

EMERGING TRENDS OF EXTREMOZYMES IN INDUSTRIAL BIOTECHNOLOGY

Abstract

Biocatalysis plays a pivotal role in achieving a green, sustainable, biobased economy, and extremozymes offer enhanced activity and stability under extreme conditions, making them valuable biocatalysts. These extremozymes possess distinctive adjustments to thrive in challenging surroundings, encompassing conditions like elevated and reduced temperatures, acidic or alkaline pH levels, substantial salinity, and notable metal concentrations. Extremozymes are capable of catalysing reactions under harsh conditions, making them valuable alternatives for industrial processes previously thought unsuitable for enzymatic activity. Extremophiles, organisms thriving in extreme conditions, offer sustainable, efficient, and cost-effective alternatives to conventional methods in various industries. They produce extremolytes, extremozymes, biosurfactants, etc., which have applications in sustainable agriculture, food, cosmetics, pharmaceuticals, bioremediation, biofuels, biorefinery, and astrobiology. These organisms help us understand the boundaries of life, the origin and evolution of life on Earth, and research in astrobiology and space exploration. However, further investigation is needed to explore their structural and biochemical properties and long-term effects of their applications. Despite their potential, the availability of extremozymes is limited, partially due to challenges in cultivating extremophiles in the lab. This review provides an overview of extremozymes, their applications in various industrial markets, explores future prospects and trends for their biotechnological applications. Extremozymes can contribute to the research and development of safe, healthy, and sustainable food products while minimizing waste generation.

Keywords: Extremozymes; Industrial Biocatalysts; Thermophiles; Acidophiles; Halophiles; Psychrophilic Enzymes.

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I. INTRODUCTION

Extremophiles are microorganisms with the ability to endure and flourish within exceedingly harsh environmental circumstances, conditions that are typically inhospitable to the majority of life forms. These circumstances encompass both elevated and reduced temperatures, exceptionally extreme pH values, heightened pressure, substantial salinity, radiation exposure, and scarceness of nutrients [1]. Extremophiles have evolved diverse molecular tactics to acclimate to these extraordinary circumstances, including the synthesis of extremolytes—organic osmolytes that safeguard biological macromolecules and cells against harm originating from external stressors [2]. They generate distinct enzymes referred to as extremozymes, characterized by exceptional attributes like tolerance to salt, thermal stability, and adaptability to cold conditions [3,4]. Enzymes from extremophiles, including amylases, proteases, lipases, cellulases, and many others, are of particular interest due to their stability and functionality under extreme conditions. The study of extremophiles and their enzymes has gained increasing attention in recent years, opening up new avenues for biotechnological and industrial advancements. These microorganisms play a vital role in various fields, including agriculture, biodegradation, chemical processing, food industry, pharmaceuticals, and bioremediation [5]. Microbiomes thriving in extreme conditions possess the capacity to generate an extensive array of bioactive compounds, secondary metabolites, and enhanced-value products. These microbiomes find utility across various domains, including white and green biotechnology, medicine, and the production of food [6]. The distinct characteristics exhibited by extremophiles and their enzymes hold significant promise for driving advancements in biotechnology, thereby fostering economic growth and unveiling fresh pathways for research and innovation.

Extremophiles are characterized into different types based on their preferred extreme habitats, such as thermophiles (thriving in high temperatures), psychrophiles (thriving in low temperatures), halophiles (thriving in high salinity), and acidophiles (thriving in acidic environments) [7]. The need for industrial enzymes continues to experience consistent growth. The worldwide enzymes market, assessed at \$6.4 billion in 2021, is projected to attain \$8.7 billion by 2026, demonstrating a compounded annual growth rate (CAGR) of 6.3% spanning from 2020 to 2026 [8]. Nonetheless, contemporary industrial biotechnology grapples with several challenges, such as insufficient enzyme stability when subjected to rigorous processing conditions, microbial contamination, subpar recyclability of biocatalysts, and restricted capability for synthetic procedures [9]. Biochemical procedures involving hydrolases often require the involvement of solvents, leading to decreased water activity. This shift in thermodynamic balance enhances the synthetic aspect of the reaction and diminishes undesired side reactions occurring in an aqueous environment [10]. Enhancing the attributes of mesophilic enzymes through chemical or genetic alteration and immobilization proves to be a time-intensive, expensive, and often ineffective process, potentially impacting reaction velocities, enzyme specificity, and stability [11]. Given these challenges, extremozymes present an inherent substitute. These enzymes are tailored to function in rugged settings and have the potential to offer feasible remedies for surpassing the constraints of conventional enzymes.

Extremophilic enzymes are highly adaptable and have numerous uses in the food and biotechnology industries. For example, thermostable enzymes are appropriate for high-temperature processes such as starch hydrolysis for glucose and fructose generation, as well

as grain fermentation for distilled spirits. Psychrophilic enzymes, on the other hand, can be used in low-temperature food processing, whereas halophilic enzymes are effective in the fermentation of salty foods such as soy sauce, salted salmon, and sauerkraut [12]. Despite their enormous potential, the number of commercially available extremophilic enzymes is still very small, and their applications in the food business are not fully realized. Recent research has highlighted the importance of these enzymes in the breakdown of dietary toxins and polymers. This review aims to explore these unique features of extremophilic enzymes and shed light on their potential applications.

Extensive research has focused on identifying extremozymes that are relevant for industrial biocatalysis. Currently, researchers are looking for microorganisms that may produce new enzymes such as amylases, hydrolases, peptidases, cellulases, and lipases that have high activity at low/high temperatures [13]. Due to their biodegradability and extraordinary stability, extremophilic bacteria are significant sources of extremozymes, which have a wide range of commercial applications [14]. Serving as robust biocatalysts, these extremozymes retain their functionality even within extreme environmental circumstances that were once deemed incompatible with biological processes. The employment of extremozymes has expanded the potential for harnessing resilient biomolecules across diverse industrial applications. Examples include extremozymes capable of withstanding cold, acid, alkali, and high salinity conditions [15].

The number of extremophilic enzymes with commercial use is currently limited, recent research in the field has identified enzymes with industrial potential. These investigations play a role in augmenting our understanding of extremophiles and their enzymatic characteristics, setting the stage for forthcoming advancements in leveraging these distinctive biocatalysts. The persistent goal in enzyme research involves uncovering enzymes with unprecedented extreme capabilities and enhanced resilience, underscoring its continued importance [16]. This review specifically focuses on the industrial applications of enzymes derived from extremophilic microorganisms, highlighting their importance in various fields.

II. UNIQUE ADAPTATION & FEATURES OF EXTREMOZYMES

Extremophiles possess unique mechanisms to withstand harsh environmental conditions, necessitating genetic alterations that subsequently lead to changes in protein sequence and structure [17].

1. Thermophiles: Extreme temperatures can lead to irreversible protein folding and exposure of hydrophobic cores, resulting in protein aggregation [17]. In response to this, thermophilic and hyperthermophilic proteins utilize tactics like oligomerization, a substantial hydrophobic core, an augmented count of disulfide bonds, surface charges, and the formation of salt bridges to achieve stabilization [18]. Heat-adapted extremozymes share structural similarities with mesophilic enzymes but exhibit differences in helix and beta sheet sizes, as well as ionic modifications in terminal portions [19]. A unique characteristic of heat-adapted extremozymes is their tightly packed protein structures, which control solvent interactions and contribute to stability by promoting proper folding, reducing protein unravelling, and controlling undesired solvent interactions. The compact arrangement, coupled with the existence of hydrophobic cores,

elevated quantities of salt bridges and disulfide bonds, and a reduced enzyme surface area in proportion to protein size, bolsters the enzyme's resistance to high temperatures [20].

Certain heat-adapted extremozymes exhibit an elevated ratio of hydrophobic amino acids, a diminished ratio of polar and charged amino acids, and a lower fraction of glycine [2]. Deep-sea thermophilic enzymes, in particular, have an excess of charged residues on their protein surfaces, which reflects the aquatic environment of the extremophiles expressing them. Heat-adapted extremozymes provide distinct benefits such as enhanced substrate solubility (particularly for polymers), lower contamination hazards, faster reaction speeds, and the capacity to maintain low solvent viscosity and miscibility [20]. Moreover, a number of thermostable enzymes retain their catalytic traits even when subjected to additional harsh conditions, including high salinity, chemical solvents, and denaturing agents [20].

The existence of disulfide bridges, which diminish the entropy of the protein's unfolded form, has a significant impact on thermal stability in these enzymes. In various studies [23, 24, 25], extremozymes featuring elongated disulfide bridges, notably those originating from the N-terminus, demonstrated enhanced thermostability. Beyond disulfide bridges, numerous additional factors play a role in upholding the conformation of thermophilic extremozymes. These factors encompass tightly packed barrel-like folding, abbreviated loops and helices, the presence of salt bridges, the distribution of surface charges, and interactions among inner hydrophobic amino acids [22]. Enzymes displaying hyperthermostability have shown a notable abundance of charged amino acids, where ionic interactions significantly contribute to their stability beyond 70°C [26]. Furthermore, the thermal adaptations observed in thermophilic enzymes are inherent to their genetic makeup, as demonstrated by their ability to maintain stability even when transplanted and expressed in mesophilic hosts [27].

- 2. Psychrophiles:** Cold Shock Proteins (CSPs) and Cold Acclimation Proteins (CAPs) are specific adaptations that allow psychrophiles to thrive in cold conditions. CSPs are overexpressed in reaction to mild cold shocks, whereas CAPs are overexpressed in response to extreme cold shocks. These proteins undergo structural changes, such as amino acid substitutions, that improve their functioning [28]. Because of reduced rigidity in the protein core and fewer connections between interdomains, the flexibility of enzymes in psychrophiles is improved, providing added stability and specificity at low temperatures [18].

Extremozymes adapted to cold conditions have garnered significant research attention due to their unique structural properties that determine their stability and activity. These enzymes find applications in various food technologies, such as milk pasteurization, lactose degradation, juice extraction, meat tenderization, and dough fermentation. The ability of cold-adapted enzymes to function under cold conditions reduces the enzyme requirements, saves energy costs, offers environmental advantages, and preserves heat-labile flavor compounds and nutrients [29]. Cold-adapted enzymes exhibit high flexibility and substrate promiscuity compared to mesophilic and thermostable enzymes [29]. They possess distinct structural features, including smaller buried amino acid moieties, higher hydrophobic amino acid content on the enzyme surface, lower arginine/lysine ratio, higher glycine levels, and reduced protein

interactions. Additionally, the number of secondary structures and oligomerization is decreased, while the number and size of loops are increased [30]. These features, along with the high conformational entropy of the unfolded protein state, play crucial roles in determining the enzymatic activities of cold-adapted extremozymes [29].

- 3. Halophiles:** Halophiles, or animals that flourish in highly saline environments, have evolved a diversity of adaptations to cope with such hostile conditions. Because salt changes protein solubility, stability, and structure, halophiles devise ways to offset these effects [31]. They regulate osmotic pressure by preventing inorganic salts from entering and creating organic osmolytes [28]. Water availability to internal proteins is reduced in salty environments, leading to dehydration and enhanced interactions between hydrophobic amino acids, resulting in aggregation formation. Proteins adapted to halophilic environments exhibit specific characteristics, including an increased count of salt bridges and a greater presence of acidic residues. Additional adaptations include a decrease in hydrophobic residues, folding influenced by salt concentration, and the incorporation of halophilic peptides [18].

Research focusing on the structural characterization of halophilic enzymes has underscored the significance of enhancing solvation to uphold activity and solubility [32]. In conditions with limited water availability, stable hydration shells can form through hydrogen interactions involving water molecules and negatively charged side chains [33]. Halophilic enzymes also exhibit fewer hydrophobic surface patches, an increased prevalence of ion-pair networks, and a greater occurrence of well-ordered side chains [34]. The resistance to salt stress is evident in the structural foundation of halophilic enzymes, such as the DNA ligase domain from *Haloferax volcanii* [35]. The impact of salt on the stability of halophilic enzymes is primarily unrelated to the overall protein charge, instead closely tied to the reduction of hydrophobicity on the exposed surface area [34]. Furthermore, experimental trials have validated the pivotal role of disulfide bonds in fortifying enzymes within halophilic organisms [36].

- 4. Acidophiles:** Protonation changes the charges of polar charged residues and proteins in acidic circumstances, reducing permeability and maintaining the proton gradient across the cell membrane. Acidophiles, which thrive in acidic conditions, use cytoplasm buffering to keep their intracellular pH balanced. The presence of an abnormally wide external loop in *Thiobacillus ferrooxidans* [37] exemplifies how these acidophiles lower membrane permeability by decreasing the size of their membrane pores [28]. Acidophiles enhance their negative surface charge as well [18]. While the comprehensive investigation of how acidophilic enzymes adapt to low pH conditions remains incomplete, insight into the pH stability of this extremozyme class can be gleaned from research on α -amylases. Acid-stable α -amylases display an abundance of glutamic acid (Glu) and aspartic acid (Asp) residues on their surfaces, alongside fewer positively charged amino acids like arginine (Arg), histidine (His), and lysine (Lys) [38]. The heightened presence of positively charged amino acids on the enzyme surface might induce repulsion, potentially triggering protein unfolding. Nonetheless, negatively charged amino acid residues exhibit a diminished negative charge at low pH, aiding in the stabilization of proteins under acidic conditions [38].

- 5. Alkaliphiles:** Phosphoserine aminotransferase, dependent on vitamin B6, is present in alkaliphiles and assembles into a homodimeric structure [37]. Despite sharing structural similarities with their mesophilic counterparts, these enzymes exhibit certain distinctions. They boast an increased count of hydrogen bonds, more hydrophobic interactions at the dimer interface, and a greater abundance of negatively charged amino acid residues. These variations contribute to the heightened stability and enhanced activity of alkaliphilic enzymes within highly alkaline surroundings [37]. Notably, alkaliphilic enzymes derived from *Bacillus* species, such as alkaline protease and alkaline cellulase, have garnered substantial research attention. Their structural attributes diverge significantly from those of neutralophilic *Bacillus* counterparts. The capacity of alkaliphilic enzymes to operate in high-pH conditions necessitates a high isoelectric point. Consequently, these enzymes feature a greater presence of amino acid residues with positively charged side chains, such as arginine (Arg) and histidine (His), while having fewer residues with low charged side chains like aspartic acid (Asp), glutamic acid (Glu), and lysine (Lys) [39]. Given the pKa of the arginine (Arg) side chain at 12.5, Arg residues acquire a negative charge within the pH range of 9–12, an optimal range for alkaliphile growth. Within this pH span, Arg residues can readily form ion pairs with acidic amino acid residues [40]. Particularly, the formation of Arg-Asp ion pairs assumes vital importance in upholding the stability of alkaliphilic enzymes within high-alkaline environments [40].
- 6. Piezophiles:** Piezophilic proteins, which are specialized for functioning in high-pressure environments, exhibit several structural adaptations. These adaptations contribute to their stability and functionality under extreme pressure conditions. One prominent feature of piezophilic proteins is the presence of hydrophobic cores. These hydrophobic regions are composed of smaller amino acids, which helps to enhance protein stability by minimizing the exposure of hydrophobic residues to the surrounding water [28]. Additionally, piezophilic proteins tend to undergo multimerization, where protein subunits come together and form complexes through hydrogen bonding. This multimerization further enhances protein stability and provides structural support under high-pressure conditions.

Proline and glycine residues, which have unique properties, are found in lower quantities in piezophilic proteins. Proline residues can disrupt helical structures, while glycine residues confer flexibility due to their small size. By reducing the presence of these residues, piezophilic proteins maintain the integrity of their helical structures and reduce conformational flexibility. This reduction in flexibility helps to counteract the compressibility of proteins and ensures their functionality in high-pressure environments [18].

In the instance of *Thermococcus barophilus*, an organism dwelling in the depths of the sea, it has been noted that it accumulates a minor organic osmolyte known as mannosylglycerate. This osmolyte functions as a protective mechanism by diminishing the hydration layer encircling proteins, especially under normal pressure conditions [41]. Through this hydration layer reduction, mannosylglycerate contributes to protein stability and guards against the adverse effects of elevated-pressure environments [41]. Additionally, bacteria inhabiting hydrothermal vents in the deep sea have developed a specialized operon system for pressure sensing. This system empowers them to modulate their growth and physiological processes in response to shifts in both temperature and

pressure. By utilizing the operon system, these bacteria manage to acclimate and thrive in the extreme circumstances encountered within deep-sea hydrothermal vents [28, 37].

III. INDUSTRIAL APPLICATIONS OF EXTREMOPHILES

1. Agricultural Industry: Extremophiles have demonstrated a pivotal and indispensable role in bolstering plant growth, development, and crop yield, particularly in regions grappling with demanding environmental conditions like frigid temperatures, elevated salinity, and drought [42,43]. These organisms serve as invaluable assets for biofertilizers, bioinoculants, and biocontrol agents. In the agricultural sphere, extremophiles present a promising avenue for enhancing water management within plants during periods of water scarcity [44,45]. Moreover, their distinctive cold-active enzymes boast versatile utility across biotechnology and diverse industries [46]. Noteworthy is the biotechnological significance of extremophiles, which hinges on their capacity to generate enzymes essential for the advancement of commercial products, facilitation of industrial processes such as the bioremediation of harmful contaminants from water and sediments, and synthesis of crucial biomolecules for both medical and industrial applications [47].

Biofertilizers and bioinoculants, which are microorganisms with a variety of functions, play critical roles in nutrient cycling, fixation, mineralization, and solubilization, making them viable alternatives to traditional agricultural technology. Furthermore, they have the ability to induce resistance, making them useful biocontrol agents [43,48]. The genetic variety of these microorganisms provides considerable prospects in the agro-industrial sector, allowing for the replacement of chemical-based goods as well as the development of cost-effective, environmentally friendly, and sustainable farming methods [49,50]. Soil salinity, defined by a high concentration of soluble sodium salts, is a major concern for the agricultural business, causing soil degradation and impeding plant growth [51].

Plant Growth Promoting Bacteria (PGPB) inhabit diverse ecosystems, including epiphytic, endophytic, and rhizospheric niches. They contribute to plant growth through the synthesis of phytohormones like indole acetic acids (IAA), gibberellic acids (GA), and cytokinins, as well as activities such as biological nitrogen fixation, nutrient solubilization, and binding (e.g., phosphorus, potassium, zinc). PGPB also exhibit 1-aminocyclopropane-1-carboxylate (ACC) deaminase activity, which helps reduce ethylene levels, a hormone that curbs plant development and, consequently, mitigates salinity stress [42]. Extremophiles like *Enterobacter* and *Gluconacetobacter* participate in nitrogen fixation, while *Methylobacterium*, *Microbacterium*, and *Ochrobactrum* produce phytohormones. In the context of salinity stress, halophilic extremophiles promote various facets of plant growth, encompassing seedling germination, root and shoot elongation, biomass accumulation, yield enhancement, and chlorophyll content. Additionally, specific halophilic extremophiles like *Haloarcula argentinensis* and *Haloferax alexandrinus* demonstrate phosphorus solubilization, enhancing phosphorus accessibility in hypersaline soils [43].

Psychrophilic extremophiles are harnessed as bio-inoculants due to their contributions in nutrient solubilization, nitrogen fixation, and synthesis of

phytohormones. This aids in fostering plant growth in cold conditions, while also enhancing disease resistance [53]. Among acidophilic extremophiles, *Azotobacter*, *Bacillus*, and *Flavobacterium* stand out for their ability to encourage plant development. This positions them as viable choices for bio-inoculants and biocontrol agents in acidic soils. Moreover, extremophiles with drought tolerance and the capability to solubilize phosphorus hold potential as bio-inoculants. Their utilization in agriculture within arid environments could play a significant role in ensuring global food security for the ever-expanding human population [54].

Extremophiles exhibit potent capabilities as biocontrol agents, harnessing their genetic expression adaptations to thrive in extreme conditions. This characteristic has captured the attention of numerous industries and biotechnological pursuits. Notably, a significant application involves employing these microorganisms for the management of biological diseases [55]. *Rhizobacteria*, for instance, play a pivotal role in safeguarding plants against pathogens by generating an array of defensive compounds, including ammonia, hydrogen cyanide, siderophores (iron-chelating compounds), chitinases, and various secondary metabolites [56]. These biocontrol agents retain their efficacy across diverse harsh environments and effectively curtail the proliferation of pathogens and nematodes by disrupting their reproductive cycles and engaging in resource competition. *Bacillus*, *Clavibacter*, *Microbacterium*, and *Pseudomonas* are exemplars of biocontrol agents that operate as inhibitors of plant pathogens [54].

- 2. Food Industry:** Extremophilic microorganisms are renowned for their capability to generate a wide array of bioactive compounds, secondary metabolites, and value-added products, rendering them of exceptional significance within the food and food processing domains [57]. These compounds not only enhance the nutritional profile of food but also bestow health benefits and contribute to the prevention of certain chronic conditions [58]. Carotenoids, among the valuable chemicals synthesized by extremophiles, fulfil significant roles in the food industry as additives, enhancers of colour, and antioxidants [59]. Carotenoids offer numerous advantages to consumers, including elevated nutritional content and enhanced oxidative stability in meat and poultry items [60]. Rich in provitamin A, they possess anti-aging properties, reinforce the immune system, and offer protection against certain cancers and physiological ailments [6]. These visually appealing, probiotic-derived colorants are incorporated into an array of products such as sauces, infant foods, processed cheese, dairy items, breakfast cereals, and fruit and energy beverages. Extremophiles like *Bradyrhizobium* sp. and *Halorubrum* sp. produce canthaxanthin, a colorant utilized in food, beverages, and even for salmon flesh colouring [57]. Riboflavin in *Ashbya gossypii* and carotene in *Blakeslea trispora* are employed for manufacturing microbial food colours [57]. Furthermore, microalgal biomass serves as a valuable source for carotenoid extraction, extensively used in dietary supplements. Astaxanthin, a dietary and feed supplement, is derived from the microalga *H. pluvialis* and extremophiles found in Antarctica's crimson snow [61].

The central processes within enzymatic starch processing are liquefaction and saccharification, both of paramount importance. Liquefaction entails the dissolution of insoluble starch in an aqueous solution, followed by partial hydrolysis using thermostable amylases. Subsequently, the saccharification stage employs glucoamylases to fully degrade oligomers into monomers. These reactions transpire within a temperature range

of 50 to 80°C, necessitating the utilization of enzymes with robust thermal stability. A diverse range of thermophilic enzymes is accessible commercially, encompassing α -amylases, pullulanases, glucoamylases, xylanases, and amylopullulanases [62]. Initial liquefaction relies on α -amylases, while glucoamylases and pullulanases come into play during saccharification. In the food sector, pullulanases and glucoamylases find application in generating glucose syrups, while β -amylases are pivotal in the pharmaceutical realm for maltose syrup production. Additionally, thermostable amylopullulanases contribute to the creation of maltose and maltotriose syrups, offering the dual advantage of simultaneous debranching and liquefaction. This makes them exceedingly sought-after for use in the food, beverage, and pharmaceutical industries [63]. Notably, within both submerged and solid-state fermentation processes, three thermophilic enzymes—glucoamylase, amylopullulanase, and α -amylase—efficiently bring about starch saccharification, eliminating the requirement for calcium or supplemental enzymes [64].

In a study conducted by Rana et al., a *thermophilic Bacillus* sp. sourced from an Indian hot spring was harnessed to produce α -amylase. This enzyme was utilized for multiple purposes, including the clarification of kiwi and apple juices, as well as the production of buns [65]. In the processing of kiwi juice, the addition of 1.25% (w/v) α -amylase led to heightened yield and substantial enhancement in taste, colour, flavour, and overall acceptability. A parallel enzyme concentration of 1.25% (w/v) proved optimal for augmenting taste, colour, flavour, and overall acceptability in apple juice as well. The enzyme's ability to break down polysaccharides yielded a reduction in viscosity and the formation of clusters in the juices, culminating in an improved juice quality. Pertaining to bun production, α -amylase was introduced before the amalgamation of ingredients such as wheat flour, sugar, yeast, and oil. At an enzyme concentration of 0.75%, the study reported a peak leavening activity of 2.60 ml/hr, translating into a significant enhancement in bun quality [65].

β -glucosidase assumes a pivotal function in the treatment of sugarcane bagasse, the residual dry fibrous material remaining after the extraction of juice from sugarcane. An *Anoxybacillus flavithermus*-derived thermostable β -glucosidase, isolated from the Tengchong hot spring in Yunnan, China, has demonstrated remarkable proficiency in cellulose hydrolysis. When this enzyme was used in combination with a commercial cellulase product (Celluclast®, Novozymes), the cellulose content of sugarcane bagasse decreased by 25%. However, when β -glucosidase (50 μ g/g sugarcane bagasse) was used together with Celluclast®, a more significant reduction of 48% in cellulose content was observed [66]. These findings indicate the synergistic action of the thermostable β -glucosidase and Celluclast® in breaking down complex sugars present in the bagasse. Given its efficiency in degrading cellulose, this thermostable enzyme holds promise for treating food industry wastes that contain high levels of complex sugars.

α -glucosidase has found practical utility in the conversion of maltose into isomalto oligosaccharides (IMO), renowned as low-calorie, high-fiber sweeteners and marketed as prebiotic fibers in China and Japan [67]. Furthermore, the thermostable α -glucosidase originating from *Thermococcus hydrothermalis* has demonstrated effective application in tandem with α -amylase and pullulanase for starch processing, yielding glucose syrup as the end product [68]. Another enzyme frequently employed within the starch industry is

the glucosidase sourced from *Aspergillus niger*, extensively utilized for generating glucose syrups and disaccharides [69].

An exceedingly heat-resistant glucoamylase, sourced from *Penicillium oxalicum* and isolated from the forest floor in China, has exhibited exceptional efficacy in the hydrolysis of raw starches from corn and cassava, facilitating the production of ethanol [70]. Similarly, a thermally stable glucoamylase produced by *Bacillus licheniformis* was utilized to break down potato starch, characterized by its large granules that are challenging for most enzymes to degrade [71]. The combination of fungal glucoamylases with α -amylase is a prevalent practice in generating glucose and fructose syrups through starch hydrolysis [72]. These syrups, rich in glucose, can be utilized to produce crystalline D-glucose or serve as a foundational material for the synthesis of high-fructose syrups.

In the realm of bread production, a recently discovered extremophilic xylanase sourced from *Aureobasidium pullulans* underwent utilization and comparison with two commercially available xylanase preparations. The enzyme, employed at a concentration of 125 U/100 g flour, yielded high-quality dough with heightened water absorption capabilities. Notably, this enzyme led to a remarkable 30% upsurge in bread-specific volume and a corresponding 30% reduction in crumb stiffness in comparison to the effects elicited by commercial enzymes [73]. Diverse microbial xylanases have been harnessed within bread manufacturing, encompassing those originating from *Bacillus subtilis*, *Aspergillus aculeatus*, *Aspergillus oryzae*, and *Trichoderma reesei* [74]. Among these, the xylanase sourced from *A. oryzae* demonstrated the most notable effectiveness as a bread improver, while the one derived from *Trichoderma reesei* exhibited superior antistaling properties [75]. Moreover, enzymes such as lipases and phospholipases have been employed as in situ emulsifiers to bolster dough stability and conditioning. Additionally, lipoxigenase and glucose oxidase have been employed to reinforce dough structure and augment bread whiteness [74].

Extremophilic lipases play an extensive role in the synthesis of structured lipids containing omega-3 fatty acids and in the extraction of omega-3 fatty acids from diverse sources. For instance, the thermostable lipase *Candida antarctica* (*Cal-A*) has been instrumental in producing highly pure docosahexaenoic acid (DHA) concentrates. These DHA concentrates find wide application in the food and pharmaceutical sectors, particularly in products necessitating elevated DHA levels, such as infant formula [76]. Another lipase from *Candida antarctica* (*Cal-B*) has been utilized to fabricate fat analogs for infant formula, enriched with arachidonic acid (ARA) and DHA [77]. Extremophilic lipases have held pivotal significance in the synthesis of an extensive array of food additives, encompassing antioxidants, flavoring agents, coloring agents, phytosterol esters, sugar esters, and conjugates of multifunctional compounds [76]. These enzymes have demonstrated their versatility within the food industry, empowering the creation of diverse functional lipids with a myriad of applications.

Microbial esterases exhibit a broad spectrum of applications across the food and beverage sectors, alongside their utility in the breakdown of synthetic materials. For instance, a p-coumaric esterase derived from *Rhizoctonia solani* has been employed to enhance the value of food processing byproducts. This enzyme effectively releases p-coumaric, caffeic, and ferulic acids from sources like wheat bran, sugar beet pectin, and

coffee pulp residues [78]. Similarly, an esterase originating from *Candida parapsilosis*, a fungal yeast isolated from marine debris along China's East Sea coast, has been employed in synthesizing taste-enhancing esters such as n-propyl acetate, isobutyl acetate, and isoamyl acetate [79]. These microbial esterases have demonstrated substantial utility across various industries, aiding in the efficient utilization of byproducts and waste materials. Furthermore, they play a key role in crafting desirable flavor compounds for the food and beverage sectors. Additionally, their capacity to degrade synthetic materials underscores their potential contribution to waste management and environmental applications.

Microbial proteases hold significance within the food domain, serving roles in both meat tenderization and peptide generation. An exceptional thermostable aspartic protease derived from *Rhizomucor miehei* stands out as a noteworthy enzyme in this field. Demonstrating remarkable effectiveness as a meat tenderizer, even at a modest dosage (0.25 mg/100 g pork), this enzyme outperformed a commercial meat tenderizer known as papain [80]. Furthermore, when employed to produce angiotensin converting enzyme (ACE) inhibitory peptides from turtle meat, this aspartic protease yielded a substantial quantity of short peptides (5,000 Da) exhibiting potent ACE-inhibitory activity [80]. These findings underscore the substantial potential of the aspartic protease sourced from *Rhizomucor miehei* as a valuable asset within the food industry, contributing to meat tenderization and the generation of bioactive peptides with potential health benefits.

A multitude of extremozymes displaying exceptional resistance to high salinity have been recorded for applications pertinent to the food industry. For instance, *Halobacterium sp.* Strain LBU50301, sourced from salt-fermented fish (budu), showcased its capacity to generate a halophilic protease capable of enduring 27.95% (w/v) NaCl [81]. Similarly, a protease that remains stable in both high temperature and solvents, originating from *Halobacillus sp.* CJ4 and isolated from the hypersaline Chott Eldjerid Lake in Tunisia, exhibited remarkable stability and catalytic efficacy even in the presence of 120 g/L NaCl (2 M) [82]. The impressive high-salinity tolerance of these extremozymes introduces intriguing prospects for their utilization in the production of high-salt foods, such as soy sauce. Leveraging their distinct attributes, these enzymes hold the potential to elevate the processing and quality of food items within high-salt environments, thereby offering valuable opportunities for advancement within the food industry.

- 3. Extremozymes Applied in Paper & Pulp industry:** Pulp, a fibrous substance comprised of cellulose extracted from wood, fiber crops, and discarded paper, has traditionally been produced through chemical and mechanical methods. These procedures entail separating cellulose fibers from other components present in wood, including hemicellulose and lignin. The conventional approach involves elevated temperatures (sometimes up to 80°C), alkaline pH levels, and the application of potent chemicals like sodium sulfide, sodium hydroxide, and chlorine. This technique has been associated with environmental concerns and substantial operational costs [83]. Enzymatic bio-pulping has garnered attention as an eco-friendly, safer, and economically feasible alternative to complement existing pulping techniques within the pulp and paper industry. Robust hyperthermophilic/alkaline enzymes have emerged as valuable enhancements to pulping processes, boosting efficiency while reducing reliance on harmful chemicals. The enzyme

market in the pulping and paper sector is poised for significant growth, particularly in Europe [83]. Among the enzymes pivotal to bio-pulping, xylanases hold a critical role as they facilitate the breakdown of hemicellulose, thus aiding in the liberation of lignin during a process referred to as bio-bleaching. Hyperthermophilic xylanases have been identified in diverse microorganisms and have shown potential in bio-bleaching procedures. Nonetheless, a greater availability of xylanases in the pulp and paper industry is required to meet the demand [84].

Laccases are also employed in bio-bleaching operations to break down lignin and enhance the brightness of the final product. Numerous fungal laccases have found utility in bio-bleaching processes, yet further investigation is required to create enzymes suitable for robust pulping conditions [85]. The management of sticky deposits affecting paper production is achieved through the use of hyperthermophilic lipases, which mitigate these troublesome residues. Furthermore, innovative hyperthermophilic esterases are under exploration to bolster pitch control and address other adhesive substances. Cellulases contribute to elevating the brightness and strength of paper sheets, along with enhancing the overall efficiency of the refining procedure. To advance environmentally conscious and efficient methodologies in the pulp and paper sector, endeavors are underway to generate high-performance enzymes tailored to the pulping industry, including hyperthermophilic pectinases and amylases [83]. Sustained research and development endeavors in this realm are indispensable for attaining sustainable and enhanced practices within the industry.

- 4. Extremozymes used in Textile Industry:** Extremozymes, which are noted for their eco-friendliness and versatility in dealing with a wide range of substrates, are increasingly being used in the textile sector to improve fabric quality and address numerous processing issues [86]. These extremozymes serve an important function in increasing fabric appeal throughout the finishing process by resisting stressors such as bending and tension that cause thread degradation. They operate well in moderate circumstances, are biodegradable, and speed up reactions by lowering activation energy through substrate specificity [87].

Desizing, a technique used to remove the protective starch layer placed during weaving that may interfere with later operations, is one key application of extremozymes [88]. Extremophiles such as *Thermus thermophilus* HB8, *Euplotes focardi*, *Alkalibacillus* sp. NM-Da2, and *Geomyces* sp. produce enzymes such as -amylase, lipase, and proteases that aid in the desizing of woven fabric, notably denim and cotton fabrics [89].

Extremozymes also find application in bioscouring, a process aimed at eliminating non-cellulosic contaminants from fabric surfaces, including substances like pectin and waxes. Pectinase, xylanase, protease, lipase, and their combinations are employed to remove impurities, with alkali-thermophilic thermozymes proving highly effective due to their ability to withstand high temperatures and alkaline pH [90]. Particularly noteworthy are extremophiles such as *Bacillus* sp. and *Pseudomonas* sp., which produce alkaline pectinases suitable for cotton bioscouring, preserving cellulose and minimizing fiber damage [91]. Extremozymes like glucose oxidase, catalase, and laccase are harnessed in bleaching processes to achieve pristine white cotton fibers by eliminating natural hues and residual hydrogen peroxide in an environmentally friendly manner [92]. Catalase and

laccase enzymes sourced from bacterial species like *Geobacillus thermopakistanensis* and *Brevibacillus agri* offer effective solutions for denim bleaching and discoloration [93]. Additionally, extremophiles such as *Vibrio sp.* and *Chromobacterium violaceum* have been investigated for their capacity to produce bio-dyes such as prodigiosin and violacein, providing sustainable alternatives for coloring wool, silk, acrylics, and other textiles [94]. The ongoing exploration in this realm holds promise for uncovering even more potent extremozymes that could revolutionize the textile industry, enhancing its sustainability and eco-friendliness.

- 5. Extremozymes in Detergent Market:** The current trend in the detergent industry revolves around cold-water detergents, which exhibit performance levels comparable to conventional detergents but operate effectively at lower temperatures. The adoption of cold-water detergents has the potential to yield advantages such as reduced energy consumption, lower CO₂ emissions, and enhanced fabric preservation. Despite these benefits, the widespread adoption of cold-water detergents has been relatively gradual, as the conventional practice of using hot water for garment cleaning remains prevalent. Nevertheless, recent endeavours focused on identifying and developing novel enzymes capable of functioning optimally in colder temperatures have garnered attention within the cleaning sector. This emergence presents a promising opportunity for the broader utilization of cold-wash detergents [95].

Ongoing research is focused on harnessing the potential of various cold-adapted enzymes to enhance the effectiveness of cold-water laundry and dishwasher detergents, both for household and industrial applications. Notably, some of the key cold-adapted enzymes under investigation include:

- Lipases:** These enzymes specialize in breaking down lipids and eliminating fatty stains from fabrics. Novozymes has developed Lipoclean®, a cold-adapted lipase that targets triglyceride stains and maintains activity even at low temperatures (20°C). Additionally, Lipex® and Lipolase® Ultra, created by the same company, offer effective performance at lower to moderate temperatures [96].
- Proteases:** Playing a crucial role in hydrolyzing peptide bonds within proteins, proteases aid in the degradation of protein-based stains like blood, egg, grass, chocolate, and perspiration [97]. Novozymes and Genencor have introduced cold-adapted proteases named Kannase® and Polarzyme® for use in laundry detergents.
- Amylases:** These enzymes are designed to break down starch-based stains originating from foods like cereals, fruits, and pasta [98]. Novozymes offers Stainzyme® and Stainzyme® Plus, both of which effectively tackle stains through moderate/low-temperature washing.
- Cellulases:** With a focus on degrading cellulose within cotton fibers, cellulases contribute to reducing fuzz and pilling. Novozymes has introduced Celluzyme®, derived from the fungus *Humicola insolens*, which remains active even at chilly temperatures (15°C) [99].

In addition to the commonly employed dishwashing enzymes, the industry is actively investigating alternative cold-active enzymes, such as mannanases and pectinases, to address specific types of stains commonly found in food and personal care products [95]. Despite the progress made in developing cold-active enzymes for the detergent sector, there remains a persistent demand for novel psychrophilic/psychrotolerant enzymes capable of effectively functioning within current cold-washing methods. Enzymes that demonstrate successful performance at low temperatures, sustain activity across a broad temperature range, and maintain

compatibility with surfactants and alkaline pH conditions hold significant potential for shaping the future of detergent applications [95]. Beyond laundry detergents, extremozymes also find utility in cleaning-in-place operations within the food, brewing, and dairy industries. In the beverage sector, enzymes are employed to clean equipment and unblock filters. Notably, lipases, proteases, amylases, and pullulanases exhibit excellent efficacy in degrading molds and biofilms present in filters and building surfaces. This leads to enhanced cleaning outcomes without the reliance on chemical detergents, surfactants, or organic solvents [100].

- 6. Biofuel Production:** Enzyme-catalyzed fermentations play a pivotal role in the direct production of biofuels from biomass. Initially, first-generation biofuels derived from sources like corn, sugar beets, and wheat faced challenges as they competed with global food supplies, leading to increased food prices (Bhalla et al., 2013). In contrast, second-generation biofuels have emerged as a more promising alternative by harnessing the potential of lignocellulose, a resource that is abundant, cost-effective, and often sourced from agricultural and forestry residues. Lignocellulose comprises three main components: lignin, cellulose, and hemicellulose, with cellulose and hemicellulose serving as primary sources for second-generation biofuel production. Given the dense and rigid nature of lignocellulose, pretreatment is essential to render cellulose and hemicellulose accessible to enzymes [101]. Effective pretreatment methods often involve elevated temperatures (exceeding 50°C) to disrupt the lignocellulose structure and facilitate enzyme penetration [101].

The destruction of lignocellulose necessitates the use of cellulase and xylanase enzymes, which work together to hydrolyze cellulose and hemicellulose, respectively. Cellulases are made up of three enzymes: endoglucanase, β -glucosidase, and exoglucanase, which all work together to completely hydrolyze cellulose into glucose [102]. In contrast, xylanases are a class of enzymes that breakdown xylan in hemicellulose into monosaccharides and xylo-oligosaccharides. The degradation of lignocellulose necessitates the use of enzyme combinations that can be structured in many ways, including the utilization of a multienzyme complex known as the cellulosome and multifunctional megazymes [103].

Multifunctional megazymes refer to enzymes that possess a minimum of two separate catalytic modules, often displaying bifunctionality. In the case of *Caldicellulosiruptor bescii*, it features a hyperthermophilic cellulase/hemicellulase system adept at breaking down xylan, microcrystalline cellulose, as well as untreated grass and rice straw. These enzymatic activities occur at elevated temperatures and specific pH levels [104]. *Clostridium thermocellum cellulosomes* and thermophilic β -glucosidase from *Thermoanaerobacter brockii* demonstrated high glucan conversion from pre-treated rice straw with significant economic benefits [105]. When compared to commercial enzymes, *C. thermocellum's cellulosome* accomplished full glucan conversion of microcrystalline cellulose [106]. Lipases, for example, play an important part in biotechnological applications and help to produce biofuels such as biodiesel. Cold-active lipases from psychrophilic extremophiles are very useful for industrial biodiesel synthesis because they accelerate reactions at extremely low temperatures [107].

Lignocellulose-degrading enzymes play a pivotal role in the degradation of lignocellulose, a highly resistant biomass comprising cellulose, hemicellulose, and lignin. These hydrolytic enzymes break down cellulose into fermentable sugars, which can subsequently be converted into ethanol. Cellulases, xylanases, lignases, lignin peroxidases, and manganese peroxidases are examples of enzymes produced by thermophilic microorganisms like *Geobacillus* sp. R7, *Phanerochaete chrysosporium*, and *Sporotrichum thermophile* [108]. Notably, *Caldicellulosiruptor bescii*, an anaerobic bacterium, exhibits efficient degradation of untreated biomass and crystalline cellulose, offering the potential for lignocellulose-to-ethanol conversion without the need for pretreatment [109]. Another enzyme of significance is α -amylase, crucial for starch hydrolysis. Extremozymes from thermophilic organisms, such as *Bacillus licheniformis*, are particularly suitable for α -amylase isolation due to their optimal activity at high temperatures [110]. These enzymes hold substantial importance in ethanol production through the processes of liquefaction, saccharification, and fermentation.

- 7. Biomining:** Biomining, also referred to as bioleaching and bio-oxidation, presents a cost-effective and environmentally advantageous approach to mineral extraction. This method involves the oxidation of metal sulfides within an acidic environment by thermophiles and sulfur-oxidizing chemolithotrophs, resulting in the formation of sulfur compounds or metal ions [111]. Alternatively, bio-oxidation focuses on breaking down the mineral matrix surrounding the targeted metal, thereby exposing it to oxidation processes. The biomining process often encounters extreme conditions such as high salt concentrations, wide temperature ranges, organic solvents, low pH levels, and elevated metal concentrations due to acid mine drainage. Polyextremophiles like *Acidithiobacillus ferrooxidans*, *Sulfobacillus* sp., and *Ferroplasma* sp. are frequently employed for the biomining of metals like copper, nickel, and uranium under these challenging circumstances. Additionally, acidophiles such as *Acidihalobacter prosperus* and *Acidihalobacter ferrooxidans* find application in bio-metallurgy processes [112]. Archaeobacteria such as *Metallosphaera* and *Sulfolobus* excel in biomining at exceptionally high temperatures, demonstrating the ability to fix carbon dioxide and thrive in aerated conditions [113].

Biomining, employing methods like roasting and smelting, stands out for its energy efficiency compared to traditional mining techniques, while also avoiding the release of hazardous gases like sulfur dioxide. This approach offers benefits for economically leaching ores of both low and high grades. Additionally, it contributes to the mitigation of acid mine drainage, thereby reducing environmental pollution [114]. In the realm of large-scale extraction, various technologies such as bio-reactors, piles, and dumps are harnessed, whereas in-situ mining and vats find use with lower-grade ores. In the creation and recycling of reagents used as lixiviants, acidophilic iron-oxidizing extremophiles play a crucial role by eliminating excessive iron, sulfate, and other impurities from hydro-metallurgical solvents. The efficiency and management of biomining have been enhanced through the utilization of genetically modified (GM) microorganisms, which have been engineered to withstand variable environments [114]. The integration of OMICs technologies (genomics, proteomics, transcriptomics, and metabolomics) has significantly contributed to an improved comprehension of the internal growth mechanisms that facilitate the adaptability of extremophiles. Ongoing research is imperative to pinpoint microorganisms with heightened metal tolerance, improved

mineral attachment, and high growth rates at elevated metal concentrations. Furthermore, the realm of synthetic biology could explore the potential of applying bioleaching and biomining techniques in scenarios like asteroid and planetary utilization [114].

- 8. Bioremediation, Biodegradation & Pollutant Revomal:** Bioremediation has assumed a vital role in the pressing need to restore contaminated and degraded landscapes. Microorganisms, particularly extremophiles, play a pivotal role in this context by actively engaging in the breakdown of heavy metals and organic pollutants, detoxifying polluted soil, wastewater, radioactive waste, and even aiding in the decomposition of plastic, a significant environmental pollutant [115]. A multitude of industrial activities contribute to the release of heavy metals and radioactive agents into the environment, posing threats to human health and ecological integrity. The exceptional abilities of extremophiles enable them to convert, immobilize, or break down these harmful contaminants into harmless compounds through diverse mechanisms such as biodegradation, biosorption, bioreduction, and bioemulsification [116].

Significantly, extremozymes produced by these exceptional microorganisms act as highly effective biocatalysts, facilitating the conversion, precipitation, and immobilization of pollutants through redox reactions, all while minimizing the generation of secondary contaminants [117]. This bioremediation process presents a promising avenue to counter environmental pollution and uphold the equilibrium and well-being of ecosystems [117]. The phenomenon of acid mine drainage (AMD) arises when sulfide minerals in the Earth are exposed during mining or large construction activities. Upon contact with water and oxygen, most sulfide minerals undergo oxidation, resulting in the production of sulfuric acid that infiltrates both surface and groundwater. AMD significantly contributes to water pollution and the release of heavy metals into the environment. Typically exhibiting a pH range of 2 to 8, AMD contains elevated levels of metals and sulfides. Traditional AMD treatment methods involve raising the acidic effluent's pH above the optimal requirements for iron-oxidizing bacteria or using crushed limestone to mitigate acid formation. However, these approaches are inefficient, operationally costly, and generate substantial quantities of solid sludge that necessitate proper disposal [118].

Acidophilic microorganisms, particularly *Acidiphilum*, *Acidithiobacillus*, *Acidisphaera*, and *Leptospirillum*, are prevalent inhabitants of AMD environments [119]. These microbes not only thrive in acidic surroundings but also possess the capability to oxidize and reduce iron and sulfur. They exhibit resilience to toxic elements like cadmium, chromium, nickel, and arsenic. In the realm of AMD bioremediation, the focus is on utilizing bioreactors containing acidophilic iron-oxidizing bacteria (e.g., *Leptospirillum ferrooxidans*) and sulfate-reducing bacteria (e.g., *Acidithiobacillus ferrooxidans*, *A. ferrivorans*) rather than specific enzymes. These bacteria secrete extracellular oxidoreductases that remain stable at pH levels significantly lower than their intracellular pH (around pH 5) [120]. The bioreactors facilitate an AMD fermentation process that creates conditions conducive for sulfate reduction and metal precipitation [121]. This process leads to sulfate reduction, which generates alkalinity by converting sulfate to sulfide. The dissolved metals subsequently combine with sulfide to form insoluble metal sulfides. The treated and neutralized drainage, devoid of metals, is then discharged from the bioreactor. Numerous instances of successful AMD treatment bioreactors achieving over 90% heavy metal removal have been documented [122].

Due to their remarkable ability to withstand high temperatures and reduce metals, thermophilic microorganisms can be effectively employed in heavy metal bioremediation for elements like Mn, U, Tc, Cr, Co, Mo, Au, and Hg. *Geobacillus thermantarcticus* and *Anoxybacillus amylolyticus*, for instance, possess a strong biosorption capacity, allowing them to bind with heavy metals such as Cr, V, and Co, facilitating their extraction from contaminated environments [123]. These thermophiles convert contaminants into non-toxic compounds. *Bacillus sp.* has also demonstrated effectiveness in eliminating aliphatic and aromatic hydrocarbons, as well as synthetic dyes, from various industries [124].

Petroleum industries and incidents involving oil spills frequently result in the contamination of soil and groundwater with harmful substances, including poly-cyclic aromatic hydrocarbons and long-chain alkanes (ranging from C10 to C32). Specific extremophiles, such as *Bacillus*, *Thermus*, and *Geobacillus*, possess the capability to remediate such pollutants [125]. For instance, the *Geobacillus SH-1* strain can degrade saturated alkanes within the C12 to C33 range as well as naphthalene. Additionally, thermophiles like *Geobacillus thermoparaffinivorans IR2*, *Geobacillus stearothermophilus IR4*, and *Bacillus licheniformis* can convert lengthy alkyl hydrocarbons (C32 and C40) into non-toxic compounds [125]. In the context of radioactive waste treatment, thermophiles like *Thermus scotoductus*, *Thermoterrabacterium ferrireducens*, *Pyrobaculum landicum*, and *Thermoanaerobacter sp.* have shown promise in reducing specific radioactive elements such as enzymatic uranium and technetium [126]. Additionally, hyperthermophilic species like *Pyrobaculum sp.* are associated with uranium reduction [127]. Furthermore, extremozymes derived from thermophilic molds such as *Talaromyces emersonii*, *Rhizopus sp.*, and *Thermomucorindicae seudaticae* demonstrate remarkable efficacy and stability at elevated temperatures, rendering them valuable for breaking down hazardous organic pollutants stemming from industrial processes [126].

Psychrophiles, which flourish in cold environments, are excellent in utilizing organic pollutants, particularly hydrocarbon mixtures and halogen compounds, rendering them non-toxic [124]. *Pseudoalteromonas sp. P29* and *Oleispira antarctica RB-8T*, for example, exhibit modifications that allow them to breakdown crude oil, jet fuel, and other contaminants [125]. Furthermore, psychrophiles play an important role in plastic breakdown, particularly when building biofilms on plastic waste [128].

Extracellular polymeric substances (EPS) produced by halophiles aid in their attachment to surfaces and the creation of biofilms, boosting their efficacy in the treatment of harmful organic contaminants [129]. These microbes are capable of decomposing hydrocarbons prevalent in hypersaline environments, such as alkanes, benzene, biphenyl, anthracene, and naphthalene [125]. They may also remove hazardous chemicals such as tributyltin, phenol, hydrocarbons, and azo dyes from diverse industrial effluents [125].

Finally, radiophiles contribute to radionuclide treatment in soils and aquatic mediums via biomineralization, biotransformation, and biosorption processes. Some radiophilic strains, such as *Shewanella* and *Geobacter* species, can reduce uranium and other radioactive contaminants, making them helpful for decontamination [125].

Extremophiles, which include thermophiles, acidophiles, psychrophiles, halophiles, and radiophiles, provide excellent solutions for the bioremediation of diverse pollutants in a variety of environmental situations.

- 9. Cosmetic Industry:** Mycosporines and mycosporine-like amino acids (MAAs) have gained significance in the cosmetic industry due to their capability to shield the skin from detrimental UV radiation. Prolonged exposure to UV rays can result in sunburn, premature aging, and even skin cancer [130]. In this regard, MAAs have demonstrated superior efficacy in safeguarding the skin compared to synthetic sunscreens containing organic filters (such as oxybenzone, avobenzone, aminobenzoic acid) or inorganic filters (like titanium dioxide, zinc oxide), or a combination of both. They offer anti-aging benefits by acting as antioxidants, fending off microorganisms, and effectively absorbing UV radiation, all while imposing minimal adverse effects on marine ecosystems and causing fewer concerns among individuals, such as allergies, phototoxicity, and disruptions in endocrine functions. Additionally, they are more ecologically friendly [130, 131]. When subjected to UV light, lichens, fungi, and cyanobacteria naturally produce MAAs, and their stability at high pH and temperatures makes them suitable as natural bioactive components in cosmetic formulations [132]. However, their protective effect against UVA radiation is more pronounced than against UVB radiation [130]. Considering that synthetic UV filters in sunscreens absorb photons rather than reflecting them, incorporating compounds rich in antioxidants is pivotal to enhancing the effectiveness of sunscreens [132]. Extremophiles showcase an array of biochemical adaptations, including the synthesis of carotenoid pigments (such as lycopene and astaxanthin), which function as natural antioxidants, safeguarding against UV radiation and mitigating skin photodamage [133].

Biosurfactants have garnered popularity in the cosmetic sector due to their favorable properties like foaming, emulsification, and water binding, which render them preferable over other surface-active agents [134]. The production of monoglyceride, a commonly used surfactant, can be enhanced through the treatment of glycerol tallow with the psychrophile *Pseudomonas fluorescens* lipase [132]. Marine organisms like *Arthrobacter*, *Pseudomonas*, *Halomonas*, and *Bacillus* present promising candidates for biosurfactant and bioemulsifier production [132].

- 10. Medical Applications of Extremophiles and their Products:** Extremophiles thrive in challenging environments and play a crucial role in providing antibiotics, antifungals, and compounds with anticancer properties. These extremophiles generate antimicrobial peptides like halocins, which exist in *Halobacteriaceae* and *Sulfolobus* species. Remarkably, these peptides efficiently eliminate archaeal cells without posing any danger to beneficial human microorganisms. [135]. Furthermore, extremophiles produce diketopiperazines, which are derived from halophiles such as *Naloterrigena hispanica* and *Natronococcus occultus* and have antibacterial, antifungal, antiviral, and anticancer activities. These diketopiperazines also have an effect on human blood coagulation, making them possible candidates for alternate treatments against drug-resistant *Pseudomonas aeruginosa* infections via regulating quorum-sensing pathways [135]. Furthermore, extremophiles may synthesize Polyhydroxyalkanoates (PHAs), which act as carbon storage for microbial cells and provide a biodegradable and biocompatible alternative to petroleum-based plastics. Because PHAs are non-cytotoxic, they are highly

adaptable as biopolymers and have uses in implants, drug delivery systems, and other areas [135]. Recombinant gas-filled vesicles produced by extremophiles such as *Haloferax terranei*, *Halobacterium sp. NRC-1*, *Halobacterium salinarum*, and *Holoquadratum walsbyi* are another fascinating breakthrough. These vesicles are largely non-toxic while provoking a strong immunological response. As a result, they have demonstrated good outcomes in mouse studies, making them prospective candidates for alternate vaccine delivery systems [135].

Thermophile-derived DNA polymerases have demonstrated their value in the fields of medicine and biotechnology. Taq, sourced from *Thermus aquaticus*, along with Pfu from *Pyrococcus furiosus* and Vent from *Thermococcus litoralis*, are notable instances. Of particular significance is Taq polymerase from *Thermus aquaticus*, which finds frequent application in PCR, a fundamental method in molecular biology [135, 136]. *Aeropyrum pernix K1* is a hyperthermophilic bacterium that produces a remarkable extremozyme called nucleoside phosphorylase, which has uses in antiviral therapy by helping in the manufacture of nucleoside analogs. Because of their capacity to act at high temperatures and with minimal substrate viscosity, thermozyms like this one has a wide range of clinical applications [130,135].

Pyochelin, a compound derived from *Pseudomonas sp.*, exhibits antifungal properties and the ability to bind iron, rendering it effective against *Candida* and *Aspergillus* species. Dried Dunaliella, classified as a halophile, possesses antioxidative and cryoprotective qualities due to the presence of antifreeze proteins [137]. Moreover, Dunaliella is a producer of β -carotene, utilized as a pharmaceutical colorant and dietary supplement [138]. Additionally, a marine *Streptomyces* strain yields two benzoxazine glycosides (arcticoside and C-1027 chromophore-V), which hinder *Candida albicans* isocitrate lyase as well as breast and colorectal cancer cells [139]. The therapeutic potential of extremolytes lies in their capacity for anti-proliferative, anti-inflammatory, and chemopreventive effects. Extremophiles generate diverse metabolites like biosurfactants, biopolymers, and peptides, all of which find a wide array of applications within the pharmaceutical sector [138].

Biosurfactants find therapeutic applications and are commonly employed within the pharmaceutical and medical sectors. These surface-active compounds offer a diverse range of therapeutic benefits owing to their antibacterial, antiviral, anticancer, and antifungal properties [138]. In the realm of pharmaceuticals, biosurfactants exhibit an extensive spectrum of uses, showcasing attributes that encompass antibacterial, antiviral, anticancer, antifungal, and even antitumor effects. An illustrative instance is the biosurfactant produced by *Bacillus circulans*, which displays notable antibacterial potency against multidrug-resistant (MDR) and other pathogenic and semi-pathogenic microbial strains [140]. In pharmaceutical formulations, biosurfactants play a role in augmenting the production of novel collagen fibers through the action of refined lactone sophorolipid [141]. Additionally, they contribute to the recovery of intracellular products by facilitating cell lysis post-fermentation [141].

Biosurfactants contribute significantly to combating the attachment and colonization of pathogenic microbes through their antiadhesive and antibiofilm attributes. Biosurfactants obtained from *Lactobacillus fermentum*, a thermo-acidophilic lactic acid

bacteria, have been demonstrated to effectively hinder *Staphylococcus aureus* infections on surgical implants. Similarly, the application of surfactant-treated PVC plates and vinyl urethral catheters impedes the development of *E. coli* biofilms [141]. Moreover, biosurfactants, particularly those based on liposomes, hold promise as potential tools for gene transfection, serving as alternative gene delivery methods and immunological adjuvants. Their favourable characteristics, such as minimal toxicity and pyrogenicity, make them well-suited for such applications [141].

Table 1 gives a comprehensive list of extremozymes, their role played in various industries.

Table1: Extremozymes and their Applications in Different Industries

Industries	Name of Enzymes	Microbe	Application	References
Agricultural Industry	Cold active enzymes	Arthrobacter and Bacillus	Aids farming at low-temperature	[54]
	Cellulase	<i>Acidothermus cellulolyticus</i>	Hydrolyzing cellulose	[1]
	Urease	<i>Bacillus sp.</i> strain TB-90	Breakdown of urea	[1]
Pharmaceutical and Medical Industry	Thermolysin	<i>Bacillus thermoproteolyticus</i>	Synthesis of dipeptides production of NAOS	[110]
	Prolidase	<i>Pyrococcus furiosus</i>	Cleavage of dipeptide	[110]
	Monoacylglycerol lipase (GMGL)	<i>Geobacillus sp.</i> 12AMOR1	Acts on monoacylglycerol substrate	[110]
	β -agarase AgaP4383	<i>Flammeovirga pacifica</i> WPAGA1	Hydrolysis of agar and recovery of DNA from agar gels, production of NAOS	[110]
	β -agarase Aga4436	<i>Flammeovirga sp.</i> OC4	Hydrolysis of agar, recovery of DNA from agar gel,	[110]
	Est11 esterase	<i>Psychrobacter pacificensis</i>	Act as catalysts	[110]
	EstO esterase	<i>Pseudoalteromonas arctica</i>	enhance the solubility of anti-inflammatory drugs	[110]
	Mercuric reductase	<i>Archaeon</i> SCGC-AAA261G05	Bacterial detoxification	[113]

	DNA polymerase	<i>Thermus aquaticus</i> , <i>Thermococcus litoralis</i> , <i>Pyrococcus furiosus</i> , Archaeon SCGC-AAA261G05,	PCR	[135]
	Nucleoside phosphorylase	<i>Aeropyrum pernix</i> K1	Synthesis of nucleoside analogs	[135]
Textile Industry	Amylase, lipase, and proteases	<i>Thermus thermophilus</i> HB8, <i>Euplotes focardi</i> , <i>Alkalibacillus</i> sp. NM-Da2, and <i>Geomyces</i> sp.	Increase the lubricity of the yarn in cases of cotton fabrics & denim	[89]
	α - Amylase	<i>Geobacillus stearothermophilus</i> , <i>Halothermothrix orenii</i> <i>Streptomyces</i> sp. TO1		[89]
	β -glucosidase	<i>Martelella mediterranea</i>	Degradation of cellulose	[16]
	Cellulase Puradax HA	<i>Bacillus</i> sp. and <i>Paenibacillus tarimensis</i>	Remove stains and protects colour from fabric	[16]
	OptimizeVR COOL and Optimize NEXT	<i>Geomyces</i> sp. P7	Desizing of woven fabric	[90]
	Pectinase	<i>Tetracladium</i> sp., <i>Bacillus</i> sp. and <i>Pseudomonas</i> sp.	Bioscouring: Removal of pectin from fabrics	[90]
	Lipase	<i>Penicillium canesense</i> , <i>Pseudogymnoascus roseus</i>	Bioscouring: Removal of fats from fabric	[90]
	Xylanase	<i>Flammeovirga pacifica</i> WPAGA1	Bioscouring	[90]
	Catalase	<i>Geobacillus thermo pakistaniensis</i>	Bleaching	[90]
	Laccase	<i>Geobacillus thermo pakistaniensis</i>	Artificial dyes	[90]

	Laccase	<i>Streptomyces psammoticus</i> and <i>Stenotrophomonas maltophilia</i>	Decolourising agents	[90]
	Laccase LacT	<i>Brevibacillus agri</i>	Biobleaching: helps in depigmentation of azo dyes	[6]
Bioremediation and Biodegradation	Hydrolytic enzymes, oxidoreductases	<i>Anoxybacillus sp.</i>	Reduce and degrade pollutants like polyaromatic hydrocarbons dyes, phenol, heavy metals, phosphates and antibiotic residues, from waste water	[6]
		<i>Talaromyces emersonii</i> , <i>Rhizopus sp.</i> , and <i>Thermomucorindicae seudaticae</i>	Degrade organic contaminants & toxic from effluents	[126]
		<i>Acidothiobacillus ferrooxidans</i> and <i>Acidothiobacillus ferrivorans</i>	Help in precipitation of Copper	[125]
		<i>Acidocella aromatica</i> PFBC	Reduce vanadium ions	[125]
		<i>Acidiphilium symbioticum</i> H8	Biosorption of Cd cations	[125]
		Nitrile hydratase/amidase	<i>Pseudomonas putida</i> , and <i>Rhodococcus sp.</i>	Elimination of acetonitrile from organic pollutants
Bioenergy, biofuels and biorefinery	Cellulases, xylanases, lignases, lignin peroxidases and manganese peroxidases (lignocellulose degrading enzymes) α -Amylase	<i>Caldicellulosiruptor bescii</i> , <i>Geobacillus sp. R7</i> , <i>Phanerochaete chrysosporium</i> , and <i>Sporotrichum thermophile</i> <i>Bacillus licheniformis</i> , <i>Pyrococcus furiosus</i> , <i>Bacillus acidocaldarius</i> , & <i>Bacillus stercorophilus</i> , and	Degrades crude biomass, crystalline cellulose and aids in bioconversion of lignocellulose to ethanol without pretreatment Production of ethanol	[108] [108]

		<i>Alteromonas sp.</i>		
	Glucoamylase	<i>Aspergillus niger</i>	Assists in saccharification	[108]
Food industry	Lipase	<i>Bacillus stearothermophilus</i>	Dairy industry	[1]
		<i>Acinetobacter calcoaceticus</i> LP009 <i>Moraxella sp.</i>	Baking industry Dairy industry	[1] [1]
	Protease	<i>Bacillus brevis</i> <i>Bacillus HUTBS62</i> <i>Bacillus HUTBS71</i> <i>Alteromonas sp.</i> <i>Bacillus sp.</i> <i>Bacillus sp. 158</i>	Baking industry, Brewing industry, Dairy industry Baking industry, Brewing industry, Dairy industry	[1]
	Xylanase	<i>Actinomadura sp. strain Cpt20</i> <i>Clostridium strain PXYL1</i> <i>Paenibacillus curdolanolyticus B6</i>	Baking industry, Baking industry Fruit juice processing	[1]
	α - Amylase	<i>Bacillus sp. isolate A3-15</i> <i>Aeromonas veronii NS07</i>	Bakery industry Bakery industry	[1]
	β - Glucosidase	<i>Fervidobacterium islandicum</i> <i>Bacillus sp.</i>	Brewing industry, Brewing industry,	[1]
	Esterase	<i>Anoxybacillus gonensis A4</i> <i>Oleispira antarctica</i>	Food industry Food industry,	[1]
	Cellulase	<i>Flavobacterium sp.</i> <i>Geomyces sp.</i> <i>Shewanella sp. G5</i>	Brewing industry, Fruit juice processing, Wine industry	[1]
Detergent industry	Lipase	<i>Geobacillus sp. SBS-4S</i>	Stain removal	[1]
	Protease	<i>Bacillus sp. JB-99</i>	Stain removal	[1]

	Xylanase	<i>Bacillus sp.</i>	Stain removal	[1]
Paper and pulp industry	Lipase	<i>Pseudomonas aeruginosa</i> BTS-2	Paper industry	[1]
	Xylanase	<i>Caldocellum saccharolyticum</i> <i>Dictyoglomus thermophilum</i>	break down hemicellulose and bio-bleaching	[1]
	Esterase	<i>Pseudoalteromonas arctica</i>	improve pitch control and address other sticky compounds	[1]
Pharmaceutical industry	Lipase	<i>Thermosyntropha lipolytica</i>	Transesterification of oils and fats	[1]
	Protease	<i>Chaetomium thermophilum</i> <i>Geobacillus collagenovorans</i> MO-1 <i>Paenibacillus tezpurensis</i> sp. nov. AS-S24-II <i>Pyrodictium sp.</i> <i>Thermococcus onnurineus</i> NA1 <i>Thermus aquaticus</i> YT-1 <i>Clostridium schirmacherense</i> <i>Flavobacterium</i> YS-80 <i>Halomonas sp.</i> <i>Pseudoalteromonas sp.</i> NJ276 <i>Pseudomonas strain</i> DY-A <i>Pseudomonas fluorescens</i> 114 <i>Streptomyces sp.</i> <i>Rheinheimera sp.</i>	Flavor modification, optically active esters; Cleavage of proteins	[1] [1]
	Esterase	<i>Pseudomonas sp.</i> B11-1 <i>Psychrobacter sp.</i> Ant 300 <i>Streptomyces coelicolor</i> A3	Increases the solubility of anti-inflammatory drugs	[1]

IV. CONCLUSIONS AND PROSPECTS

Extremophilic microbes' production of extremozymes has captured the attention of researchers due to their remarkable stability and ability to thrive in hostile surroundings. Despite their immense potential, the current availability of extremozymes remains limited. The significance of thermophilic enzymes in biotechnology lies in their remarkable resistance to extreme temperatures, chemicals, organic solvents, and pH variations. These enzymes find paramount importance in sectors such as agriculture, food and beverage, pharmaceuticals, detergents, textiles, leather, pulp and paper, as well as biomining. The pursuit of commercial applications for extremozymes and the effort to meet the escalating demand for inventive biocatalysts within the biotech industries stand as central objectives in the realm of extremophile research.

The discovery and utilization of extremophiles and their products have already demonstrated their superiority over conventional methods. With further research and development, their potential applications can extend to various industries that have yet to be explored. Advancements in nanotechnology can enhance the specificity of extremozymes, benefiting sectors like bioremediation, nuclear power, and textiles. Additionally, genetic modification of extremophiles can boost biofuel production and aid in the disposal of radioactive waste. The economic potential of extremophiles is significant, and further studies should focus on their genetic modification, biochemical properties, and long-term effects. Securing government funding and fostering collaboration among institutions are indispensable factors in advancing research and achieving the sustainable and effective utilization of extremophiles across diverse industries.

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