Futuristic Trends of Extremophilic Bacteria in Industrial Biotechnology

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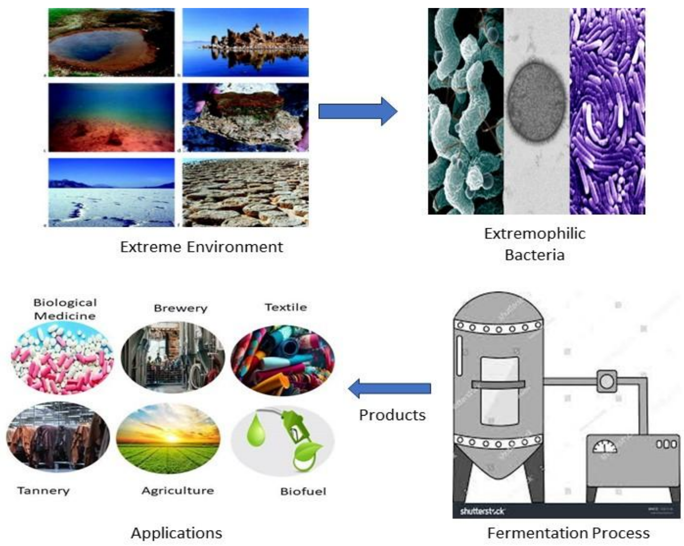

Abstract

Extremophilic microorganisms, capable of thriving in extreme environmental conditions, have garnered significant attention in industrial biotechnology. This chapter provides an overview of the futuristic trends surrounding extremophilic microorganisms in this field. After introducing extremophiles and highlighting the importance of industrial biotechnology, the chapter explores various types of extremophiles, including thermophiles, psychrophiles, acidophiles, alkaliphiles, halophiles, and xerophilies, detailing their characteristics and potential applications in industrial biotechnology. The study then delves into the futuristic trends, including enzyme production and biocatalysis, biofuel production, bioremediation, and pharmaceutical and chemical production, showcasing how extremophiles are poised to revolutionize these areas. Additionally, the chapter addresses the challenges and opportunities associated with extremophiles, such as cultivation, genetic engineering, and ethical considerations. In conclusion, this abstract emphasizes the importance of further research and development in the field of extremophilic microorganisms, highlighting their potential to transform industrial biotechnology and shape the future of sustainable and efficient processes.

I. Introduction

In fascinating world of microbiology certain organisms display an exceptional ability to thrive and flourish in extremes of environment, these extraordinary entities are known as extremophiles, have captivated scientists and researchers alike owing to their remarkable resilience against extreme physical (pH, temperature, pressure and salanity) and chemical (macro and micro nutrients required) conditions. These encompass a diverse array of microorganisms, predominantly within the Archaea and Bacteria domains. The study of these extremophiles has not only expanded our understanding of the diversity of life on Earth but has also paved the way for groundbreaking applications in industries. This chapter focusing on three major subsections delves into the intriguing world of extremophiles, exploring their diverse adaptations, the enzymes they produce—and their profound significance in industrial processes.

A. Extremophiles: Nature's Resilient Pioneers

Extremophiles represent the pioneers of resilience, pushing the boundaries regarding the conditions in which life can thrive. For instance, hyperthermophiles, a subset of extremophiles, survive in the scorching hydrothermal vents deep within the ocean floor home, where temperatures exceed 80°C (Bakir & Metin, 2016). In similarly astonishing fashion, psychrophiles have adapted to frigid environments, with optimal growth temperatures as low as -10°C. These remarkable microorganisms can be found in icy polar regions and high-altitude environments. Likewise, acidophiles flourish in highly acidic surroundings, with pH levels below 3, such as acid mine drainage sites. Alkaliphiles, on the other hand, embrace alkaline environments with pH values exceeding 9, like soda lakes and alkaline soils (Jeong et al., 2020). These organisms survive in harsh conditions as well as produce bioproducts such as extremozymes, pharmaceutical compounds, biofuels etc. These organisms defy conventional wisdom by not only surviving but thriving in such extreme conditions.

Extremozymes: Enzymatic Marvels of Extreme Conditions

One of the most captivating aspects of extremophiles is their ability to produce extremozymes—enzymes that exhibit exceptional stability and activity under extreme conditions. These extremozymes have found their way into a multitude of industrial applications, revolutionizing processes across various sectors. For instance, thermophiles are masters of heat, and their enzymes have revolutionized fields such as biofuel production, where high-temperature reactions can be catalyzed efficiently and sustainably (Zhu et al., 2020). Cold-active enzymes from psychrophiles have transformed the biotechnology landscape, enabling processes that require low temperatures, such as dairy and food industries (Sarmiento et al., 2015). In the realm of bioremediation, acidophiles and alkaliphiles contribute their extremozymes to cleanse contaminated environments, showcasing their potential in environmental sustainability (Martins et al., 2022).

B. Industrial Applications and Beyond

The impact of extremophiles and their extremozymes is undeniable across various industries. The biopharmaceutical sector harnesses their unique abilities to synthesize complex molecules under extreme conditions, redefining drug discovery and production (Lailaja et al., 2013). In the realm of biorefinery and bioenergy, extremozymes from thermophiles and halophiles are catalyzing reactions that hold the promise of sustainable energy production (Bonfá et al., 2011). Furthermore, the detergent industry benefits from the powerful enzymes of alkaliphiles, enhancing the efficacy of cleaning products even in high-pH environments (Priji et al., 2017).

In this chapter, we embark on a journey through the extremes of life, exploring the remarkable adaptations of extremophiles and the unparalleled capabilities of their extremozymes. As we uncover the intricate mechanisms that enable these microorganisms to thrive in seemingly inhospitable conditions, we delve into their industrial significance, revolutionizing biotechnology, energy production, and environmental restoration. The collaboration between nature's resilient pioneers and human ingenuity opens doors to a future where extremophiles and their extremozymes propel us toward innovative and sustainable solutions for the challenges that lie ahead.

II. Extremophilic bacteria and its types

Extremophile organisms are living beings that possess the remarkable ability to flourish and propagate in environments characterized by extreme physical conditions such as temperature, pressure, and radiation, as well as challenging chemical parameters like salinity, pH, and redox potential. Most extremophiles belong to the microorganism category, specifically within the Archaea and Bacteria domains. Among these microorganisms, there are polyextremophiles that exhibit the extraordinary capability to withstand and thrive in multiple extreme conditions simultaneously (Dalmaso et al., 2015).

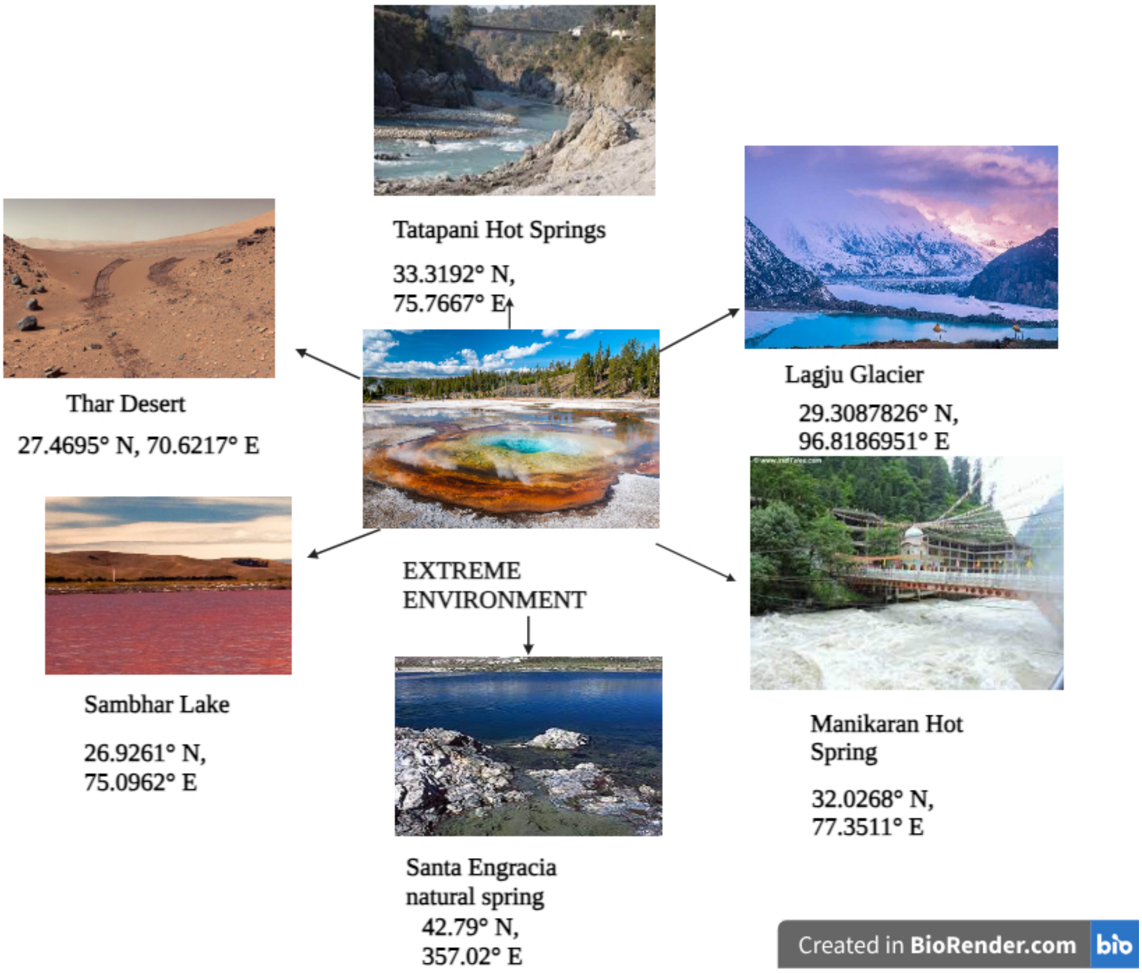

Figure 1: Environmental source of extremophiles- A figure represents different environmental conditions with their geographical locations from which different types of extremophiles can be isolated.

Overview on the mechanisms of extremophiles

It is important to study mechanism of extremophilic bacteria, as they have diverse mechanisms to survive in harsh conditions, at extremes of environment. For instance, extreme halophilic bacteria forms osmoprotecctants such as ectoine and proline etc. These extremophiles can be studied and applied in industrial biotechnology for bioproducts formed by them. It is also necessary to study their mechanisms, that how they are surviving at extremes of environment. It is becoming important to study functioning of these bacteria as research era is shifting towards to isolate extremophiles, what type of potent proteins and enzymes they have, which can be utilized in industrial biotechnology to produce different byproducts. Figure 1, depicts the graph of increasing trends of research towards extremophilic bacteria

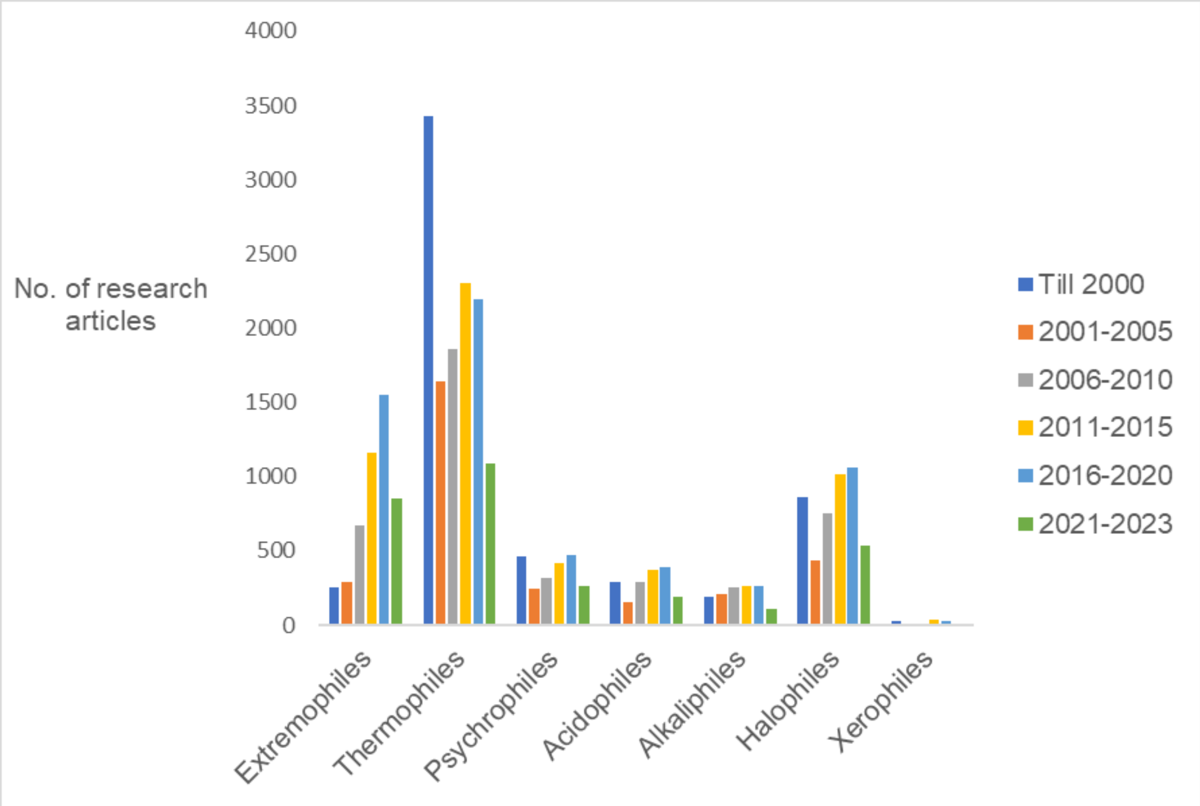

Figure 1: Graph of increasing studies on extremophilic bacteria vs different extremophilic bacteria

A graph depicting the growth in research focused on extremophilic bacteria in relation to various types of mesophilic bacteria.

This data is correct of our knowledge, and collected from pubmed on 14 August, 2023

- Protein stabilization: Extremophilic bacteria produce proteins that are adapted to withstand harsh conditions such as high temperatures, extreme pH levels, or high salinity. These proteins have unique structural features that enhance their stability and function under extreme conditions (Kumar et al., 2018). For instance, this has been observed in proteins from *P. furiosus*. Enzymes from *P. furiosu*s have highly packed hydrophobic cores with many ionic pairs and buried atoms to help diminish unfavorable solvent interactions (Sarmiento et al., 2015)
- Membrane adaptations: The cell membranes of extremophilic bacteria are modified to maintain integrity and functionality in extreme environments. This includes alterations in lipid composition, membrane fluidity, and the presence of specialized transport proteins to regulate ion and nutrient uptake (Siliakus et al., 2017). For example, Xerophilic bacteria modifies their cell membrane by phospholipid and fatty acid compositions. In *S. enterica*, the lipid A palmitoleoyl acyltransferase gene ddg, which replaces lipid A laurate with palmitoleate, is up-regulated in response to desiccation, increasing the fluidity of the outer membrane (Lebre et al., 2017)
- Osmoregulation: Extremophilic bacteria employ osmoregulatory mechanisms to balance internal and external osmotic pressures. They accumulate compatible solutes or osmoprotectants, such as sugars or amino acids, to maintain cellular hydration and prevent dehydration in environments with low water availability (Slama et al., 2015).
- DNA repair systems: Extremophilic bacteria have efficient DNA repair systems that enable them to rectify DNA damage caused by exposure to extreme conditions such as high levels of radiation or oxidative stress (Confalonieri et al., 2011).
- Spore formation: Some extremophilic bacteria can form spores, which are dormant and highly resistant structures. Spore formation allows bacteria to survive extreme conditions such as desiccation, high temperatures, or high levels of radiation until more favorable conditions arise (Sarma et al., 2023).

These mechanisms collectively enable extremophilic bacteria to adapt and thrive in extreme environments that would be detrimental or lethal to most other organisms.

Table1: Types of extremophilic bacteria and their optimum environment (adapted from Sarma et al., 2023) - The table gives information about categories of extreme bacteria and their favorable environment of growth

Extremophile Microorganism	Favorable Environment for Growth
Hyper Thermophilic	Optimum growth at temperatures above 80 °C
Thermophilic	Grows at temperatures between 60 °C and 85 °C
Psychrophiles	Grows at temperature from 0°C to 15°C
Acidophile	Optimum pH for growth—Below 3
Alkaliphile	Optimum pH for growth—Above 10
Halophile	Requires at least 1M salt for growth
Xerophile	Grows in low water availability, resistant to desiccation

The upcoming section of the chapter deals with the different categories of extremophiles as mentioned in Table 1.

A. Thermophiles

Thermophiles are heat-loving organisms, which not only tolerate high temperatures but usually require the same for their growth and survival. A thermophile as defined by Brock (1978) is "an organism capable of living at temperatures at or near the maximum for the taxonomic group of which it is a part." Temperatures for their growth typically range from 50°C to 121°C, which is the temperature used for sterilization in autoclaves. These microorganisms have further been classified into moderate thermophiles, extreme thermophiles, and hyperthermophiles depending on the range of temperatures they tolerate (Rasuk et al., 2016).

Thermophiles have several mechanisms to tolerate extreme temperatures. It is believed that the thermostability of cellular components such as ATP, amino acids, and peptides may exceed 250 °C, suggesting that the maximum temperature for life goes beyond the temperatures that have been observed until now. Extreme thermophile bacteria produce thermostable proteins that can be readily crystallized to obtain stable enzymes for structural and functional studies. Proteins from hyper/thermophiles require sufficient structural rigidity to resist unfolding. As a classical instance is the bacteria *Thermus thermophilus* that was originally isolated from a thermal vent within a hot spring in Izu, Japan, and is frequently used in genetic manipulation studies. The DNA gyrase from this extremophile has been used as an anti-drug target model. DNA gyrase is a type IIA topoisomerase that introduces negative supercoils into closed circular bacterial DNA using ATP hydrolysis. It is an important antibacterial target that is sensitive to the widely used fluoroquinolone drugs (Zhu et al., 2020). These advantages are observed owing to high solubility of the substrate, a lower risk for contamination of the system, and lowering the solution viscosity and increasing the miscibility of the solvent ultimately promoting faster reactions. Several thermophiles and thermostable enzymes are used in the biorefinery industry, first and second-generation biofuels, paper, and bleaching industries, the crucial ones of which are compiled in Table 2 (Sarma et al., 2023).

Table 2: Types of Extreme thermophiles - Extreme thermophiles, with their optimum temperature, enzymes produced and their application**s.**

Extreme Thermophile	Optimum Temperature (◦C)	Extremozyme Enzyme	Industrial Application	Reference
Thermophilic Anoxybacillus sp. GXS-BL	60	α-amylase	Bioenergy industries, Food, pharmaceutics, textile, detergent	Liao et al., 2019
Dictyoglomus turgidum Thermostable	80	Thermostable β-glucosidase	Biorefinery, food	Fusco et al., 2018

Anoxybacillus flavithermus Bacillus licheniformis	60	β-galactosidase	Food, bioremediation, biosensor	Rani et al., 2019
Bacillus mojavensis SO-10	70	α-amylase	Biorefinery, food, detergent	Ozdemir et al., 2018
Anoxybacillus thermarum FRM-RBK02	80	α-amylase	Biorefinery, food, detergent	Mantiri et al., 2019
Janibacter sp. strain R02	80	Thermophilic and halophilic esterase	Detergents, pharmaceutical, leather, food, bioremediation	Castilla et al., 2017
Metagenome	115	Thermoactive endoglucanase	Biorefinery	Suleiman et al., 2019

B. Psychrophiles

Psychrophilic microorganisms typically thrive within a temperature range of 1-4◦C, whereas mesophilic microorganisms prefer temperatures between 30-37◦C. In contrast to mesophilic microorganisms, which have a preferred temperature range of 30-37◦C, psychrophilic microorganisms can maintain cellular metabolism even at temperatures below 0◦C. To adapt to these harsh conditions, psychrophiles have evolved several physiological adaptation mechanisms, including control of membrane fluidity, action of molecular chaperones, and synthesis of antifreeze molecules (Jeong et al.,2020)

These microorganisms can withstand the negative effects imposed by cold environments and are frequently found in such habitats (Rizvi et al., 2021).

Cold-adapted enzymes, also known as psychrophilic enzymes, possess specific adaptations in their structural features that provide them with greater flexibility compared to mesophilic and thermophilic enzymes. This flexibility allows for high catalytic activity at low temperatures while maintaining thermolability. These adaptations are the result of long-term selection and are characterized by specific genetic changes. Recent reviews on psychrophilic enzymes have highlighted several important adaptations that contribute to maintaining high flexibility and activity at low temperatures. These adaptations include:

(a) Decreased core hydrophobicity and increased surface hydrophobicity of cell membrane,

(b) Changes in amino acid compositions, such as a lower arginine/lysine ratio, an abundance of glycine residues for enhanced conformational mobility, fewer proline residues in loops but more in α-helices, and an increased presence of non-polar residues on the protein surface,

(c) Weaker protein interactions, including inter-domain and inter-subunit interactions, fewer disulfide bridges, reduced hydrogen bonds and electrostatic interactions, and fewer/weaker metal binding sites.

(d) Decreased secondary structures and oligomerization, coupled with an increase in the number and size of loops.

(e) Increased conformational entropy of the unfolded protein state.

Table 3:Types of Extreme psychrophiles- Extreme psychrophile with their optimum temperature, enzymes produced and their applications

Extreme Psychrophiles	**Optimum Temperature °C**	**Extremozyme**	**Industrial Application**	**Reference**
Pseudomonas sp. MM15	4°C to 42°C.	Endoglucanase (Cel5M)	Cellulose degradation	Yang and Dang (2011)
Arthrobacter sp. 20B	30–37°C	galactosidase	Food processing	Wierzbicka -Wos

				et al. (2011)
Planomicrobium sp. 547	20-21°C	Protease	detergent and pharmaceutical	Xiangsheng et al. (2011)
Cryptococcus diffluens	32 and 40°C	D-galacturonate reductase	Food, pharmaceutical	Hamada et al. (2011)
Bacillus sp. N2a (BNC)	40°C	Catalase	food industry	Wang et al. (2008)

C. Acidophiles

Microorganisms that are adapted to acidic environments, known as acidophilic microorganisms, have the remarkable ability to survive under extremely low pH conditions (less than pH 3). They achieve pH homeostasis by effectively controlling proton permeation. For instance, microorganisms belonging to genera such as *Thermoplasma, Ferroplasma*, and *Sulfolobus* are capable of regulating proton permeation even under these extremely low pH conditions. This is achieved through the presence of a highly impermeable cell membrane, primarily composed of tetraether lipids. These lipids possess a diverse range of polar head groups and a bulky isoprenoid core, contributing to the membrane's impermeability and enabling these microorganisms to thrive in acidic environments (Jeong et al., 2020).

Acidophilic microorganisms have evolved various mechanisms to survive and thrive in acidic environments. A key adaptation is their cell membrane, which exhibits impermeability to protons. In the Archaea branch of life, this impermeability is attributed to specific features like tetraether lipids, distinct lipid head-group structures, a bulky isoprenoid core, and the resistance of ether linkages to acid hydrolysis, setting them apart from Bacteria and Eukarya domains (Siliakus et al., 2017). Acidophiles also employ strategies such as reducing membrane channel pore size, observed in *Acidithiobacillus ferrooxidans*, and maintaining a net positive charge inside the cell to counteract the high concentration of H^+ ions in their acidic surroundings. Some acidophilic species, like *Bacillus* and *Thermoplasma*, utilize active proton pumping for intracellular pH regulation. While an identifiable acid response signature in acidophile genomes remains elusive, it is interesting to note that acidophile genomes tend to be smaller than those of neutrophiles, though the reasons and potential evolutionary advantages of this difference are yet to be fully understood. These adaptations provide valuable insights into the unique biology of acidophilic microorganisms and their ability to thrive in acidic environments (Coker et al., 2019). Tabe 4 lists the type of acidophilic bacteria, and their industrial application.

Table 4: Types of Extreme Acidophile-Types of extreme acidophilic bacteria with their optimum pH, enzymes produced and their industrial applications.

Extreme Acidophiles	Optimum pH	Industrial Application	Reference
Acidianus brierley	1.5–2.0	Ferric iron-reducing	Plumb et al., 2007
Acidianus copahuensis	2.5–3.0	Ferric iron-reducing	Giaveno et al., 2013
Acidianus manzaensis	1.2–1.5	Ferric iron-reducing	Yoshida et al., 2006
Acidianus sulfidivorans	0.8–1.4	Ferric iron-reducing	Plumb et al., 2007
Acidothiobacillus ferrooxidans BY-3	<1.8	Bioleaching	Chen, Pet al., (2011)

Extreme Acidophiles	Optimum pH	Industrial Application	Reference
At. Ferrooxidans	1.5–4.5	Bioleaching	Romero-González et al., (2016)
Acidothiobacillus ferrivorans	2.5	Bioprecipitation	Jameson et al., (2010)
Acidocella aromatica	2.5	Bioreduction	Okibe et al., (2016)

D. Alkaliphiles

Alkaliphiles are organisms that grow in alkaline habitats (pH > 9), usually showing optimal growth around a pH range up to 10. These extremophiles are classified into two main physiological groups: obligate and facultative alkaliphiles. Depending on their ability to tolerate alkaline habitats, these have been categorized as facultative and obligate. Facultative alkaliphiles can grow in the pH range of 7.0–9.5, whereas obligate alkaliphiles (e.g., *Bacillus krulwichiae*) have shown optimal growth between pH 10.0 and 12.0. Alkaliphiles may coexist with neutrophilic microorganisms such as under mild basic pH conditions and live in specific extreme environments.

Alkaliphile bacteria have molecular defenses against high pH that include symporter (proteins that simultaneously transport two molecules across a membrane in the same direction) and antiporter (membrane protein that transports two molecules at the same time in the opposite direction) system activation. An electrochemical gradient of Na^+ and H^+ is produced by electrogenic antiporters, and the symporter system allows the uptake of Na^+ and other solutes into the cells. These systems enable the influx of protons and solutes inside the cell due to the alteration in the distribution of ions (e.g., Na^+), maintaining the hydro saline homeostasis and thermodynamic stability of the cell. The transporters are controlled, probably by signaling from a transmembrane pH sensor (Orellana et al., 2018). Table 5 consists of extreme alkaliphiles, their pH at which they function and their potential use.

Table 5: Extreme alkaliphiles- Industrial application of extreme alkaliphiles with their optimum pH is listed.

Source	Optimum pH	Stable pH range	Optimum temperature (◦C)	Reference
Aneurinibacillus thermoaerophilus lipase expressed in E. coli (LipAT)	10	7-10	45	Zottig et al. (2017)
Microbulbifer sp. YNDZ01	10	7-10	70	Gu et al. (2021)
Burkholderia gladioli BRM58833	9	8-10	50	Martins et al. (2022)
Serratia sp. W3	9	5-10	55	Eddehech et al. (2019)

Burkholderia gladioli BRM58833	9	8-10	50	Martins et al. (2022)
Bacillus mycoides strain CV18	9	7-10	30	Sharma et al. (2021)
Anoxybacillus flavithermus HBB-134 9 6-11 50 Bakir and Metin, 2016	9	6-11	50	Bakir and Metin, 2016
Bacillus smithii BTMS11	8	7-10	50	Lailaja and Chandrasekaran, 2013
Pseudomonas sp.	8.2	7-9	45	Priji et al. (2017)

E. Halophiles

Extreme halophiles are a specific group of microorganisms that require high salt for their growth. They are categorized based on their optimal NaCl concentration for growth, which includes slight halophiles (0.2 M), moderate halophiles (0.5–2.5 M), borderline extreme halophiles (>2.5–4.0 M), and extreme halophiles (>4.0–5.9 M). Halophilic microorganisms can be found in various environments such as salars, saline lakes, oceans, polar ice, and coastal areas. On the other hand, halotolerants are microorganisms capable of growing both in the presence and absence of NaCl. Among halotolerants, those that can thrive in the presence of >2.5 M NaCl are considered extremely halotolerant **(**Orellana et al., 2018).

Halophiles have evolved two primary adaptation mechanisms to prevent the diffusion of NaCl into their cells and thrive in hypersaline environments. The first mechanism involves the accumulation of inorganic ions, particularly KCl, to balance the osmotic pressure. This strategy is primarily employed by aerobic and extremely halophilic archaea, as well as some anaerobic halophilic bacteria. On the other hand, most halophilic bacteria and eukarya utilize a different approach by accumulating water-soluble organic compounds of low molecular weight known as compatible solutes or osmolytes. These compatible solutes serve to maintain a low intracellular salt concentration and act as stabilizers for biological structures, enabling the cells to adapt not only to high salt concentrations but also to conditions such as heat, desiccation, cold, and even freezing. Remarkably, this allows halophiles to thrive in environments with pH levels as high as 10 and temperatures exceeding 50°C. Some halophiles synthesize osmolytes such as ectoine, which are small organic molecules and maintain the integrity of cells. These organic molecules do not intervene in enzymatic activity. Some halophiles scavenge osmoprotectants or compatible solutes from other organisms by using transporter systems as they do not produce their own compatible solutes. For example, Halobacterium salinarum has been known to show chemotactic activities toward osmoprotectants (Sarma et al., 2023).

Table 6: Types of halophile- Extreme halophiles, with their optimum temperature, enzymes produced and their applications.

Strain	**Salt tolerance (M)**	**Enzymes**	**Potencial Use**	**Reference**

Haloferax sp.	3.4	α-amylase	surfactants and detergents.	Bajpaiet al., 2015
Halomonas nitroreducens 11ST	0.5–3.4	poly(3-hydroxybutyrate) PHB	bioplastics	Hernández-Núñez et al., 2019
Shewanella sp. Asc-3	0–0.5	fibrinolytic enzyme	treat and prevent CVDs.	Vijayaraghavan et al., 2015
Exiguobacterium sp. SH31	0.4	not yet known	capable of reducing arsenate and chromium and explored for bioremediation applications.	Orellana et al., 2018
Microbacterium sp.	0–1.2	carbohydrate-active enzyme (CAZyme)	polysaccharides degradation.	Guptaet al., 2022

F. Xerophiles (least evaluated)

Xerotolerant extremophile organisms have the remarkable ability to survive in arid environments where the water activity level is less than $0.75a_w$ (low water activity) (Orellana et al., 2018)**.**

Xerotolerant bacteria have different adaptations such as:

Behavioral Adaptations

First, in dry environments, xerotolerant bacteria utilize spore formation, which allows them to enter a non-replicative viable state ; Second, formation of exopolysaccharide and biofilm formation which help them to maintain hygroscopic nature, that ultimately saves cell from desiccation. The hydrophilic properties of EPS also contribute to the rapid water absorption rates. (Lebre et al., 2017).

Physiological Adaptations

First: Cell membrane adaptations: As the main barrier between the intracellular space and the external environment, the cellular membrane of bacteria is severely affected by changes in the external water availability (FIG. 1). Bacteria exposed to extreme fluctuations in water status typically have modified membrane phospholipid and fatty acid compositions, including increases in the ratio of saturated to unsaturated fatty acids and trans- to cis-mono-unsaturated fatty acids, as well as increased conversion of monoenoic to cyclopropane fatty acids

Accumulation of compatible solutes: In desiccating conditions, the intracellular accumulation of small molecules and salts restores the osmotic equilibrium and permits continued protein function at low aw, which allows cells to adapt to xeric stress. Extreme halophiles use a salting-in‘ strategy in which they import inorganic ions, referred to as osmolytes, to match the extracellular osmotic pressure . On the other hand, xerotolerant bacteria use a bi-phasic salting-out process. Initially, they rapidly accumulate charged solutes (such as potassium and glutamate) in response to osmotic stress; then the charged solutes are replaced by neutral organic solutes that are more compatible with organic reactions, maintain a long-term osmotic balance and function as stabilizers by limiting the unfolding and denaturation of proteins and other macromolecules (Lebre et al., 2017). The study of xerophilic bacteria till now is limited to their isolation and to study their growth characteristics which is given in Table 7, Types of xerophilic bacteria, growth characteristics and their source.

Table 7: Extreme xerophilic bacteria- Table describes about different strains of xerophiles and their growth characteristics along with their source

Extremophilic	**Organisms**	**Growth characteristics**	**Geographical location/source**

Xerophile	*Arthrospira platensis, Bacillus halophilus, Chromohalobacter canadiensis, C. marismortui, C. israeliensis, Dunaliellaspp., Halospirulinarapelicola, Halomonas campisalis, H. elongata, H. salino, H. halophila, Methanococcusdoii, Natrococcusoccultus, Oreniasalinaria, Salinibacterruber, Zygogaccharoccharomycesrouxii*	Organisms able to grow at low water activity, and resistant to high desiccation	Atacama Desert in Chile, Brackish Sea water, Great Salt Lake, Rock surfaces, Soda lakes (Egypt, Kenya, Tanzania), Salterns (Spain, Mexico), Subterranean halite

III. **Applications of extremophiles in industrial biotechnology**

The chapter so far clearly suggests that extremophiles and extremozymes exhibit remarkable abilities to facilitate catalytic reactions across a diverse spectrum of conditions, spanning extreme environments, as well as heightened catalytic efficiency. These intriguing attributes of extremophiles and extremozymes hold substantial potential for various practical applications. They play a significant role in fields such as bioremediation, agriculture, polymer production, bioenergy generation, and diverse industrial sectors (Rathinam et al., 2018) which are compiled in Figure….. Certain most widely used and crucial applications have been described in detail in the upcoming sections:

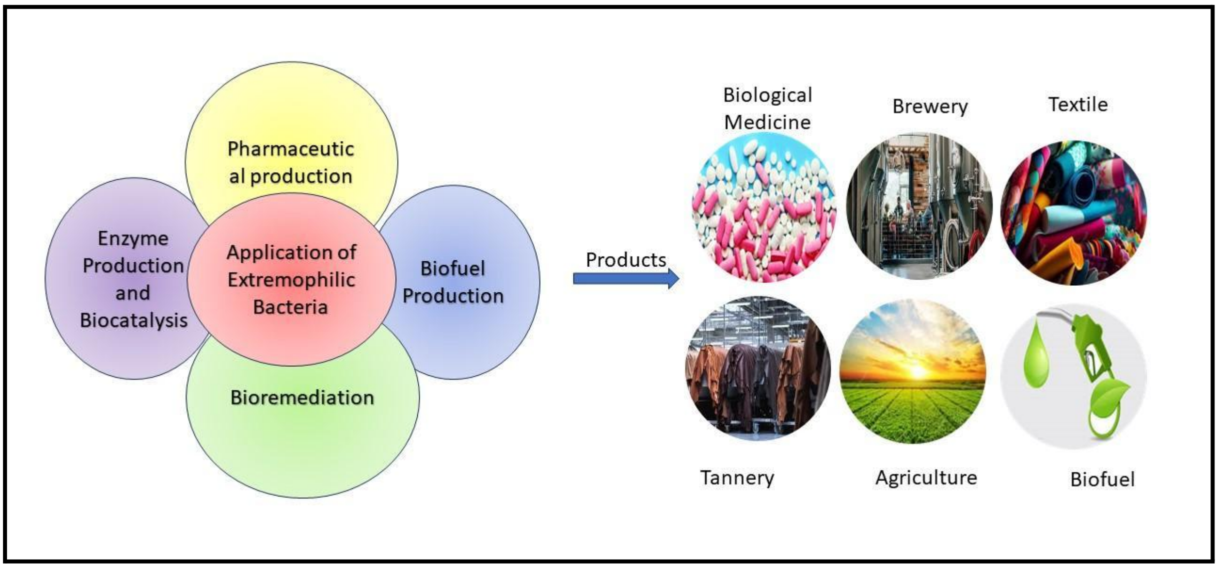

Figure 2: Application of Extremophiles -A diagram describes application of extremophilic bacteria in different industries such as production of bioactive compounds, biofuels, extremozymes and cleaning of environment at harsh conditions.

A. Enzyme production and biocatalysts

The need of an hour is to work with extremophiles as mesophilic enzymes are tailored for standard conditions while extremozymes are isolated from extremophilic bacteria so they can survive in extreme scenarios, making them crucial players in industries requiring robust performance amidst adversities (Porter et al., 2016). They can be used in different industries such as to permit them in biorefinery, agriculture, the chemical industry, bioremediation, biomedicine, and environment pollution control.

These microorganisms hold significant promise for the large-scale synthesis of enzymes. The present industrial enzyme market, valued at approximately US$ 7,100 million, is witnessing a consistent annual growth rate of 8%. Projections indicate that by 2024, enzymes derived from microorganisms will establish dominance in the market. The substantial industrial demand for microbial enzymes can be attributed to their ready availability and cost-effectiveness in production (Orellana et al., 2018)

Table 8: Comparison between normal enzymes and extremozymes - This table deals with the difference between enzymes produced by mesophiles and extremophiles.

Characteristic	Mesophilic Enzymes	Extremozymes
Temperature Sensitivity	Optimal at 20-50°C	Can function at high temperatures (50-121°C)
pH Range	Optimal pH around 6-8	Can tolerate extreme pH values (acidophiles (<3) or alkaliphiles (pH <9))
Stability	Relatively stable under normal conditions	More stable under extreme conditions
Applications	Common in various industries and research	Used in extreme condition-dependent processes (e.g., bioremediation, biofuels)
Enzyme Engineering	Subject to enzyme engineering for optimization	Engineered for enhanced performance or adaptation
Industrial Importance	Enzymes used in traditional processes like food, pharmaceuticals, textiles, etc.	Essential for processes requiring extreme conditions, e.g., high-temperature food processing, biofuel production from extreme environments, and bioremediation in extreme pH environments.

The utilization of extremophilic microorganisms within industrial processes has experienced significant growth over the past two decades. More than 3,000 enzymes have been successfully isolated and identified from extremophiles, with a considerable proportion finding application in biotechnological and industrial contexts. The extremozymes play a pivotal role as they are highly stable and there is low risk of contamination by mesophilic organisms while their cultivation as they are grown in harsh conditions as comparable to them. The polymer degrading enzymes are important as it is difficult to hydrolyse polymers for instance cellulose, starch, and polyethylene glycol etc. It is important to hydrolyse them as they are abundant on earth which becomes pollutants for humans. These enzymes are classified as polymer-degrading agents, including amylases, proteases, cellulases, and xylanases. Moreover, ongoing research indicates that extremozymes hold promise as innovative catalysts for diverse industrial applications. Notably, certain extremophiles have transitioned into commercial availability, as outlined in Table 9.

Table 9: Commercially available extremozymes- This table deals with commercially available enzyme, their brand and year of commercialisation

Brand	Enzyme	Company	Application	Reference
Optimax®	Glucoamylase and pullulanase	Genencor	Starch saccharification	Chettri et al., 2021
IndiAge® NeutraFlex	Cellulase	Genencor	Textile and garment processing	Chettri et al., 202
Lipoclean®, Lipex®, Lipolase® Ultra, Kannase, Liquanase®, Polarzyme®,	Lipases	(Novozyme)	Detergent	Mesbah et al., 2022
Novoshape® Pectinase 62L Lallzyme®	Pectinases	Novozymes Biocatalysts Lallemand	Food and beverages	Chettri et al., 202
Luminase® PB-100 and PB-200	Xylanases	Verenium	Pulp and paper	Sarmeinto et al.,2015

B. Biofuel production

Extremophiles and their enzymes are likely to play important roles in many kinds of bioprocessing, including conversion of nonfood biomass into biofuels. Extremophiles grow under extreme conditions of temperature, acidity, alkalinity, or salinity and have been reported to produce not only biofuels but also value-added products with unique properties. The processes employing extremophilic microorganisms to produce biofuels and value-added products can be cost effective as they have (i) low risk of unwanted microbial contamination, (ii) increased reaction kinetics, (iii) higher yields of products, and (iv) minimal environmental hazards (Bibra et al., 2014).

A cost-effective pretreatment method is required for the biofuel-based industry, and recent interests have been looking at a single step process using extremophiles and their enzymes as other methods of pretreatment are more complex and costly and create pollution. Another reason to produce extremozymes is they hydrolyse crop residues by their special enzymes such as amylases and cellulases etc. (Martinez-Hernandez et al., 2018).

Extremophiles' contributions to biofuel production have become tangible and are growing fast. The development of thermophilic whole cell biocatalysts of industrial relevance is one of the most significant recent contributions. Developments in genetic systems and strain production will continue to push new innovations to achieve a sustainable supply of biofuels (PDF2).

C. Bioremediation

The accumulation of hazardous contaminants in the environment poses a significant threat to both the ecosystem and human health, resulting from various anthropogenic and natural factors. Mitigating the contamination levels has become a formidable challenge, necessitating the exploration of effective strategies. Among these approaches, bioremediation has emerged as a promising, cost-effective, and sustainable solution. Extremophile-based bioremediation has garnered considerable attention. These unique microorganisms, adapted to thrive in extreme environments, offer potential for efficient and targeted remediation of contaminants. Harnessing the capabilities of extremophiles presents a promising avenue for addressing the environmental impacts of hazardous contaminants.These microorganisms possess unique enzymatic features and physiological properties that render them highly promising for diverse biotechnological applications. Notably, these applications encompass the bioremediation of hazardous pollutants present in water and sediments, along with the production of essential biomolecules for medical and industrial purposes. Among these microorganisms, metalophiles and acidophiles, which have adapted to thrive in environments with high concentrations of heavy metals, are particularly valuable in processes such as bioremediation and biomining (Chowdhury et al., 2022). Their remarkable capabilities offer considerable potential for addressing environmental challenges and advancing various industries. On the contrary, radiophiles have proven to be well-suited for the management of environments contaminated with nuclear waste. In the agricultural context, extremophilic desert bacteria that can endure low water activity conditions present potential advantages in water management for drought-stressed plants. These diverse applications showcase the adaptability and untapped potential of extremophilic microorganisms in tackling various environmental and industrial issues (Raddadi et al., 2015).

Halophilic microorganisms have demonstrated their usefulness in bioremediation processes owing to their unique structural and functional properties such as their cell wall, capsule, S-layer proteins, extracellular polymer substances (EPS), and siderophores which enable them to effectively biosorb metals even under extreme environmental stress (Gunjal Aparna et al., 2021).

There are different types of pollutants which are degraded by extremophilic bacteria, and are listed in table 10.

D. Pesticide degrading microbes as extremophiles

Pesticides are chemicals that repel, neutralize, destroy, or otherwise inhibit insects or pests. Despite their usefulness, pesticides have the potential to pollute soil, water, grass, and other plants. Pesticides are a threat to humans, as they can damage the neurological system, digestive system, and endocrine system (Nicolopoulou-Stamati et al., 2016). The extensive and widespread usage of pesticide has resulted in significant soil contamination and soil degradation. Extremophiles have been reported to successfully degrade many components of pesticides that make their way into the environment. The organophosphorus insecticide, monocrotophos, was removed from wastewater through bioremediation by *Arthrobacter atrocyaneus*, *Bacillus megaterium*, and *Pseudomonas mendocina*. A psychrotolerant *Sphingobacterium sp. C1B* isolated from Shimla, Himachal Pradesh, India was able to degrade the organophosphorus pesticide chlorpyrifos at varying temperatures and is the prospect for remediation of chlorpyrifos in a cold environment (Verma et al., 2020).

→ **Removal of hydrocarbons**

The crude oil extraction and transportation sometimes involve oil spills, and therefore, contaminate extreme environments. In such environments, the traditional microorganisms used in bioremediation have lesser metabolic capacity and therefore, result in poor degradation, as they are either unable to perform optimally, or survive in extreme environments. The traditional microorganisms cannot withstand harsh physical and chemical conditions of growth. Hence, extremophilic microbes should be considered for the bioremediation of crude oil contaminated extreme habitats, as extremophiles may adapt to adverse environmental conditions (Rajkumari et al., 2019).

E. Removal of heavy metals:

Extremophiles can be used in those industries, which use heavy metals to produce their products such as leather making industries (tannery), paper manufacturing industry, and lead- acid battery manufacturing factory. Bioleaching and alkylation and reduction are two types of techniques followed by extremophilic microrganism to bioremediation heavy metal contamination site.

- Bioleaching: Both pyrometallurgy and hydrometallurgy are favorable for efficient and rapid treatment of metal-bearing sludge. These processes use highly acidic environments and are done at elevated temperatures. However, these methods have various environmental issues. Some produce toxic pollutants such as dioxins, highly acidic water, and furans. Therefore, extremophile microorganisms are appropriate to extract the various valuable metals from e-waste through an economical and ecofriendly approach (Venkatesa Prabhu et al., 2021). Biomining is usually conducted by extremophilic bacteria and archaea for the recovery of M&R from ores and mine/metal rich/nuclear wastes, through biooxidation (minerals oxidation for metal release) and/or bioleaching (metal solubilization). These bioprocesses take advantage of the anaerobic metabolism, redox pathways, intercellular communication, biofilm formation (Vera et al., 2013), and resistance to heat, acid and metals of (thermo) acidophiles consortia (e.g., *Leptospirillum spp*., *Acidithiobacillus spp*., *Sulfobacillus spp*., *Ferroplasma spp*., *Acidiplasma spp*.) (Orell et al., 2010 2013). Insoluble metal sulfides are converted into soluble metal sulfates by iron- and sulfur-oxidizing extremophiles, thereby facilitating the recovery of economically relevant metals (e.g., Cu, Fe, Au, Ni, and Zn) (Marques et al., 2018).

F. Alkylation and reduction:

Extremophiles can mobilize heavy metals by alkylation and reduction reactions. *Herminiimonas arsenicoxydans* ULPAs1 can oxidize As^{+3} to As^{+5} (Ramadan et al., 2019).

- Metal immobilization Bioaccumulation: Metal immobilization is the process in which heavy metal for instance, hexavalent chromium is transformed to non toxic trivalent chromium.
- An energy-dependent import of heavy metals and radionuclides and subsequent physiologic use or storage by extremophiles is called bioaccumulation. The extremophiles are tolerant to high concentration because of which, they reduce heavy metal from toxic form to non- toxic form. The imported metal species can be sequestered in various proteins and peptide ligands (Fomina M et al., 2014).
- Biotransformation: Extremophiles convert heavy metals and radionuclides into non-toxic or recoverable forms through biotransformation. Biotransformation is of two types – (1) redox conversion of inorganic forms and (2) interchange between organic and inorganic forms via methylation–demethylation reaction. Extremophiles can obtain energy through the oxidation of heavy metals like Fe, Sulfur (S), manganese (Mn), and arsenic (As) or can utilize arsenic (As), selenium (Se), chromium (Cr), and uranium (U) in anaerobic respiration as terminal electron acceptors via dissimilatory reduction. Certain microbes also utilize metals as a part of their metal resistance pathway. Such as aerobic and anaerobic reduction of Cr (VI) to Cr (III); reduction of Se(VI) to elemental selenium ; reduction of U(VI) to U(IV) ; and reduction of Hg(II) to elemental (Chowdhury et al., 2022).

G. Removal of radionuclides

A radionuclide refers to an unstable atom containing surplus nuclear energy, often generated through processes such as fission, neutron stimulation, cyclotrons, and generators. These radionuclides find application in various industries and mining operations, playing a role in inspecting welds, detecting leaks, assessing corrosion rates, erosion, and other factors. However, the presence of radionuclide contamination is linked to severe health risks, including cancer development and DNA damage (Manobala et al., 2019). Certain microorganisms, known as radiophilic or radiotolerant organisms, exhibit the ability to thrive in environments with high levels of radiation, and survive in high levels of ionizing radiation for example gamma rays and uv rays. Leveraging this capability, radiophilic microorganisms can be employed to address radionuclide-related issues using techniques like biosorption, biomineralization, bioprecipitation, biostimulation, and biotransformation (Manobala et al., 2019). Among these extremophiles, *Deinococcus radiodurans* stands out as one of the most resilient microorganisms discovered so far in terms of remediating radionuclide pollution. This remarkable organism, due to its exceptional radiotolerance, has demonstrated effectiveness in mitigating uranium contamination by efficiently removing uranyl ions from the environment (Chowdhury et al., 2022). This category of extremophiles is important as it is surviving in radiation and can help clean those environments which consist of radio- waste. Table 10 consists of the type of extremophile, and the pollutant that they degrade.

Table 10: Pollutants degraded by type of extremophilic bacteria - This table deals with type of contaminant, type of extremophilic microorganism

Type of Contaminant	Type of Extremophile	Microorganism	References
Hydrocarbon	Halophile	*Acinetobacter* *Marinobacter Pseudomonas* *OchrobactrumEnterobacter cloacae,* *Stenotrophomonas maltophila* *Cycloclasticusare Achromobacter* *Rhodococcus Micrococcus* *Arthrobacter* *Rhodanobacter*	Arulazhagan et al., 2017
	Thermophile	*Bacillussp. strain JF8* *Bacillusthermoleovorans* *Bacillussubtilis BUM* *A. fulgidus 24*	Shimura et al., 2001 Annweiler et al., 2000 Zhao Z et al., 2010 Khelifiet al., 2014
	Psychrophile	*Rhodococcus,* *Sphingomonas or Pseudomonas*	Aislabie et al., 2006
	Acidophile	*Acidocella 26* *Acidiphilium*	Stapleton RD et al., 1998
Heavy metals	Thermophile	*Anoxybacillus sp. 28*	Goh KM et al., 2013
	Metal Tolerant	*Pseudomonas strain As-11 29*	Jebelli MA et al., 2017
Radio nuclide	Radiophile	*Deinococcus radiodurans* *Geobacter* *Bacillus* *Micrococcus*	Manobala T et al., 2019 Cologgi DL et al., 2011 Haferburg G et al.,2007
Pesticide		*Arthrobacter atrocyaneus* *Bacillus megaterium* *Pseudomonas mendocina*	Bhadbhade BJ et al., 2002
	Psychrophile	*Sphingobacterium sp. 35*	Verma S et al., 2020

H. Pharmaceutical and chemical production

Extremophilic microorganisms exhibit significant potential for generating a diverse array of biologically active compounds relevant to biomedical applications, which are in high demand in various industries. Sahli et al. (2017) highlighted the extraction of bioactive agents from extremophilic plants, *Juncus maritimus* and *Limonium virgatum*, demonstrating attributes such as antiradical, antimicrobial, antiviral, and cytotoxic properties (Rathinam et al., 2018). However, capitalizing on the medical potential of extremophiles presents challenges, notably the intricate process of isolating and refining extremolytes (Babu et al., 2015). Even when suitable extremolytes are successfully isolated and their applications identified, the transformation of these compounds into specific drugs is a protracted and laborious endeavor. Furthermore, the current regulatory framework imposes constraints on the expeditious development of these potential drugs. This primarily results from the complexities involved in conducting comprehensive functional analyses of specific molecules derived from extremophiles (Babu et al., 2015). Table 11 provides a list of bioactive compounds produced by different bacteria.

Table 11: Bioactive compounds produced by extremophile- Type of extremophile, bioactive compounds produced by them and their application.

Extremophile	Category of extremophile	Bioactive compound	Application	Reference
Halomonas smyrnensis	Halophile	Microbial levan production	organic fertilizer	Sarilmiser et al., 2015
Pseudoalteromonas haloplanktis	Psychrotrophic	Sterols/steroids	biopharmaceutical production	Gelzo et al. 2014
Psychrobacter namhaensis	Marine psychrophile	Probiotics	as feed diet additive	Makled et al., 2017
Leptospirillum ferriphilum	Acidophiles	Glycolic acid	bioactive compound	Rathinam et al., 2018
Pseudomonas aeruginosa	___	Glycolipids	Bioremediation	Mahjoubi et al., 2018
Bacillus subtilis	___	Lipopeptides	Biomedical application	Mahjoubi et al., 2018
Rhodococcus, Mycobacterium	___	Trehalolipid	Bioremediation	Mahjoubi et al., 2018
Arthrobacter	___	Trehalolipid	Biocontrol agent	Mahjoubi et al., 2018

IV. Challenges and Opportunities

Cultivating extremophilic bacteria, which thrive in extreme conditions like high temperature, high salinity, or extreme pH, poses significant challenges. These microorganisms demand specialized environmental mimicry, often necessitating the replication of harsh conditions not typical in standard laboratory settings. Finding and collecting extremophiles from their often remote and harsh natural habitats can be logistically demanding, while maintaining sterile conditions to avoid contamination is crucial. The development of growth media that accurately mirrors the nutrient and chemical compositions of extreme environments, such as high-temperature or high-pressure conditions, requires meticulous formulation. Additionally, factors like slow growth rates, the need for specialized equipment to maintain extreme conditions, and ethical considerations around sample collection further complicate the cultivation and study of extremophilic bacteria. Nevertheless, these challenges are met with enthusiasm because extremophiles offer valuable insights into the limits of life on Earth and possess biotechnological potential.

A. **Obstacles at large scale production-** The constrained expansion rate of these organisms, along with the modest output of essential compounds, and the specialized machinery essential for their cultivation, have imposed restrictions on the volume of these organisms produced (Babu et al., 2015). Scaling up the manufacturing of extremozymes presents challenges as well. For example, when employing halophilic bacteria to synthesize Polyhydroxylalkanoate (PHA) under severe conditions, the demand for a high-salinity environment leads to recurrent and costly equipment maintenance (Zhu et al., 2020).

B. **Designing suitable growth media:** Overcoming these obstacles can involve innovative strategies like employing bioreactors tailored to endure the unique environmental extremities required by these organisms. Another approach is the insertion of genes related to extremozymes into mesophilic hosts, enabling them to function in more manageable conditions. Bridging various disciplines is essential to uncover the underlying mechanisms of these biological systems and to characterize them for enhanced comprehension and biotechnological applications.

C. **Scarce biocatalytic resources:** Despite the inherent benefits of extremozymes, the pool of available extremophilic biocatalytic tools remains limited. Working with extremophiles or extremozymes necessitates adapting or creating novel methodologies, assays, and techniques that function under non-standard conditions. Many conventional tools from microbiology and biochemistry aren't applicable to extremophilic research due to their inability to withstand extreme conditions. For instance, standard agar-based plating is impractical for hyperthermophiles due to high temperatures causing agar to melt and water to evaporate. Technical disparities persist between laboratory enzyme production and the eventual commercial product, posing a challenge for novel biocatalyst development. Addressing these scientific hurdles is crucial to fully exploit the potential of extremozymes (Sarmiento et al., 2015).

D. **Technical limitations:** Challenges arise not only during the discovery of novel biocatalysts but also when optimizing these biocatalysts for industrial use. Utilizing extremophiles directly as producers of extremozymes is ideal but presents complexities. Operating bioreactors under extreme conditions, such as high or low pH, high temperatures, or high salt concentrations, can shorten the lifespan of sensors and seals in these systems. In some cases, extremophiles do not thrive optimally in bioreactors, attributed to issues like the accumulation of toxic compounds resulting from Maillard reactions at high temperatures. This is exemplified in the cultivation of *Aeropyrum pernix* (Kim et al., 2003).

V. Biosafety and biosecurity concerns

The apprehensions related to black biology are centered on its potential implications for pathogens, particularly those with a historical association or potential for use in biological weapons (BW) and bioterrorism activities. The intention behind introducing genetic modifications into pathogens encompasses a wide array of objectives. These span from extending the longevity of preserved pathogens in controlled environments to conferring resistance against antibiotics or vaccines. Additionally, there is the aim to enable pathogens to evade natural immune responses, such as resisting fever or avoiding macrophage endocytosis, as well as increasing the lethality rate among infected hosts, including humans, livestock, and crops.

To illustrate, Daly's work delves into how extremophiles and their genes, bearing specific traits, could be harnessed for the development of genetically enhanced biological weapons. In a specific scenario, thermophiles—organisms adapted to extreme heat—could provide attributes for creating more resilient and heat-resistant BW. This could enable the BW to endure explosive dispersal from a missile or withstand elevated temperatures within human hosts during infection (Lawrence et al., 2013).

VI. **Conclusion**

The chapter deals with different types of extremophilic bacteria and their robust mechanism that is surviving in those conditions in which life cannot survive. They can stablilized their proteins, enzymes, cell membrane at extremes of physical and chemical conditions. They are different types of extremophiles such as thermophiles, psychrophiles, acidophiles, alkaliphiles, and halophiles.Extremophiles have already demonstrated their utility on an industrial scale. Their robust enzymes, known as extremozymes, have revolutionized processes across diverse sectors, including biofuels, pharmaceuticals, and waste management. The inherent stability of these enzymes allows for enhanced activity under both extreme and moderate conditions, contributing to more efficient and sustainable industrial processes.

Despite their immense potential, there are challenges associated with utilizing extremophiles in industrial biotechnology. Scaling up their cultivation poses obstacles due to the need for specialized equipment and stringent control of extreme conditions. Furthermore, the transition from laboratory-scale success to large-scale industrial application requires overcoming technical barriers and refining the production processes.Addressing biosafety and biosecurity concerns is paramount in harnessing the power of extremophilic bacteria. The unique mechanisms that allow extremophiles to survive extreme conditions must be thoroughly understood to prevent unintended consequences. Mismanagement or accidental release of extremophiles with potentially harmful traits could have far-reaching consequences.

Moreover, the potential misuse of extremophiles in bioterrorism or biological warfare presents a significant challenge. Genetic modifications could be introduced to pathogens, enhancing their virulence, resilience, and evasion capabilities. This highlights the need for strict regulations, robust containment protocols, and international collaboration to ensure the responsible handling of extremophilic organisms.

In conclusion, the integration of extremophilic bacteria into industrial biotechnology offers a promising path toward innovation and progress. Capitalizing on their unique adaptations and enzymatic capabilities can lead to more sustainable and efficient industrial processes. However, a balanced approach is crucial, considering both their benefits and potential risks, to ensure that extremophiles are harnessed safely and ethically for the betterment of society.

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