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Industrial Products from Halophiles: A Review

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Abstract: *Halophiles are microorganisms living in conditions with increased levels of Sodium chloride. The members of halophiles belong to the categories of Bacteria, Archaea and Eukarya. Since they live in a stressful environment their products possess more stability and activity compared to those obtained from inhabitants of normal environment. They are recently explored for a number of industrially important products like compatible solutes, enzymes, biopolymers, nutraceuticals, halocin and other important proteins. They have also found application in processes like biodegradation and bioremediation. Halocins include a number of antimicrobial substances obtained from halophiles. These are peptide or protein antibiotics that have either narrow or broad spectrum of activity against other microorganisms. Since the available antibiotics are failing due to resistance developed by infectious microorganisms, finding out new antibiotics from an unexplored or least explored environment is the best possible solution available. Hence halocins could be a useful target to explore further in this regard. This review presents a summary of information about the halophiles, industrially relevant products explored from halophiles and also depicts the future prospects in exploring halophiles for halocin production.*

Keywords: *halophiles, biopolymers, ectoine, archaea, biodegradation, halocin*

I. INTRODUCTION

The role of halophiles in bioprocess industries has become inevitable for a number of reasons. They are proving successful in overcoming the limitations of bioprocesses involving conventional bacteria. The major issues reported in fermentation industry include high substrate cost, high processing cost and risk of contamination by undesirable organisms [1], [2], [3], [4]. Halophiles can utilize low cost substrates like agro-industrial wastes and do not require pre-treatment of substrates which can directly influence the process cost. Also they survive in extreme salt concentration in which other conventional bacteria cannot grow and contaminate.

II. HALOTOLERANTS AND HALOPHILES

Halotolerants are a group of microorganisms which does not require higher concentration of NaCl (>0.1M) for their growth but can tolerate their presence [5]. Halophiles are salt lovers and thrive only in conditions of slight, moderate and extreme NaCl concentrations. Hypersaline regions are predominant with moderate and extreme halophiles which can live up to 5M NaCl [6]. The intrinsic mechanisms available in such microbes like accumulation of osmolytes [7], [8], [9] or organic solutes like amino acids and sugars in cytoplasm make them survive in extreme environment [10], [11]. They predominantly accumulate equal concentration of K⁺ in the intracellular environment to prevent the osmotic pressure. The taxonomy of halophiles covers both the prokaryotic and eukaryotic domains [12], [13], [14], [15]. Halophilic archaea are grow in extreme concentration (> 3M) of NaCl and are revealed to be different from conventional prokaryotes. They are rich in GC content and possess information related to survival in extreme environment [16].

III. FERMENTATION PRODUCTS FROM HALOPHILES

A variety of fermentation products are obtained from halophiles with cheap substrates and simple process parameters. Table 1 shows the representative products from halophiles isolated from different geographical locations. In majority of the process, the stability and activity of were also studied and found to be higher [17], [18], [19], [20], [21], [22], [23], [24].

TABLE1: Representative Fermentation Products From Halophiles

S.No.	Name of the halophile	Name of the fermentation product	Reference(s)
1.	<i>Halomonas</i> sp. AAD6	Exopolysaccharide	[25]
2.	<i>Halomonas boliviensis</i>	Ectoine and poly (3-hydroxybutyrate)	[26]
3.	<i>Halomonas boliviensis LC1</i>	Poly (β-hydroxybutyrate)	[27]
4.	<i>Halomonas TD01</i>	Polyhydroxybutyrate	[28]
5.	<i>Pseudomonas AP-MSU 2</i>	Phytase	[29]

6.	<i>Salicola sp. IC10</i>	Lipase and protease	[30]
7.	<i>Halobacillus karajensis</i> , <i>Halobiforma sp.strain</i> <i>BNMIITR</i>	Protease	[31], [32]
8.	<i>Halomonas meridiana</i>	α -amylase	[33]
9.	<i>Streptomonospora sp. YIM</i> <i>90494</i>	xylanase	[34]
10.	<i>Marinococcus M52</i>	hydroxyectoine	[35]
11.	<i>Halorubrum sp. TBZ112</i>	Carotenoid	[36]
12.	<i>Halomonas sp. BS4</i>	Biosurfactant	[37]

IV. ANTIBIOTICS RESISTANCE: THE CHALLENGE

Resistance is defined as the ability of the infectious microorganisms to evade the mechanism of action of the antibiotics. Resistance was due to the repeated exposure of the antibiotics to the infectious microorganism [38]. The unregulated usage of antibiotics by the patients themselves is found to be the major reason lying behind this great issue [39]. The transfer of genetic materials through plasmids and transposons are also claimed to be the reasons for resistance development [40], [41], [42], [43]. Resistant microbes are available for almost all known classes of commercial antibiotics [44]. The problem has grown to a huge strength and now multidrug resistant microorganisms are the biggest challenge to be treated [45], [46]. The pharmaceutical industries are working at an alarming rate to get out of this problem but the entire process is limited by a series of challenges like inability of the synthetic or semi synthetic compounds to penetrate the cell wall, failure to adopt drug likeliness properties as proposed by Lipinski, the inherent toxicity of newly developed compounds and majorly the low returns on investment [39], [47]. Rather than looking for synthetic compound that shows activity against a infectious microorganism, the best solution for this disappoint is to tap the natural resources which are least explored. Calling for a revival of natural product drug discovery will definitely end up with positive results [48], [49], [50]. Looking into known microbial sources for antibiotics will require high time and work and may or may not end up with isolation of a new class of antibiotics. It is estimated that the atleast 10^7 strains must be screened before reaching a new class of antibiotics [39]. The pharmaceutical companies definitely will not be interested in doing such cumbersome process with less probability for success. Hence identifying a better source for searching a new antibiotics class with a minimal investment of energy, tie and money will be preferred.

V. UNTAPPED NATURAL RESOURCES FOR ANTIBIOTIC RESEARCH

Majority of the world biodiversity remains unexplored. Only 250 – 3,00,000 species have been identified, reported and deposited [51], [52]. Many of the microbes are unculturable and the estimate goes to 99% of the total microbial population [50], [53]. They are generally not culturable under laboratory parameter setup [54], [55]. Natural products research is the available route to explore new antibiotics from untapped natural resources. Microbes living in unique surroundings and extreme environments are one of the least explored living forms in this context [56], [57], [58]. Extreme conditions of salinity, pH, and temperature can be digged in to isolate novel organisms with good antimicrobial properties. Searching the sources including marine soil and water and weeds will yield new antibiotics [59], [60]. Halophiles are the potent targets that can be isolated and cultured in laboratory for the extraction of antibiotics. Nearly all bacteria possess the ability to produce antimicrobial substance and so are halophiles. The antibiotics produced by halophiles are called by the name halocin [61].

VI. HALOCIN

Of all the fermentation products produced by halophiles, halocin is gaining importance largely due to the resistance issues of existing antibiotics. Nearly all halophiles have a universal behavior to secrete halocin as a measure for protection and survival in an environment. Halocins extracted and characterized so far belong to different categories as peptide and protein halocins based on their molecular weight. So far 7 halocin were identified and reported. Of them 5 belong to peptide halocin and the rest 2 belong to protein halocin. The molecular weights of these halocins lie within 3 – 35 kDa with varying thermal, pH stability and salt dependence. These are generally expressed in the transition between exponential and stationary phases. Halocin has proven records for its activity against other closely related microbes [62].

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