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# Archaea Domain as Biocatalyst in Environmental Biotechnology and Industrial Applications: A Review

**Mohd Asyraf Kassim[1*], Noor Haza Fazlin Hashim[2,3] and Nur Athirah Yusof[4]**

*[1]Bioprocess Technology Division, School of Industrial Technology, Universiti Sains Malaysia (USM), Malaysia.*
*[2]School of Biosciences and Biotechnology, Faculty of Sciences, Universiti Kebangsaan Malaysia (UKM), Malaysia.*
*[3]Water Quality Laboratory, National Hydraulic Research Institute Malaysia (NAHRIM), Seri Kembangan, Malaysia.*
*[4]Biotechnology Research Institute, Universiti Malaysia Sabah (UMS), Malaysia.*

### *Authors' contributions*

*This work was carried out in collaboration between all authors. Author MAK manage the outline and literature search and wrote the first draft of the manuscript. Authors NHFH and NAY helped in the writing certain part of the manuscript such as introduction and revised the manuscript. All authors read and approved the final manuscript.*

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## ABSTRACT

Achaea constitute a considerable fraction of the prokaryotes which colonize marine and terrestrial ecosystem especially in the extreme environments. These microorganisms play crucial roles and contribute significant impacts on global energy cycles. In fact, the extremophilic characteristics acquired by many archaeans display unusual properties of adaptations to extreme conditions which make them a potentially valuable resource in exploring new biotechnological processes and a wide range of industrial applications. In this review, the role of archaea domain as biocatalysts in environmental biotechnology and industrial applications were summarized and discussed. This review has been categories into three main sections, (a) archaeal characteristics and their extremozymes (b) environmental biotechnology that covers on bioremediation, hydrocarbon biodegradation and biomining (c) industrial applications, which discusses on the production of polyhydroxyalkanoates (PHA), biosurfactant, and antibiotic produced by archaea domain.

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**Corresponding author: E-mail: asyrafkassim@usm.my, asyrafkassim@gmail.com;*

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## 1. INTRODUCTION

Archaea are prokaryotic microorganisms that can be found in the extreme environments. Due to their capability to live under extreme conditions, the exploration on the potential of archaea as biocatalysts for industrial applications has become the subject of intensive research, aiming on the cell structures, enzyme characterizations and its adaptability under extreme conditions. These exclusive properties make them as a valuable resource with great potential applications in a wide range of new technologies.

Moreover, the study on archaeal enzymes that are able to maintain their activity under extreme conditions such as high temperature, salinity, pH and pressure has also gain great interest among researchers. The discovery of extremophilic archaea and their enzymes has lead to significant effects conspicuously on biocatalysis activities. In addition, extremozymes produced by archaea are widely used in the synthesis of pharmaceutical products, antibodies, cosmetics, dietary supplements, enzymatic preparations, bioremediation, renewable energy, as well as all kinds of chemical compounds production. The application of extremozymes from archaeal cells has allow great improvements in multiple industry sectors and help to reduce the quantity of waste production, energy usage and material consumption. Thus, archaeal applications harbor promise for creating cheaper technology, cost-effective sustainable energy sources and environmentally friendly.

The main hallmarks of this review are to discuss and provide a comprehensive review on the future prospects of achaea as biocatalysts in environmental biotechnology and other industrial applications. In this review, the emphasis encompasses on the type of extremozymes that are produced by different group of achaea, enzymes and metabolites production and their potential industrial applications. This review would be beneficial to scientists and researchers in understanding the potential of achaea as tools for various value-added products and revolutionize the current industrial applications.

## 2. ARCHAEA

In general, Archaea have similar characteristics as bacteria in terms of shape, size and appearance. Archaeal cells can take all types of shapes, ranging from spherical, spiral, oblong, rectangular to rod. One of the distinguishing features of archaea is the structure of their membrane glycolipids; where archaea do not contain murein at their cell wall. Archaea exhibit unique features of cell surface organelles that are not present in bacteria such as flagella, hami, cannulaeand pili [1].

Year 1977 marked a history when Carl Woese, a microbiologist discovered two distinct groups of organisms that were not related to one another than they were to eukaryotes [2]. Later, a new classification was proposed based on comparisons of gene sequences of the small ribosomal subunit (SSU), which was accepted until now; three domains of life consist of Eukarya, Bacteria and Archaea [3]. After the discovery by Woese, molecular biology techniques have been the preferred choice to distinguish between archaea and bacteria. Indeed, the organization and information processing system in archaea point to a closer relationship to eukaryotes rather than bacteria. Apart from that, the structures of ribosomes and chromatin, presence of histones and sequence similarity contribute to the classification of archaea [4,5]. In contrast, the metabolic pathways of archaea show similarity to prokaryotic rather than eukaryotic counterparts [6]. Table 1 shows the comparison of characteristics between bacteria and archaea.

## 3. BIOCATALYST

The trend to an increasing number of researches on genome data of extremophilic microorganisms worldwide has able to discover hundreds of enzymes with great potential in white biotechnology. Currently, extremozymes are highly in demand in industries as they are able to withstand harsh processes for a long period of time. Overall at present, microbial enzymes are currently on demand in various industries as they contribute immense advantages such as reducing the risk of contamination, improving the transfer rates, lowering viscosity and increasing the solubility of substrates. Majority of the industrial enzymes have been derived from bacteria and fungi. Nowadays, archaeal enzymes are in the limelight of intensive investigations due to their nature that grow optimally at extreme conditions. In terms of definition, extremozymes are enzymes that are able to withstand harsh and extreme conditions in industrial

**Table 1. Comparison of the distinctive characteristics of Archaea and Bacteria**

| | **Archaea** | **Bacteria** |
|---|---|---|
| **Ribosome** | Present | Present |
| **Cell wall** | Pseudopeptidoglycan | Peptidoglycan/Lipoposaccharide |
| **Habitat** | Extreme environment: hot spring, salt lake, ruminant | Soil, water, animal, plant and etc. |
| **Growth** | Asexually by the process of binary fission, budding and fragmentation | • Asexually by the binary fission, budding and fragmentation<br>• Ability to form spore |
| **Genomic organization** | | |
| • Topoisomerase | I | I/III |
| • Recombinase | RadA | *RecA* |
| • DNA ligase | NAD dependant | ATP dependant |
| • Replicative helicase | HelicaseA | DnaB |
| • DNA polymerase | Family B polymerase | DNA E polymerase (PolIII) |
| • Histones | Yes | No |
| • Introns | Some present | Rare/none |
| • Protein synthesis | Methionine as start codon | Formylmethionine as start codon |
| **Example** | Family Euryarchaeota (*Aciduliprofundum boonei*) and Crenarchaeota (*Sulfolobus solfataricus)* | Family Enterobactericeae (*Escherichia coli*) and Streptococaceae (*Streptococcus pneumoniae*) |

processes [7]. Perhaps, the high demands of the biotech industries for tailor-made novel biocatalysts, and the rapid development of new techniques such as genomics, proteomics and metabolomics are the main factors contributing the enhancement of the development of novel extremozymes. Here, this review will focus on enzymes that are derived from extremophilic archaea and their relevance for industrial applications.

## 3.1 Thermophilic Extremozymes

Thermophiles can be further categorized either as thermophiles or hyperthermophiles. Hyperthermophiles can grow optimally up to 115°C, whereas thermophiles grow best between 50 and 70°C. Majority of thermophiles/ hyperthermophiles are identified to date belong to the archaeal domain mainly from Crenarchaeota, Euryarchaeota, Korarchaeota and Nanoarchaeota [8]. Most common habitats where archaea are naturally found are in the volcanic areas, geothermal systems and hot springs. To date, protein structural studies on thermophilic enzymes show several factors which contribute to the enzymes stability at high temperature such as increased hydrophobicity and surface charge, higher hydrogen bonds, shorter loops structure, reduction in thermolabile amino acid, and lowered in surface area to volume ratio [9]. Owing to that, thermophilic enzymes are currently on demand in vast industries which require superior biocatalysts that are capable to work at high temperatures. Moreover, reactions at high temperatures reduce the probability of undesired by-products and microbial contamination. In addition, thermophilic archaea also show high resistance under high pressure and presence of chemical denaturants such as solvent and detergents [10].

Glycoside hydrolases are large group of enzymes involve in carbohydrate hydrolysis. Enzymes in this group are greatly in demand especially those that are able to perform at high temperatures. Glucose production from starch for instance, involves two-step processes where both are carried out at high temperature of (60-105°C) and acidic pH of (4.5–6.0) [11]. The usage of thermostable amylolytic enzymes (α-amylases, α-glucosidases, α-pullulanases) provides advantages as novel energy alternatives, cost saving, as well as environmentally friendly process. Currently, hydrolytic enzymes from *Bacillus stearothermophilus* and *B. licheniformis* are currently being used in the industry. Interestingly, several studies have reported higher activities of thermostable hydrolases enzymes from archaea compared to bacterial enzymes. On the other hand, hyperthermophilic amylases are also reported from archaea of the genera *Sulfolobus, Thermophilum*, *Desulfurococcus* and *Staphylothermus*, which are recorded to be active at a broad range of temperatures ranging from 40–100°C [12]. In addition, another study on thermostable α-amylase from *Pyrococcus furiosus* reported that the enzyme has a half life activity at 120°C after autoclaving for 2 hours and fascinatingly still exhibit residual activity at 140°C [13]. In another study, thermophilic pullulanases which usually belong to the type II class acquired enzymes that are able to hydrolyze both α-1,4- and α -1,6-glycosidic bonds in branched polymers [11]. A heat-active pullulanase with an optimum temperature of 100°C has been discovered in *Thermococcus kodakarensis* KOD1 [14]. α-glucosidases are involved in the final step of starch degradation, hydrolyzing terminal glucose residues. Thermophilic archaeal *P. furiosus* α-glucosidase has been characterized extensively where it works optimally at the range of temperatures between 105–115°C [15].

Similarly, xylanases have been widely studied due to their ability to degrade *hemicelluloses*; the most abundant natural resources. This type of enzymes advocates attractive value to the paper bleaching industry; as an alternative to current chemical treatment; thus promoting an environmentally friendly industry [16]. However bleaching process performs optimally only at high temperature therefore, the need of thermostable xylanase is crucial. Recently, a thermostable xylanase was reported from *Thermotogathermarum*, Xyn10A with a maximal activity exhibited at 95°C, pH 7.0 [17]. In addition, it has demonstrated high thermostability over broad range of pH 4.0–8.5 and temperature 55-90°C upon the addition of 5 mM Ca2+. On the other hand, a xylanase from *Thermococcus zilligii* is reported active at 100°C and has preferences to different substrates [18].

DNA polymerase; the key enzyme that is responsible in molecular biology especially for DNA amplification in polymerase chain reaction, has drawn high interest in biotechnology industries. The first DNA polymerase used, Taq was isolated from thermophilic bacteria, *Thermusaquaticus* [19]. Recently, polymerases from archaeal have been developed since these polymerases show prominent advantages such as stringent proofreading ability and five to tenfold lower of error rates compared to Taqpolymerase. Several DNA polymerases from archaea are already isolated and exhibited high commercial values such as from *Thermococcus celericrescens* (TceI) [20], *Thermococcus fumicolans* (Tfu) [21], *Thermococcus zilligii* (Tzi) [22], *Pyrococcusabyssi* (IsisTM) [23].

## 3.2 Psychrophilic Extremozymes

Psychrophiles are defined as microorganisms that are able to proliferate at 0–10°C, metabolically active at subzero temperatures and also able to survive as low as −45°C [24]. Psychrophiles can be found either in permanently cold environments such as permafrost, sea ice, polar, glacier or artificially cold environment such as the refrigerator. In order to adapt, psychrophiles produce enzymes that are able to work optimally at cold temperatures. Generally, cold adapted enzymes have higher structural flexibility and catalytically effective at cold. Several features of cold adapted proteins have been reported to show unique characteristics compared to their mesophilic and thermophilic counterparts. These include fewer disulfide bonds and salt bridges, more solvent interactions, lower number of hydrogen bonds at domain interfaces, lower core hydrophobicity, and longer loops structure [25].

Studies on psychrophilic archaea mainly focus on methanogens as they play important roles in anoxic permanently cold environment like lake sediments, deep sea and permafrost. Genome and proteome analysis on *Methanococcoides burtonii* have disclosed mechanisms for its survivability at cold environment [26,27]. The usages of cold adapted enzymes are currently the center of attention of many researchers due to their natural properties that able to grow/work optimally at cold temperatures. However, studies of archaea and cold adapted enzymes from archaea are still in infancy level compared to bacteria. To date, several applications have been reported of using archaea in wastewater treatment and methane production [28,29]. Similarly, archaeal enzymes/cofactors are also reported to involve in metabolic, light-harvesting complexes and ether-linked lipids, which show impressive values in biotechnology applications [30,31].

### 3.3 *Haloarchaeal* Extremozymes

Halophiles are organism that is able to thrive optimally at high salt concentration (> 0.6M NaCl; seawater salt concentration). In this context, archaea have been discovered in several ecological niches like Dead Sea and Great Salt Lake, where most of the isolated archaea are able to adapt with the osmotic changes in their environments [32,33]. Enzymes from halophiles remain active and stable although being exposed to high salt concentration due to the presence of unique properties in their proteins like high acidic amino acids content, less hydrophobic surface contact and presence of specific ion binding site [34,9].

Due to the ability to withstand extreme salt concentrations, halophiles have been first chosen to be applied in various industries. Many enzymatic activities of halophilic archaea have been characterized, however no commercial applications have yet been developed for such enzymes [35]. Still, some archaeal enzymes have triggered some potential interests, such as the amylase of *Haloarcula* sp. that functions optimally at 4.3 M salt at 50°C and known to be stable in the presence of benzene, toluene and chloroform [36]. In addition, halophilic galactosidases from *Haloferax alicante* that are active at 4M NaCl with the ability to cleave broad galactosidases excluding lactose have been long identified [37]. Besides, the archaeon *Haloferax mediterranei* has been reported to be able to produce up to 38% Poly-β-hydroxyalkanoate (PHA) compound from its dry weight grown at 150 g/L salt under phosphate limitation [38].

### 3.4 Piezophilic Extremozymes

Organisms that are able to thrive at high pressure are generally called as piezophilic. Often they colonize in habitats like deep sea and extreme heat of hydrothermal vents. Piezophilic archaea are usually characterized as thermophilic as they are mainly being isolated from thermophilic habitats [39]. The general properties of piezophilic enzymes usually similar to their temperature adaptation but with additional features; exist as multimers, smaller hydrogen bonding amino acids and packed hydrophobic core [9]. Paradoxically, research on piezophiles archaea are limited due to the difficulties in culturing the strain at high pressure. Albeit, the piezophiles are usually coupled with either high or low temperature adaptations mechanisms that making them as a great candidates in the industrial applications especially in food processing.

## 4. BIOREMEDIATION

Bioremediation is a process of utilizing natural or genetically engineered living organisms such as fungi, bacteria and archaea to transform pollutant and contaminants from the environment into less toxic compound. Accordingly, bioremediation has been proven to degrade hydrocarbon and other aromatic compounds in soil and water. The success of this technology depends on the ability to establish and maintain the favor of microbe to grow and enhance the biodegradation rates in the contaminated environment. Hence, it is unsurprising that the suitable conditions such as pH, temperature and salinity have been reported to influence the microbe growth and biodegradation metabolic activity [40,41]. Moreover, the physical and chemical characteristics of oil and oil surface also play crucial role to ensure the bioremediation success. Though this technology has been proven to be able to remediate contamination, however there is a limitation for the bioremediation process in extreme condition such as high salinity and temperature. This is due to the fact that not many microorganisms have the capability to grow in these harsh conditions. Archaea are one of the microbes that have gained much attention to remediate hydrocarbon contamination especially in the extreme conditions. Analysis of microbial community on soil sample contaminated with petroleum hydrocarbon in the European Alps, using fish-in-situ hybridization (FISH) and identification via 16S rRNA, revealed that a number of archaea related to the orders of *Methanomicrobiales*, *Methanosarcinales*, *Methanobacteriales* and *Thermoplasmatales* have been detected in that area [42]. In another study, a range of archaeal community that has functions in hydrocarbon-degradation, production of surfactant and methanogenesis during the displacement of oil such as *Thermus*, *Thermincola*, *Thermanaeromonas* have been found in high-temperature oil reservoir [43].

On a large scale, many researchers have reported on the potential of archaea as biocatalyst in bioremediation [44-46]. Mainly, as archaea can grow in hypersaline condition and encapsulate great catabolic activity compared to bacteria and fungi hence, archaea probably comprise excellent selections as best possible biocatalyst candidates [47]. On top of that, archaea can growth in either high or low temperatures and extreme pH conditions, contrariwise to bacteria which are commonly used for bioremediation but are unable to survive in these harsh conditions [43,48]. This unique ability clearly provides advantages for archaea especially to remediate contaminations that occur in extreme environments. Fascinatingly, it has also been reported that some archaea show high resistant towards variety of antibiotics including *cycloheximide*, streptomycin and penicillin, which turn archaea as a great potential to be applied in bioremediation in the presence of antibiotic [49].

## 4.1 Hydrocarbon Biodegradation

Studies on bioremediation using archaea have been reported previously by other researchers [49,50]. Table 2 shows the isolated halophilic archaea that have been reported to demonstrate capability to degrade hydrocarbon. *Archaebacterium* strain EH4 which was isolated from sail-mash was found to be able to grow in medium supplemented with 20% NaCl [50,51]. This study reported that this archaea could grow and degrade eicosane up to 62% of biodegradation in 10 hours of generation time. In another study, three extreme halophilic *Haloferax*, *Halobacterium* and *Halococcus* have been isolated from hypersaline coastal area of Arabian Gulf. All of these archaea are able to use crude oil as sole carbon source for energy. This study also demonstrates that these strains are able to use and degrade n-alkanes and mono- and polyaromatic compounds as carbon and energy source [49]. Interestingly, these archaea could degrade crude oil up to 47% after 3 weeks of incubation at 40-45°C. Similar observation has been reported by Tapillatu et al. [46], who isolated *Haloarcula* and *Haloferax* sp. that could degrade 95% heptadecane at 40°C after 30 days of incubation. Based on previous studies, these findings suggested that halophilic archaea have the capability to degrade crude oil at high temperatures and are probably the most suitable candidates to be applied in bioremediation process at extreme environment conditions.

## 4.2 Aromatic Compound Degradation

Apart from degrading aliphatic hydrocarbon, archaea have also been reported to acquire the ability to degrade aromatic hydrocarbon. Several studies have been conducted to isolate and determine the archaea that could degrade aromatic hydrocarbon. It has been reported that Haloarchaea *Haloferax* sp. has the capability to degrade phenanthrene [46,49]. Study by Emerson et al. [53] reported that *Haloferax* strain D1227 isolated from soil contaminated with oil brine was able to use aromatic hydrocarbon such as benzoate, cinnamate and phenylpropanoate as carbon source with 70% degradation. Similarly, Bonfa et al. [44] who investigated the potential of *Haloferax* sp. to degrade aromatic reported that this archaea was able to degrade the mixture of aromatic compound. For this particular study, *Haloferax* sp. was cultured in a medium with aromatic compound mixture of benzoic acid, p-hydroxybenzoic acid, salicylic acid and mixture of *polycyclic* aromatic hydrocarbon. It was found that this archaea was able to grow and degrade these compounds. In another study, other archaea members such as *Halobacterium piscisalsi*, *Halorubrum ezzemoulense*, *Halobacterium salinarium*, *Haloarcula hispanica*, *Haloferax* sp., *Halorubrum* sp., *Haloarcula* sp. isolated from Camalti Saltern, Turkey have also exhibited capability to degrade aromatic hydrocarbon compound [45]. It was also reported that *Halorubrum* sp. and *Halorubrum ezzemoulense* could grow in medium supplemented with 20% NaCl.

**Table 2. Halophilic archaea that are able to grow and use hydrocarbon as carbon and energy source**

| Archaea | Hydrocarbon | References |
|---|---|---|
| *Haloferax* sp. | n-alkane $C_{10}$-$C_{30}$ | [46] |
| *Haloferax* sp. | Heptadecane | [46] |
| *Haloarcula* sp. | Heptadecane | [46] |
| *Halobacterium* sp. | n-alkane $C_{10}$-$C_{34}$ | [49] |
| *Halococcus* sp. | n-alkane $C_{10}$-$C_{34}$ | [49] |
| Strain EH4 | Tetradecane<br>Hexadecane<br>Eicosane<br>Heneicosane | [51] |
| *Halobacterium* sp. | n-alkane $C_{10}$-$C_{30}$ | [52] |

### 4.3 Biomining

Metals and mining sector is considered as one of the major industries that is dedicated for extraction of metal and valuable minerals from lode, orebody, seams, and reef reserves in the world. These minerals are gold mine for profit and widely used in a vast range of industrial applications, for instance, jewelry making, construction, ceramics, automobiles, electronics, plastics and paper. Current mineral extraction involved high temperature and chemicals which potentially lead to environmental pollution. Therefore, biomining using microbial has been considered to be an alternative approach to overcome the problem. In this process, microbes are utilized to recover mineral resources such as copper and other metals or minerals from low-grade ores, waste, slag and sludge. This technique experimentally showed that it could improve recovery rate, reduce operational cost, require less energy and reduce pollution problems. Biomining of minerals is carried out on different scale with different type of microbes including bacteria and archaea. The biomining process artificially can be divided into two modes namely bioleaching and bioxidation. Bioleaching- can be related to solubilization of metals such as copper, nickel, and zinc from ores by microorganisms. While, biooxidation is used for bioleached solubilized metals which wrapped/locked in sulfide minerals such as gold and silver.

There are several recent reviews on the biomining mechanisms that can be carried out by microbes. The bioleaching process of metal could also contributed by the type of metals, its properties and mineral species [54]. There are two different reaction mechanisms that control the dissolution of metal sulfides: the thiosulfate pathway and the polysulfate pathway. The oxidation of acid-insoluble metals sulfide (pyrite, molybdenite, tungstenite) and acid-soluble metal sulfide (chalcopyrite and pyrrhotite) can be categories into the thiosulphate intermediate pathway and polysulphide intermediate pathway (Fig. 1) [55]. The thiosulphate pathway is a process where the metal is solubilized by ferric ion that generated by microbial process. In this pathway, the acid-insoluble metals sulfide such as pyrite ($FeS_2$), molybdenite ($MoS_2$) or tungstenite ($WS_2$) are exclusively oxidized via electron extractions by ferric (Fe(III)) ions and thiosulphate is generated as main intermediate product. On the other hand, the polysulphate pathway is a mechanism that the acid soluble metal sulfide such as sphalerite (ZnS) and chalcopyrite (CuS) are solubilized by combination attacked of ferric ion and proton. In this process, an element such as stable sulfide cation ($H_2S^+$) is generated as main intermediate. However, this sulphate can spontaneously dimerize to free disulfide ($H_2S_2$) and further oxidized by sulphur-oxidizing microbes such as archaea and bacteria via higher polysulfides and polysulfide radical to generate sulfur element.

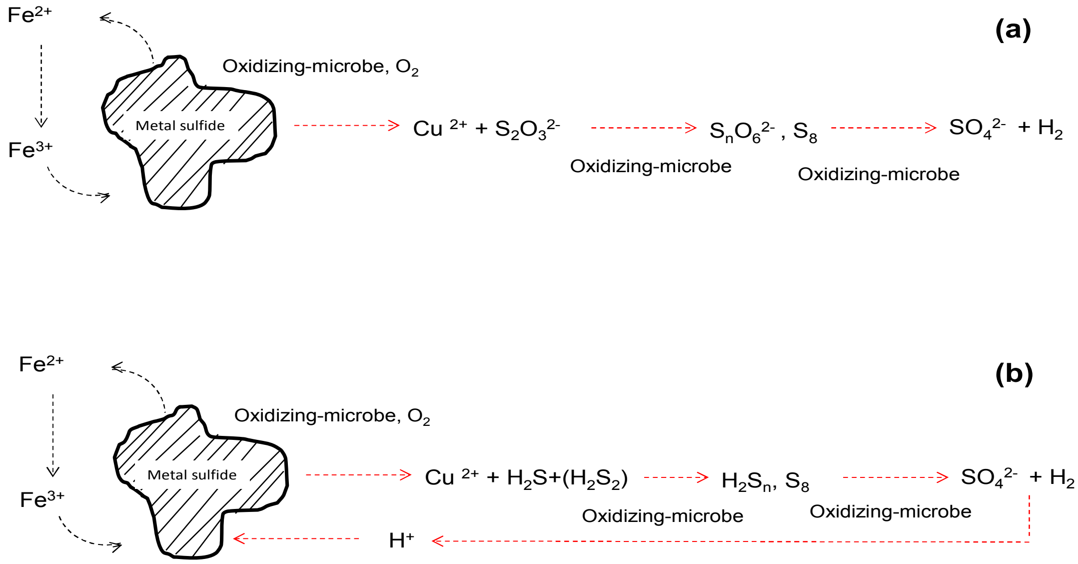

**Fig. 1. The schematic diagram of the bioleaching mechanisms (a) The thiosulfate pathway (b) The polysulfate mechanisms**

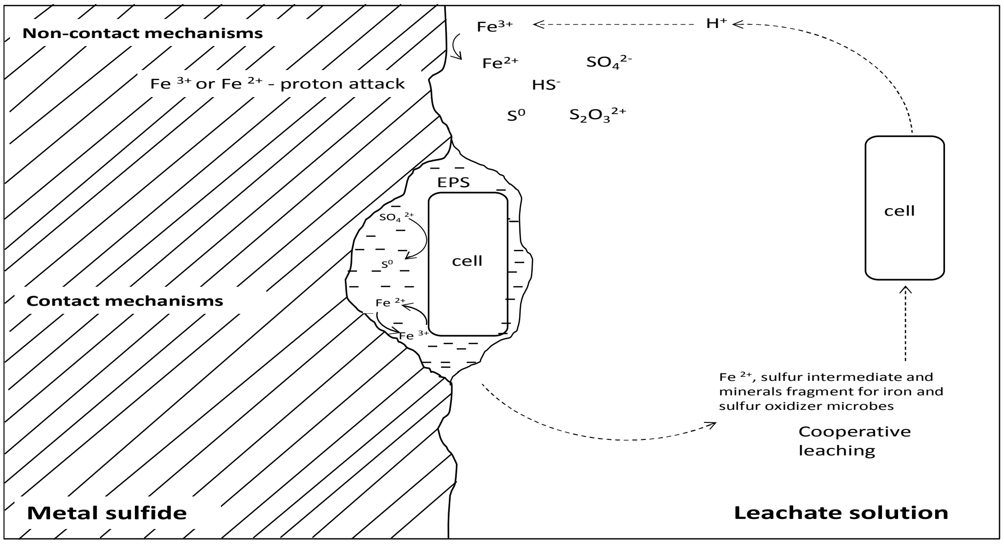

**Fig. 2. Contact and non-contact leaching mechanisms by microbes (Archaea and bacteria)**

Removal of metals and minerals from ore can occur in two different processes: contact and non-contact reactions [56]. Contact bioleaching is where the microbe acts on the ore directly to extract metals and minerals which involve oxidation and direct enzymatic reaction by the microorganisms. In this mechanism, the cells attach to the mineral surface where this process takes place within minutes or hours. Microorganisms typically form an exopolysaccharide (EPS) layer when attach to the surface of minerals and provide a space for biooxidation reaction in the compound (Fig. 2). While for non-contact bioleaching, it occurs when the microbe produces some strong oxidizing chemical substances like ferric ions and sulphuric acid that lead to the solubilization of metals and minerals (iron and sulfur) from ore. This mechanism involves oxidation of reduced metal which is mediated by ferric ions ($Fe^{3+}$) formed from the microbial oxidation of ferrous ion ($Fe^{2+}$) compounds present the mineral. In this matter, acidic environment is important in indirect bioleaching in order to keep the ferric ion and other metals in solution form. This can be done through continuous oxidation of iron, sulphur, metal sulphides and carbonate in solution.

The following equations (1-12) describe the contact and non-contact biomining mechanisms of various type of metals by microorganisms:

**Contact mechanism:**

In this process, metal sulphides are oxidized directly by bacteria or archaea to soluble metal sulphates as shown in equation 1.

$$MeS + 2O_2 \rightarrow M^2 + SO_4{}^{2-} \tag{1}$$

Theoretically, the mechanism can be continued until all the substrate orr metal sulfide (MeS) is converted to product ($MeSO_4$). The oxidation of other metal sulfides are represented as follows:

Chalcopyrite:

$$4CuFeS_2 + 17O_2 + 2H_2SO_4 \rightarrow 4CuSO_4 + 2Fe_2(SO_4)_3 + 2H_2O \tag{2}$$

Pyrite:

$$4FeS_2 + 15O_2 + 2H_2O \rightarrow 2Fe_2(SO_4)_3 + 2H_2SO_4 \tag{3}$$

Chalcocite:

$$2Cu_2S + 5O_2 + 2H_2SO_4 \rightarrow 4CuSO_2 + 2H_2O \tag{4}$$

Covellite:

$$Cu_2S + 2O_2 \rightarrow CuSO_4 \tag{5}$$

**Non-contact mechanism:**

In non-contact bioleaching, the microbes generate chemicals that will oxidize the sulfide minerals. The process for non-contact mechanism is represented by the oxidation of sulphide minerals by ferric ions as shown in equation 6. This particular reaction occurs by the action of archaea or bacteria whereas the chemical reaction in equation 7 occurs without any association of microbes.

$$4FeS_2 + 2H_2SO_4 + 2O_2 \rightarrow 2Fe(SO_4)_3 + 2H_2O \quad (6)$$

$$MeS + Fe_2(SO_4) \rightarrow MeSO_4 + S^0 \quad (7)$$

$$2S^0 + 3O_2 + 2H_2O \rightarrow 4H^+ + 2SO_4^{2-} \quad (8)$$

Metal dissolution takes place by a cyclic process between reactions shown in equation 6 and 7 and the generation of $H^+$ during sulphide oxidation in equation 8 enhances the overall efficiency. The following equations represent chemical oxidation processes;

Chalcopyrite:

$$CuFeS_2 + 2Fe_2(SO_4)_3 \rightarrow CuSO_4 + 5Fe_s\,(SO_4)_3 + 2S^0 \quad (9)$$

Pyrite:

$$FeS_2 + Fe_2(SO_4)_3 \rightarrow 3FeSO_4 + 2S^0 \quad (10)$$

Chalcocite:

$$Cu_2S + Fe_2(SO_4)_3 \rightarrow 4CuSO_4 + 3\,FeSO_4 + S^0 \quad (11)$$

Covellite:

$$CuS + Fe_2(SO_4)_3 \rightarrow 4CuSO_4 + 3FeSO_4 + 2S^0 \quad (12)$$

According to Stott et al. [57] based on their study on the bioleaching of chalcopyrite by 11 different microbes found that the process in archaea and bacteria were identical. To date, thermoacidophile archaea such as *Sulfolobus metallicus*, *Ferrroplasma*, *Sulfobacillus*, *Acidianus* and *Metallosphaera* are among the archaea that have been reported to be able to thrive in this extreme environment [56,58]. *Sulfolobus acidocaldarius* and *Sulfolobus brierleyi* which are thermophilic and acidophilic archaea respectively are among the archaea that involve in bioleaching of copper and molybdenum from chalcopyrite and molybdenite [58,59]. Additionally, another archaea that is commonly used in biomining is *Metallosphaera sedula*, which is a single-cell microorganism that produce enzymes to alter metal-sulfur compound and produce elemental form of the metal that can be used for industrial application [59]. Study by Kozubal et al. [60], who isolated *Metallosphaera* strain MK1 from geothermal spring in Yellowstone National Park indicated that this archaea showed a maximum bioleaching activity under an extreme condition of pH value of 2.5 and temperature of 70°C. In another study, the optimum growth of *Ferrosplasm athermophilum* sp. nov. isolated from leaching bioreactor was obtained when the process was carried out at temperature of 45°C and pH value of 1 [61]. Most of these archaea show optimum bioleaching activity under extreme temperature (>60°C) and the pH value below 3 (Table 3).

The capability of archaea in bioleaching and biooxidation activity is highly attributed by several factors such as types of archaea, quantity of minerals, ore type, nutrient addition, pH, temperature, pulp density and agitation [67-69]. In order to obtain high extraction yield, there is a need to optimize the operating conditions which could provide favorable conditions for the archaea growth, acid consumption and enhance metals recovery [70]. In the biomining process, there are two major important factors that need to be considered: (1) pH and (2) temperature [71,72]. Generally, the leach dump for biomining process is in acidic condition due to the presence of acidic mine water supplied during the process. On top of that, the temperature in the dump may probably high due to the overheating from the bioprocessing of ores, which release a great deal of heat that could kill or hinder the microbes growth during the process. Thus, in order to increase the efficiency of biomining activity, the microbial strain that have capability to survive in low pH and high temperature is required.

**Table 3. Optimum temperature and pH for bioleaching by different extremophile archaea**

| Archaea | Temperature (°C) | pH | References |
|---|---|---|---|
| *Ferroplasma acidophilum* | 35 | 2.2 | [62] |
| *Acidianus brierly* | 70 | 2 | [63] |
| *Sulfolobus metallicus* | 75 | 6 | [64] |
| *Sulfolobus acidocaldarius* | 65 | 1.3-1.7 | [65] |
| *Acidianus manzaensis* | 65 | 1.5 | [66] |

The pH value and ores quality play a major role in leaching of material into solution [73,74]. Dynamic bioleaching can be reduced by the presence of alkaline content in the materials. Study by Zhu et al. [74] on bioleaching of low-grade ore by four different microorganisms namely, *Sulfolobus metallicus*, *Acidithiobacillus ferrodixine*, *Acidianus brierleyi*, *Leptospirillum ferriphilum* indicated that pH and ore quality significantly affect the microbial growth and metal recovery. It is found that, the archaea *S. metallicus* exhibits better growth in high cuprum concentration up to 0.5%. Besides, reducing pH value 3 to 1 would enhance *S. metallicus* growth. This could be due to the fact that low pH provides $Fe^{3+}$ and S° for microbial growth and lead to the more proton consumption of the mineral surface. Temperature is also one of the important parameters that guarantee the bioleaching process [75]. The bioleaching process is carried out from a wide range of temperatures from ambient to high temperatures up to 90°C. Basically, the optimum temperature for the bioleaching process is highly dependent on the type of archaea used in the process. Study on the effects of temperature on Cu removal by *Sulfolobus* sp. shows that rise of temperature reaction from 50 to 75°C would enhance Cu removal from low-grade granitic chalcophyrite [58]. It is found that the maximum removal of 85% is obtained at 75°C, as compared to other temperature tested; 59% at 50°C, 63% at 60°C and 74.2% at 65°C respectively.

The role of archaea in biomining industry has been proven to recover valuable minerals and metals from low-grade ore and it is now actively being practices in developing countries. However, there are few limitations that have been identified which can be improved in order to sustain this process. The crucial limitation of bioleaching is the slow kinetics of metal recovery by the archaea. In order to increase the reaction, a new technique should be adopted by targeting on the new biocatalyst reaction that can accelerate the growth and metal recovery activity. This can be achievable by selecting enzymes that have (1) better activation on the mineral surface (2) enzyme inhibition activity and (3) provide more electrons for the microbes during the bioleaching process. On top of that, the development of bioreactor for bioleaching process should also be taken as part of the approaches to improve future impact of the bioleaching process. Stirrer-tank or bioreactor with better aeration and controlled conditions would provide favorable environment for archaea to grow and for mineral removal. Besides, new bioreactor with additional features like less corrosive, cost effective material that can withstand high temperature and highly versatile where may be applied to any type of ore may bring advantages to bioleaching process. Apart of the reactor materials, the understanding of the interaction between microbes available at the bioleaching site, which consisted of wide range of different mixed culture either autotrophic, heterotrophic, thermophilic, acidophilic and etc may be useful towards understanding to improve the bioleaching and mineral bio-oxidation sector/industry. In principle, the continuation of archaeal activity exploration by determination of the proteins and metabolites as industrial bioindicators for bioleaching purposes through omic technologies should be able to provide a comprehensive overview on the reactions that occur during the process. Therefore, by understanding the mechanisms and interactions involved in the archaea, the bioleaching process could be optimized effectively and efficiently.

## 5. METHANE PRODUCTION BY METHANONGENIC ARCHAEA

Production of biomethane as renewable bioenergy from anaerobic fermentation of various organic matters such as dead animals and plant materials, manure, sewage and organic waste is one of the alternative approaches to overcome global energy issues. The biomethane is a non-poisonous, odorless and colorless gas, where this gas is produced from the series of complex anaerobic reaction of nutrient-rich substrate by several bacteria and methanogenic archaea [76]. Methanogenic archaea or methanogens are one of the important groups of the microorganisms that play a significant role in conversion of carbon dioxide ($CO_2$) and other bacteria waste byproducts in order to produce methane as the final metabolic byproduct [77-79].

### 5.1 Methane Production

Generally, production of biomethane involves three different stages, (1) conversion and hydrolysis of raw materials by acidogenic bacteria into simpler organic acids, sugars and amino acids (2) production of $H_2$, $CO_2$ and acetate from organic acid by hydrogen producing bacteria (3) methanogenesis (Fig. 3). The methanogenesis process is the formation of methane from $CO_2$ and acetate by methanogenic archaea. According to Liu and Whittman [80,65], methanogenesis can occur through six different reactions, where these reactions are highly dependent on the type of methanogens and substrates availability.

### 5.2 Methanogenic Archaea

There are 5 well established methanogenic archaea orders that involve in methanogenesis namely, *Methanobacteriales*, *Methanococcales*, *Methanomircobiales*, *Methanosarcinales*, and *Methanopyrales* [80]. Table 4 shows the major taxonomic groups of methanogens that play important roles during methanogenesis phase. Methanogens of different orders contain different cell envelope structures, lipid compositions, substrate range and other biological properties.

The first order which is the *Methanobacteriales* are generally the methane producers which use $H_2$ as electron donor and $CO_2$ as electron acceptor. In most general terms, the cells are non-motile, rod shaped and can be found in higher pH range 6 to 9. For the second order which is the Metanococcales, are cocci that have flagella and utilize $CO_2$ and $H_2$ for methane production. Most of these archaea have been isolated from marine habitats and require sea salt for optimum growth. In addition, the third order which is the Methanomicrobiales, most of these archaea in this order acquire the ability to utilize acetate to produce methane. This group can normally be found in lower temperatures between 30–55°C. For the fourth group, the *Methanosarcinales*, are rod shaped methanogen that have the widest substrate ranges among all methanogens. Most of the *Methanosarcinales* produce methane by disproportionating the methyl group in the organic compound or splitting acetate. Some of the group could also reduce $CO_2$ with $H_2$. This group is found mostly in low temperatures and has different types of cell shapes. The last methanogen order is the Methanopyrales, which are rod-shaped, motile and capable of reducing $CO_2$ and $H_2$ for methanogenesis. The only member for this group is *M. kandleri* which has been identified as a thermophilic methanogenic archaea. This species was reported to be able to grow at high temperatures ranging from 84–110°C.

Due to the ability of methanogens to degrade organic materials efficiently, these organisms are also widely been used in wastewater treatment plant. Analysis on the archaea distribution in wastewater has been reported by other researchers [81,82]. Tabatabei et al. [81], who analyzed the archaea community in palm oil mill effluent using 16S ribosomal RNA (rRNA)-targeted fluorescent in situ hybridization combined with polymerase chain reaction (PCR)-cloning found the presence of *Methanosaeta* sp. and *Methanosarcina* sp. cells where *Methanosaeta concilii* dominated the sample.

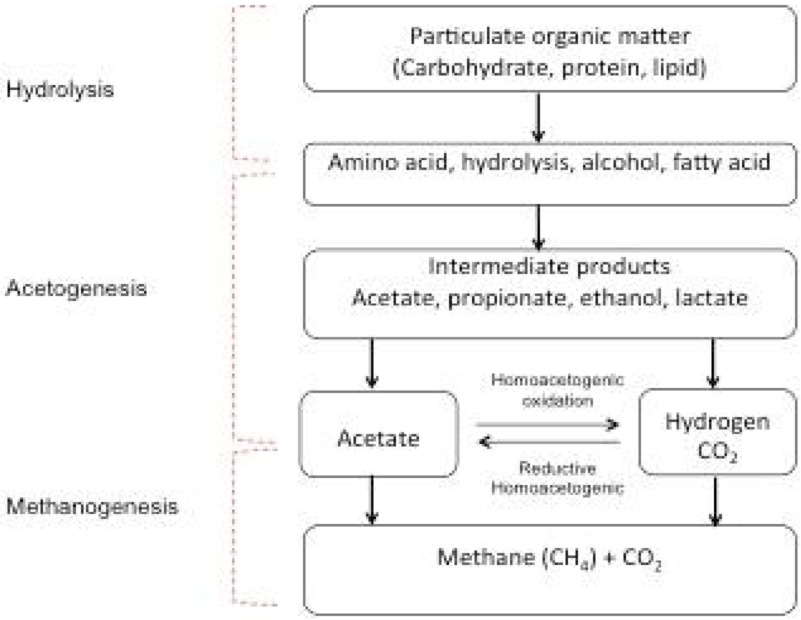

**Fig. 3. Methane production by microorganisms (Adapted and modified from [80])**

**Table 4. Characteristics of major taxonomic group of methanogens [80]**

| Order | Family | Genus | Temperature (°C) |
|---|---|---|---|
| *Methanobacteriales* | *Methanobacteriaceae* | *Methanobacterium* | 37–45 |
| | | *Methanobrevibacter* | 37-40 |
| | | *Methanobacter* | 55-65 |
| | *Methanothermaceae* | *Methanothermus* | 80-88 |
| *Methanococcales* | *Methanocaldococcaceae* | *Methanocaldococcus* | 35-40 |
| | | *Methanotorris* | 60-65 |
| | *Methanococcaceae* | *Methanococcus* | 80-85 |
| | | *Methanothermococcus* | 88 |
| *Methanomicrobacteriales* | *Methanomicrobiaceae* | *Methanomicrobium* | 40 |
| | | *Methanoculleus* | 20-55 |
| | | *Methanofollis* | 37-40 |
| | | *Methanogenium* | 15-57 |
| | | *Methanolacinia* | 40 |
| | | *Methanoplanus* | 32-40 |
| | *Methanospirillaceae* | *Methanospirillum* | 30-37 |
| | *Methanocorpusculaceae* | *Methanosorpusculum* | 30-40 |
| *Methanosarcinales* | *Methanosarcinaceae* | *Methanosarcina* | 35-60 |
| | | *Methanococcoides* | 23-35 |
| | | *Methanohalobium* | 40-55 |
| | | *Methanohalobphilus* | 35-40 |
| | | *Methanolobus* | 37 |
| | | *Methanmethylovorans* | 20-50 |
| | | *Methanimicrococcus* | 39 |
| | | *Methanosalsum* | 35-45 |
| | *Methanselacaea* | *Methanoseala* | 35-60 |
| *Methanopyrales* | *Methanopyraceae* | *Methanophyres* | 98 |

Furthermore, Vanwonterghem et al. [82] reported the discovery of divergent methyl-coenzyme M reductase genes in population genomes recovered from anoxic environments with high methane flux that belong to a new archaeal phylum, the *Verstraetearchaeota* from palm oil mill effluent (POME). These archaea encode the genes required for methylotrophic methanogenesis, and may conserve energy using a mechanism similar to that proposed for the obligate $H_2$-dependent methylotrophic *Methanomassiliicoccales*. Even though methane is one of the potential negative impacts on the global warming, it has also been suggested to capture the methane and use it as a renewable energy source [76]. Nevertheless, research and thorough understanding are needed in order to increase methane production and sustain the process. Since methane production involves other microorganisms such as bacteria at early stage of the process, thus the knowledge on microbial ecology distribution and interaction between bacteria and archaea are required for better biological control of the process. The considerable attempt for example, determination of microbial community structure using molecular approaches and metabolite analysis would definitely provide more information on the activity and microbial involvement during the methane production process.

## 6. VALUE ADDED PRODUCTS

Archaea produce variety of secondary metabolites and proteins during their metabolisms. These proteins and metabolites such as wide range of extremophile enzymes have adapted to function under extreme conditions, which can be applied in wide range of biotechnology applications.

### 6.1 Exopolysaccharides

Extracellular polymeric substances (EPS) are high molecular polysaccharides and major functional component released by archaea as protection mechanisms against several environmental stress such as dessiccation, predation and ultraviolet radiation. The EPS molecules have several industrials application such as bioaggregation in wastewater treatment process and also as gelling or emulsifying agents in food industry [83,30]. The EPSs produced by microorganisms have exhibited immense advantages, like short fermentation process, easily formed and stable emulsion [84].

Several extremophilic archaea mainly belong to the thermophilic and halophilic groups have been reported to produce EPSs [85,86]. Among the thermophilic archaea that could produce EPSs are *Thermococcus*, *Sulfolobus*, *Archaeoglobus fulgidus* and *Thermococcus litoralis* [85]. While, for the halophilic archaea, *Haloferax*, *Haloarcula*, *Halococcus*, *Natronococcus*, and *Halobacterium* are among the most common archaea that have been reported to be able to produce EPSs [87-89]. It has been reported that archaea *Haloferax* sp. could produce EPS in order to remove heavy metal from environment that contained high salt [90]. On the other hand, the common EPS producing *Halomonas*such as *H. maura*, *H. eurihalina*, *H. ventosae* and *H. anticariensis* have been reported to produce EPS that contained high sulphate content and uranic acids which corresponding to their good gelifying agent properties [91,92].

The EPSs produced from the archaea has been characterized by many researchers [83,82]. It was found that most of the EPSs produced by archaea contain heteropolysaccharide such as mannose, glucose and galactose with different ratio depending on the type of archaea [86,93]. For instance, sugar analysis of EPSs produced by *Haloferaxginnonsii* (ATCC 33959) indicated that the extracellular polysaccharide contained D-Man, D-Glc, D-Gal and L-Rha in the ratio of 2:1:3 respectively. While in another study by Nicholaus et al. [87], who isolated *Haloarcula japonica*, which was an obligate halophilic archaea revealed that EPSs produced by this archaea consisted of mannose, galactose and gluconic acid with relative ratio of 2:3:1 respectively.

The EPSs produced by microorganisms can be applied in wide range of industries. At present, the most well known products such as xanthan, dextran, gellan and curdlan are among the products that are obtained from EPSs produced by microorganisms. Even though the EPSs have exhibited potential characteristics for industrial applications, however, these non-toxic and biodegradable EPSs only contribute a small fraction in polymer market. This is due to the high production cost and poor physiochemical characteristics compared to the industrial EPSs from starch, cellulose, pectin and seaweed, which make the EPSs from archaea unsuitable for big markets [84,85]. Besides, the production of EPSs by archaea is highly depending on the fermentation condition especially types of substrates used during the fermentation process. Parallel to these findings, another study has reported that the fermentation media contributed approximately 30% of the EPS production cost. Thus, in order to maximize the cost-effective process, utilization of cheaper substrate such as molasses, biomass spent grains and industrial wastewater should be adopted in biotechnology industries. Hence, development and improvement on the archaea strains and identification of their potential usage in the high-value market niches such as cosmetic and pharmaceutical should be established in order to ensure the EPS from archaea is marketable.

### 6.2 Polyhydroxyalkanoates (PHA)

Production of PHA from microorganisms has gain great attention globally due to its characteristics that have high biodegradability in different environments, flexible thermoplastic polymer and high potential sustainable replacement production of fossil-fuel plastic. PHA has wide range of applications based on its characteristics. Currently, PHA is used in film packaging mainly for containers, paper coating and disposable plastic items such as razor, utensils, diaper, cosmetic container and cups [94,95]. The PHA is also useful as a biodegradable carrier for drugs, hormones, insecticides and herbicides in agriculture industry [96]. It is can also be used in medical and pharmaceutical applications, for instance as osteosynthetic in bone plates, surgical sutures and blood vessel replacement [84,80]. However, there is a limitation on PHA application in medical and pharmaceutical industries due to the slow degradation and high hydraulic stability in sterile tissues [97]. In this context, PHA can be synthesized by microorganisms including archaea. Generally, PHA is produced as reserve energy during stationary phase in the presence of excess carbon and during nutrient depletion [95].

There are a number of producers of PHAs as shown in Table 5. Most of the PHA produced by archaea are from *Haloarchaea*. Most of the *Haloarchaea*, *Haloarcula*sp, *Halobiforma haloterrestris* strain 135T *and Halopiger aswanesnsis* 56 exhibit high PHA content up to 63% of their cell dried weight. A previous study also indicated that supplying different nutrient sources during fermentation

**Table 5. List of PHA archaea producers supplied with different types of nutrient sources [84]**

| Microorganism | Carbon source | Type | Yield |
|---|---|---|---|
| *Haloarcula hispanica* | YE/Glc | PHB | 2.4% |
| *H. hispanica* | YE/Glc | PHVB | 0.58* |
| *H. marismortui* | YE/Glc | PHB | 21% |
| *Haloarcula* sp. IRU1 | Glc | PHB | 63% |
| *H. japonica* T5 | Glc | PHB | 0.5% |
| *Halobacterium noricence* | YE/Triptone | PHB/PHVB | 0.03-0.08% |
| *Halobiforma haloterrestris* 135T | YE/butyric acid | PHB | 40% |
| *H. haloterrestris* 135T | YE/casamino acid/proteose | PHB | 15% |
| *Halococcus dombrowskii* | YE/HyCase | PHB/PHBV | 0.15% |
| *Halococcus salifodinae* | YE/HyCase | PHB/PHBV | 0.05% |
| *Haloferax mediterranei* | YE/Glc | PHB | 17% |
| *H. mediterranei* | Glc | PHVB | 23% |
| *H. mediterranei* | Starch | PHB | 6.48% |
| *H. mediterranei* | Casamino acid/YE | PHVB | 1.33% |
| *H. mediterranei* | YE/Stach | PHVB | 1.74% |
| *Haloferax gibbonsii* | YE/Glc | PHB | 1.2% |
| *Haloferax volcanii* | YE/Glc | PHB | 7% |
| *Haloterrigena hispanica* | YE/Casamino acid | PHB | 0.14% |
| *Halopiger aswanesnsis* 56 | YE/ Sodium acetate/ butyric acid | PHB | 34% |
| *Natronobacterium gregoryi* | YE/Casamino acids | PHB/PHVB | 0.03-0.1% |

**YE: Yeast extract, Glc: Glucose*

could affect the PHA production in archaea [98]. Replacing glucose with extruded cornstarch was found to enhance *H. mediterranei* growth and increased 43.3% of PHA content [99]. In another study, fermentation of *H. mediterranei* with hydrolyzed whey, glucose and galactose in fed batch system resulted in high PHA content up to 72.8% [100].

Production of PHA from halophilic archaea is pointed to produce more advantages than non-halophile microorganisms due to its ability to operate under high salinity, which also can prevent traces of contamination. Apart from that, its applications can also reduce operation cost as only low energy is required for sterilization of the equipment and fermentation medium. On the other hand, another advantage of PHA production from halophilic archaea is the simple polymer recovery which can be performed through hypoosmotic shock with salt-deficient water. Thus, its applications are seen to greatly benefit the cost by reducing the downstream processing cost which contributes approximately 40% of the total production cost [101].

## 6.3 Biosurfactants

Biosurfactants (BS) are amphiphilic compounds produced by a wide range of organisms including archaea. These extracellular compounds contain a mixture of glycolipids, fatty acids, proteins, and sugars, which act by reducing surface tension (ST) and interfacial tensions between individual molecules at the surface and interface, respectively. Biosurfactants have displayed many advantages compared to traditional chemically derived surfactants by being renewable, nontoxic, biodegradable and active under a range of extreme conditions [102]. These compounds have been proven can be applied in bioremediation of oil in soil and water samples [103]. Besides, it can also be applied in wide range of industries for instance food, cosmetic and pharmaceutical industries [104].

Several halophilic archaea have been identified to produce biosurfactants at the highest salt concentration recorded [105]. Gana et al. [105] has screened and isolated two biosurfactant archaea *Halovivax* strain A21 and *Haloarcula* strain D21 from a pond in Ain Salah, Algeria. It was found that both archaea were able to produce high biosurfactant at high salinity condition. The capability of archaea *Haloferaxmediterranei* and *Haloarcula japonica* to produce biosurfactant have also been reported elsewhere. Both of these archaea produced high sulphated EPS and acid heteropolysaccharide, where high sulphated-EPS was reported inhibited viral penetration into the cell [106]. In another study, Selim et al. [107] has successfully isolated 29 strains of biosurfactant haloalkaphilic archaea from water and sediment of Soda Lakes of Wadi An Natrun, Egypt. The isolates have been identified from *Natrococcus*, *Natronolimnobius*, *Halorubrum* and *Natromonas* genera, where most of these archaea have shown their capability to emulsify crude oil. Furthermore, the isolated archaea can also stand extreme conditions hence they are proposed to be good candidates to be applied in bioremediation especially to remediate harsh environment contaminated sites. Recently, an extreme halophilic archaeon *Natrialba* sp. that has the capability to emulsify both aliphatic and aromatic hydrocarbon has been isolated from contaminated saline water [108]. It has been reported that this archaea is probably a potential candidate to be applied for remediation especially with high aromatic hydrocarbons at extreme environment conditions.

### 6.4 Antibiotics

Most antibiotic peptides by archaea can be found widely amongst Haloarchaea (termed halocins) and more recently from the *Sulfolobus* genus (sulfolobicins) [109]. Furthermore, other archaea such as *Natrinema* sp, an extreme halophilic archaea have also been reported to be able to produce halocin [110]. The production of halocin by *Haloferax larsenii* has also been reported by previous study [111]. The halocin produced by *H. larsenii* isolated from Pachpadra in Rajasthan has been characterized and it was found that this halocin was stable up to 100°C and in pH range 5.0-9.0. Halocin are either peptide (<10kDa: microhalochin) or protein (>10kDa) antibiotics that commonly produced by members of archaea Halobacteriaceae. The microhalochins are hydrophobic and robust, where they can undergo desaltation without losing their activities. In addition, it is also relatively insensitive to heat and can be stored for a long period of time up to 7 years [112]. The antimicrobial property of halochin has narrow range that only affects their close relatives. As for sulfolobicins, the antibiotic activity is predominantly associated with the cells [113]. The apparent sulfolobicin antimicrobial activity is recorded to be restricted only to other members of *Sulfolobales*. To date, the application of this antibiotic is not yet well established. However, a particular application that is relevant to halocin producing archaea is the textile industry, where high amount of salt is used during the tanning process. This condition could allow the growth of other halophilic organisms, which resulted to the damage of the products. The presence of this halocins was found to inhibit the undesirable halophilic growth [112]. Additionally, halocins which are produced by archaea mostly acquire tolerant to high salt concentrations where they inhibit growth of undesirable strains of other haloarchaea thus promoting them as great potential to be applied in salted food preservation.

## 7. CONCLUSION

As a summary for this review, it is clear that archaea which have unique characteristics cater immense potentials to be applied in variety of industries. Their capability to grow at extreme conditions provides advantages to these organisms to be applied in the environmental biotechnology fields especially for bioremediation and biomining activity. Among the archaea members, *Haloferax*, *Haloarcula*, *Halobacterium* and *Sulfolobus* play important roles in bioremediation and biomining of mineral processes. Similarly, peptides, proteins and enzymes (PHA, biosurfactants, extremophile enzymes and archeocins) produced by archaea can potentially be used in other industries such as food processing, agriculture, and pharmaceutical industry. Although numerous studies and reports on archael studies have been made recently, more information especially on the gene regulation, enzymes and metabolites related to the archaea metabolisms and activity are still required in order to improve the efficiency of the process. It is imperative that we continue to study archaea as comprehensive investigations will likely unveil additional industrial capabilities resulting in inexpensive and eco-friendly alternative resources. Overall, it is clear that archaea serve as great biocatalysts that can be applied in wide range of industries.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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