mechanisms. *Journal of Microbiology*, *55*(7), 499-507.
[97] Agostini, H. J., Carroll, J. D., & Minton, K. W. (1996). Identification and characterization of uvrA, a DNA repair gene of Deinococcus radiodurans. *Journal of bacteriology*, *178*(23), 6759-6765.
[98] Makarova, K. S., Aravind, L., Wolf, Y. I., Tatusov, R. L., Minton, K. W., Koonin, E. V., & Daly, M. J. (2001). Genome of the extremely radiation-resistant bacterium Deinococcus radiodurans viewed from the perspective of comparative genomics. *Microbiology and molecular biology reviews*, *65*(1), 44-79.
[99] Rajpurohit, Y. S., Sharma, D. K., & Misra, H. S. (2021). PprA protein inhibits DNA strand exchange and ATP hydrolysis of Deinococcus RecA and regulates the recombination in gamma-irradiated cells. *Frontiers in cell and developmental biology*, *9*.
[100] Rajpurohit, Y. S., Bihani, S. C., Waldor, M. K., & Misra, H. S. (2016). Phosphorylation of Deinococcus radiodurans RecA regulates its activity and may contribute to radioresistance. *Journal of Biological Chemistry*, *291*(32), 16672-16685.
[101] Tanaka, M., Narumi, I., Funayama, T., Kikuchi, M., Watanabe, H., Matsunaga, T., ... & Yamamoto, K. (2005). Characterization of pathways dependent on the uvsE, uvrA1, or uvrA2 gene product for UV resistance in Deinococcus radiodurans. *Journal of bacteriology*, *187*(11), 3693-3697.
[102] Mishra, S., Chaudhary, R., Singh, S., Kota, S., & Misra, H. S. (2019). Guanine quadruplex DNA regulates gamma radiation response of genome functions in the radioresistant bacterium Deinococcus radiodurans. *Journal of Bacteriology*, *201*(17), e00154-19.
[103] Webb, K. M., & DiRuggiero, J. (2012). Role of Mn2+ and compatible solutes in the radiation resistance of thermophilic bacteria and archaea. *Archaea*, 2012.
[104] Zivanovic, Y., Armengaud, J., Lagorce, A., Leplat, C., Guérin, P., Dutertre, M., ... & Confalonieri, F. (2009). Genome analysis and genome-wide proteomics of Thermococcus gammatolerans, the most radioresistant organism known amongst the Archaea. *Genome biology*, *10*(6), 1-23.
[105] Barbier, E., Lagorce, A., Hachemi, A., Dutertre, M., Gorlas, A., Morand, L., ... & Breton, J. (2016). Oxidative DNA damage and repair in the radioresistant archaeon Thermococcus gammatolerans. *Chemical Research in Toxicology*, *29*(11), 1796-1809.
[106] Rodrigues, J. V., Abreu, I. A., Cabelli, D., & Teixeira, M. (2006). Superoxide reduction mechanism of Archaeoglobus fulgidus one-iron superoxide reductase. *Biochemistry*, *45*(30), 9266-9278.
[107] Leprince, O., & Buitink, J. (2010). Desiccation tolerance: from genomics to the field. *Plant Science*, *179*(6), 554-564.
[108] Alpert, P. (2005). The limits and frontiers of desiccation-tolerant life. *Integrative and comparative biology*, *45*(5), 685-695.
[109] Blasius, M., Hübscher, U., & Sommer, S. (2008). Deinococcus radiodurans: what belongs to the survival kit?. Critical reviews in biochemistry and molecular biology, 43(3), 221-238.
[110] LeBlanc, J. C., Gonçalves, E. R., & Mohn, W. W. (2008). Global response to desiccation stress in the soil actinomycete Rhodococcus jostii RHA1. *Applied and environmental microbiology*, *74*(9), 2627-2636.
[111] Cytryn, E. J., Sangurdekar, D. P., Streeter, J. G., Franck, W. L., Chang, W. S., Stacey, G., ... & Sadowsky, M. J. (2007). Transcriptional and physiological responses of Bradyrhizobium japonicum to desiccation-induced stress. *Journal of bacteriology*, *189*(19), 6751-6762.
[112] Harland, C. W., Rabuka, D., Bertozzi, C. R., & Parthasarathy, R. (2008). The Mycobacterium tuberculosis virulence factor trehalose dimycolate imparts desiccation resistance to model mycobacterial membranes. *Biophysical journal*, *94*(12), 4718-4724.

[113] Ding, T., Yu, Y. Y., Hwang, C. A., Dong, Q. L., Chen, S. G., Ye, X. Q., & Liu, D. H. (2016). Modeling the effect of water activity, pH, and temperature on the probability of enterotoxin a production by Staphylococcus aureus. *Journal of food protection*, *79*(1), 148-152.

[114] Beblo, K., Rabbow, E., Rachel, R., Huber, H., & Rettberg, P. (2009). Tolerance of thermophilic and hyperthermophilic microorganisms to desiccation. *Extremophiles*, *13*(3), 521-531.

[115] Molina-Romero, D., Baez, A., Quintero-Hernández, V., Castañeda-Lucio, M., Fuentes-Ramírez, L. E., Bustillos-Cristales, M. D. R., ... & Muñoz-Rojas, J. (2017). Compatible bacterial mixture, tolerant to desiccation, improves maize plant growth. *PloS one*, *12*(11), e0187913.

[116] Niu, X., Song, L., Xiao, Y., & Ge, W. (2018). Drought-tolerant plant growth-promoting rhizobacteria associated with foxtail millet in a semi-arid agroecosystem and their potential in alleviating drought stress. *Frontiers in microbiology*, *8*, 2580.

[117] Azua-Bustos, A., & González-Silva, C. (2014). Biotechnological applications derived from microorganisms of the Atacama Desert. *BioMed research international*, 2014.

[118] Okoro, C. K., Brown, R., Jones, A. L., Andrews, B. A., Asenjo, J. A., Goodfellow, M., & Bull, A. T. (2009). Diversity of culturable actinomycetes in hyper-arid soils of the Atacama Desert, Chile. *Antonie Van Leeuwenhoek*, *95*(2), 121-133.

[119] Kour, D., Rana, K. L., Yadav, A. N., Yadav, N., Kumar, V., Kumar, A., ... & Saxena, A. K. (2019). Drought-tolerant phosphorus-solubilizing microbes: biodiversity and biotechnological applications for alleviation of drought stress in plants. In *Plant growth promoting rhizobacteria for sustainable stress management* (pp. 255-308). Springer, Singapore.

[120] Esbelin, J., Santos, T., & Hébraud, M. (2018). Desiccation: an environmental and food industry stress that bacteria commonly face. *Food microbiology*, *69*, 82-88.

[121] Ophir, T., & Gutnick, D. L. (1994). A role for exopolysaccharides in the protection of microorganisms from desiccation. *Applied and environmental microbiology*, *60*(2), 740-745.

[122] Anderson, K. L., Apolinario, E. E., & Sowers, K. R. (2012). Desiccation as a long-term survival mechanism for the archaeon Methanosarcina barkeri. *Applied and environmental microbiology*, *78*(5), 1473-1479.

[123] Fagliarone, C., Napoli, A., Chiavarini, S., Baqué, M., De Vera, J. P., & Billi, D. (2020). Biomarker preservation and survivability under extreme dryness and Mars-like UV flux of a desert cyanobacterium capable of trehalose and sucrose accumulation. *Frontiers in Astronomy and Space Sciences*, *7*, 31.

[124] Zeidler, S., & Müller, V. (2019). The role of compatible solutes in desiccation resistance of Acinetobacter baumannii. *Microbiologyopen*, *8*(5), e00740.

[125] Vriezen, J. A., De Bruijn, F. J., & Nusslein, K. (2007). Responses of rhizobia to desiccation in relation to osmotic stress, oxygen, and temperature. *Applied and environmental microbiology*, *73*(11), 3451-3459.

[126] Jin, M., Xiao, A., Zhu, L., Zhang, Z., Huang, H., & Jiang, L. (2019). The diversity and commonalities of the radiation-resistance mechanisms of Deinococcus and its up-to-date applications. *AMB Express*, *9*(1), 1-12.

[127] Wang, X., Cole, C. G., DuPai, C. D., & Davies, B. W. (2020). Protein aggregation is associated with Acinetobacter baumannii desiccation tolerance. *Microorganisms*, *8*(3), 343.

[128] Saad, S., Cereghetti, G., Feng, Y., Picotti, P., Peter, M., & Dechant, R. (2017). Reversible protein aggregation is a protective mechanism to ensure cell cycle restart after stress. *Nature cell biology*, *19*(10), 1202-1213.

[129] García, A. H. (2011). Anhydrobiosis in bacteria: from physiology to applications. *Journal of biosciences*, *36*(5), 939-950.

[130] Lagerloef, G. (2001). Satellite measurements of salinity. *Encyclopedia of Ocean Sciences*, 2511-2516.

[131] Loganathan, P., Naidu, G., & Vigneswaran, S. (2017). Mining valuable minerals from seawater: a critical review. *Environmental Science: Water Research & Technology*, *3*(1), 37-53.

[132] Gunjal, A. B., & Badodekar, N. P. (2022). Halophiles. In *Physiology, Genomics, and Biotechnological Applications of Extremophiles* (pp. 13-34). IGI Global.

[133] Menasria, T., Aguilera, M., Hocine, H., Benammar, L., Ayachi, A., Bachir, A. S., ... & Monteoliva-Sánchez, M. (2018). Diversity and bioprospecting of extremely halophilic archaea isolated from Algerian arid and semi-arid wetland ecosystems for halophilic-active hydrolytic enzymes. *Microbiological research*, *207*, 289-298.

[134] Ruginescu, R., Gomoiu, I., Popescu, O., Cojoc, R., Neagu, S., Lucaci, I., ... & Enache, M. (2020). Bioprospecting for novel halophilic and halotolerant sources of hydrolytic enzymes in brackish, saline and hypersaline lakes of Romania. *Microorganisms*, *8*(12), 1903.

[135] Villanova, V., Galasso, C., Fiorini, F., Lima, S., Brönstrup, M., Sansone, C., ... & Scargiali, F. (2021). Biological and chemical characterization of new isolated halophilic microorganisms from saltern ponds of Trapani, Sicily. *Algal Research*, *54*, 102192.

[136] Corral, P., Amoozegar, M. A., & Ventosa, A. (2019). Halophiles and their biomolecules: Recent advances and future applications in biomedicine. *Marine drugs*, *18*(1), 33.

[137] Manjula, D., Jeevitha, P., Ramya, I., Hemapriya, J., & Ravi, A. (2018). Biotechnological Applications of Halophilic Pigments–An Overview. *International Journal of Current Microbiology and Applied Sciences*, *7*(7), 4392-4398.

[138] Arun, N., & Singh, D. P. (2016). A review on pharmacological applications of halophilic alga Dunaliella.

[139] Kanekar, P. P., Kulkarni, S. O., Dhakephalkar, P. K., Saxena, N., & Pathan, H. M. (2021). Bacteriorhodopsin Producing Halophilic Archaea Isolated from Solar Salt Pan Saline Environment for Conversion of Light Energy into Electrical Energy. *ES Energy & Environment*, *13*, 57-64.

[140] Li, Y. T., Tian, Y., Tian, H., Tu, T., Gou, G. Y., Wang, Q., ... & Ren, T. L. (2018). A review on bacteriorhodopsin-based bioelectronic devices. *Sensors*, *18*(5), 1368.

[141] Flores, N., Hoyos, S., Venegas, M., Galetović, A., Zúñiga, L. M., Fábrega, F., ... & Gómez-Silva, B. (2020). Haloterrigena sp. strain SGH1, a bacterioruberin-rich, perchlorate-tolerant halophilic archaeon isolated from halite microbial communities, Atacama Desert, Chile. *Frontiers in microbiology*, *11*, 324.

[142] Das, D., Kalra, I., Mani, K., Salgaonkar, B. B., & Braganca, J. M. (2019). Characterization of extremely halophilic archaeal isolates from Indian salt pans and their screening for production of hydrolytic enzymes. *Environmental Sustainability*, *2*(3), 227-239.

[143] Houde, A., Kademi, A., & Leblanc, D. (2004). Lipases and their industrial applications. *Applied biochemistry and biotechnology*, *118*(1), 155-170.

[144] Waghmode, S., Suryavanshi, M., Dama, L., Kansara, S., Ghattargi, V., Das, P., ... & Satpute, S. K. (2019). Genomic insights of halophilic Planococcus maritimus SAMP MCC 3013 and detail investigation of its biosurfactant production. *Frontiers in microbiology*, *10*, 235.

[145] Gomes, M. B., Gonzales-Limache, E. E., Sousa, S. T. P., Dellagnezze, B. M., Sartoratto, A., Silva, L. C. F., ... & Oliveira, V. M. (2018). Exploring the potential of halophilic bacteria from oil terminal environments for biosurfactant production and hydrocarbon degradation under high-salinity conditions. *International Biodeterioration & Biodegradation*, *126*, 231-242.

[146] Eslami, M., Amoozegar, M. A., & Asad, S. (2016). Isolation, cloning and characterization of an azoreductase from the halophilic bacterium Halomonas elongata. International journal of biological macromolecules, 85, 111-116.

[147] Yadav, A. N., & Saxena, A. K. (2018). Biodiversity and biotechnological applications of halophilic microbes for sustainable agriculture. *J Appl Biol Biotechnol*, *6*(1), 48-55.

[148] Zolfaghar, M., Amoozegar, M. A., Khajeh, K., Babavalian, H., & Tebyanian, H. (2019). Isolation and screening of extracellular anticancer enzymes from halophilic and halotolerant bacteria from different saline environments in Iran. *Molecular biology reports*, *46*(3), 3275-3286.

[149] Simó-Cabrera, L., García-Chumillas, S., Hagagy, N., Saddiq, A., Tag, H., Selim, S., ... & Martínez-Espinosa, R. M. (2021). Haloarchaea as cell factories to produce bioplastics. *Marine Drugs*, *19*(3), 159.

[150] Russell, N. J. (1989). Adaptive modifications in membranes of halotolerant and halophilic microorganisms. *Journal of bioenergetics and biomembranes*, *21*(1), 93-113.

[151] DasSarma, S., Capes, M. D., Karan, R., & DasSarma, P. (2013). Amino acid substitutions in cold-adapted proteins from Halorubrum lacusprofundi, an extremely halophilic microbe from Antarctica. *PLoS One*, *8*(3), e58587.

[152] Kunte, H. J. (2009). Osmoregulation in halophilic bacteria. *Extremophiles*, *2*, 263-77.

[153] Matarredona, L., Camacho, M., Zafrilla, B., Bonete, M. J., & Esclapez, J. (2020). The role of stress proteins in Haloarchaea and their adaptive response to environmental shifts. *Biomolecules*, *10*(10), 1390.

[154] Gerday, C. (2002). Extremophiles: basic concepts. *Knowledge for Sustainable Development. An Insight into the Encyclopedia of Life Support Systems. UNESCO Publishing/EOLSS Publishers, Oxford*, *1*, 573-598.

[155] Tripathi, S., Singh, K., & Chandra, R. (2021). Adaptation of bacterial communities and plant strategies for amelioration and eco-restoration of an organometallic industrial waste polluted site. In *Microbes in Land Use Change Management* (pp. 45-90). Elsevier.

[156] Salwan, R., & Sharma, V. (2020). Physiology of extremophiles. In *Physiological and Biotechnological Aspects of Extremophiles* (pp. 13-22). Academic Press.

[157] Putri, A. Z., & Nakagawa, T. (2020). Microbial α-Amylases in the Industrial Extremozymes. *Reviews in Agricultural Science*, *8*, 158-169.

[158] Satyanarayana, T. Acidic α-amylase of Bacillus acidicola: Attempts in Ameliorating Catalytic Efficiency and Production.

[159] Sharma, A., Parashar, D., & Satyanarayana, T. (2016). Acidophilic microbes: biology and applications. *Biotechnology of Extremophiles*:, 215-241.

[160] Shah, A. R., Shah, R. K., & Madamwar, D. (2006). Improvement of the quality of whole wheat bread by supplementation of xylanase from *Aspergillus foetidus*. *Bioresource technology*, *97*(16), 2047-2053.

[161] Soni, S. K., Magdum, A., & Khire, J. M. (2010). Purification and characterization of two distinct acidic phytases with broad pH stability from Aspergillus niger NCIM 563. *World Journal of Microbiology and Biotechnology*, *26*(11), 2009-2018.

[162] Do, T. T., Quyen, D. T., & Dam, T. H. (2012). Purification and characterization of an acid-stable and organic solvent-tolerant xylanase from Aspergillus awamori VTCC-F312. *ScienceAsia*, *38*(2012), 157-165.

[163] Mirete, S., Morgante, V., & González-Pastor, J. E. (2017). Acidophiles: diversity and mechanisms of adaptation to acidic environments. In *Adaption of microbial life to environmental extremes* (pp. 227-251). Springer, Cham.

[164] Baker-Austin, C., Dopson, M., Wexler, M., Sawers, R. G., Stemmler, A., Rosen, B. P., & Bond, P. L. (2007). Extreme arsenic resistance by the acidophilic archaeon 'Ferroplasma acidarmanus' Fer1. *Extremophiles*, *11*(3), 425-434.

[165] Chen, X. (2021). Thriving at Low pH: Adaptation Mechanisms of Acidophiles. In *Acidophiles-Fundamentals and Applications*. IntechOpen.

[166] Navarro, C. A., von Bernath, D., & Jerez, C. A. (2013). Heavy metal resistance strategies of acidophilic bacteria and their acquisition: importance for biomining and bioremediation. *Biological research*, *46*(4), 363-371.

[167] Dopson, M., & Holmes, D. S. (2014). Metal resistance in acidophilic microorganisms and its significance for biotechnologies. *Applied microbiology and biotechnology*, *98*(19), 8133-8144.

[168] Preiss, L., Hicks, D. B., Suzuki, S., Meier, T., & Krulwich, T. A. (2015). Alkaliphilic bacteria with impact on industrial applications, concepts of early life forms, and bioenergetics of ATP synthesis. *Frontiers in bioengineering and biotechnology*, *3*, 75.

[169] Sarethy, I. P., Saxena, Y., Kapoor, A., Sharma, M., Sharma, S. K., Gupta, V., & Gupta, S. (2011). Alkaliphilic bacteria: applications in industrial biotechnology. *Journal of Industrial Microbiology and Biotechnology*, *38*(7), 769.

[170] Horikoshi, K. (2011). 2.8 enzymes isolated from alkaliphiles. *Extremophiles handbook*, 162-177.

[171] Battan, B., Sharma, J., & Kuhad, R. C. (2006). High-level xylanase production by alkaliphilic *Bacillus pumilus* ASH under solid-state fermentation. *World Journal of Microbiology and Biotechnology*, *22*(12), 1281-1287.

[172] Al-Johani, N. B., Al-Seeni, M. N., & Ahmed, Y. M. (2017). Optimization of alkaline α-amylase production by thermophilic Bacillus subtilis. *African Journal of Traditional, Complementary and Alternative Medicines*, *14*(1), 288-301.

[173] Ding, Z. G., Li, M. G., Zhao, J. Y., Ren, J., Huang, R., Xie, M. J., ... & Wen, M. L. (2010). Naphthospironone A: an unprecedented and highly functionalized polycyclic metabolite from an alkaline mine waste extremophile. *Chemistry–A European Journal*, *16*(13), 3902-3905.

[174] Garland, P. B. (1977). Energy transduction in microbial systems. In *Symp Soc Gen Microbiol* (Vol. 27, pp. 1-21).

[175] Van De Vossenberg, J. L. C. M., Driessen, A. J., & Konings, W. N. (2000). Adaptations of the cell membrane for life in extreme environments. *Environmental Stressors and Gene Responses*, 71-88.

[176] Masato, T. A. K. J. L., Fujisawa, M. M., & Hicks, M. I. D. B. (2010). 2.6 Adaptive Mechanisms of Extreme Alkaliphiles. *Extremophiles Handbook*, 119.

[177] Mamo, G. (2019). Challenges and adaptations of life in alkaline habitats. *Alkaliphiles in Biotechnology*, 85-133.

[178] Matsuno, T., & Yumoto, I. (2015). Bioenergetics and the role of soluble cytochromes c for alkaline adaptation in Gram-negative alkaliphilic Pseudomonas. *BioMed research international*, *2015*.

[179] Krulwich, T. A. (2006). Alkaliphilic prokaryotes. *The prokaryotes*, *2*, 283-308.