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Review

# Sources of marine superoxide dismutases: Characteristics and applications

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ABSTRACT

The ability of marine organism to cope with oxidative stress is one of the main factors that influence its survival in the marine environment, when senescence conditions prevail. The antioxidative defense system includes enzymatic and non-enzymatic components. Among the enzymatic system, superoxide dismutases are the first and most important of the antioxidant metalloenzymes. Four different types of metal centers have been detected in SODs, dividing this family into Cu/Zn, Ni, Mn and Fe-SODs. Its use was limited to non-drug applications in humans (include: cosmetic, food, agriculture, and chemical industries) and drug applications in animals. This paper is a review of the recent literatures on sources of marine SODs, the need for SOD and different applications in industry, covering the last decades. The most recent paper, patents and reviews on characterization and application are reviewed.



**Contents**



## 1. Introduction

Reactive oxygen species (ROS) are highly reactive oxygen-containing molecules produced during normal aerobic respiration process. The level of ROS control by the antioxidant system of the body [1,2]. Excessive amounts of ROS can damage macromolecules (e.g. proteins, lipids, and DNA) and cell membranes [3]. The antioxidative defense system includes enzymatic and non-enzymatic components [4]. Among the enzymatic system, superoxide dismutases (SOD; EC1.15.1.1) are the first and most important of the antioxidant metalloenzymes was reported by McCord and Fridovich (1969) when they observed dismutation of $O_2^-$ into $H_2O_2$ and $O_2$ [5–7]:

$$2O_2^- + 2H^+ \rightarrow H_2O_2 + O_2$$

$H_2O_2$ is converted by other enzymes like catalase (CAT) and peroxidases (GPx) into harmless product water (Fig. 1) [2,4]. The combined actions of these enzymes keep the levels of the superoxide anion ($O_2^-$) and hydrogen peroxide ($H_2O_2$) low [8]. SOD is ubiquitous to all forms of life. SODs are classified based on the type of metal bound at the active site: Cu/Zn-SOD, Mn-SOD, Fe-SOD, and Ni-SOD [7,9].

Cu/Zn-SOD and Mn-SOD are found in both prokaryotes and eukaryotes, Cu/Zn-SOD is generally homodimeric and is present in diverse locations in different organisms [1,5]. It is found in the periplasm of gram-negative bacteria (sodC), cytoplasm and

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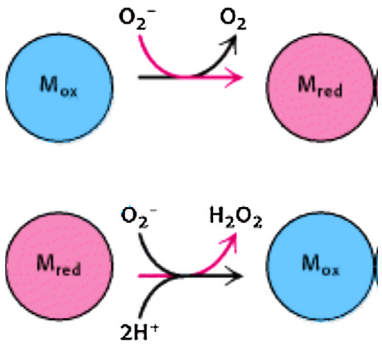


**Fig. 1.** Superoxide dismutase mechanism. The oxidized form of superoxide dismutase ($M_{ox}$) reacts with one superoxide ion to form $O_2$ and generate the reduced form of the enzyme ($M_{red}$). The reduced form then reacts with a second superoxide and two protons to form hydrogen peroxide and regenerate the oxidized form of the enzyme [2].

chloroplast of plants, intermembrane space of mitochondria, and several compartments such as nucleus, lysosome, peroxisome, cytosol (sod1), and extracellular milieu (sod3, EC SOD) in animals [7,9]. Unlike other organisms, plants have been two main subgroups of Cu/Zn-SODs: chloroplastic and cytosolic [10,11]. Cu/Zn-SOD plays important role in stationary phase survival and aerobic growth in bacteria and fungi [12]. Additionally, the periplasmic Cu/Zn-SOD in gram-negative pathogenic bacteria has been proposed to confer protection against the host defense responses [13].

Fe-SOD is found in prokaryotes (sodB), protozoans, and chloroplasts of algae and in plants two families of Fe-SODs have been found: the chloroplastic localized and the plastidial localized [3,5,14]. Fe and Mn-SODs are typically homodimers or homotetramers that probably evolved from a common ancestor. Due to their structural and sequence conservation, they can frequently bind both Fe and Mn, but attain significant activity with only the permitted metal cofactor [15]. Mn-SOD occurs in prokaryotes (sodA) and mitochondria of the eukaryotes (sod2), has the ability to catalyze the toxic superoxide anion into molecular oxygen and hydrogen peroxide [6,15]. Additionally Ni-SOD has recently been purified from several aerobic soil bacteria of Streptomyces [5,16]. Three common isoforms could be distinguished by their differential sensitivities to different chemicals. Cu/Zn-SOD is very sensitive to $H_2O_2$ and cyanide while Mn-SOD is insensitive to $H_2O_2$ and cyanide, and Fe-SOD cannot be inhibited by cyanide, but it is very sensitive to $H_2O_2$ [14].

In the 1990s, an antioxidant enzyme SOD was introduced into the market. Although the enzyme initially showed great promise in therapeutic applications, it did not perform up to expectations. Consequently, its use was limited to non-drug applications in humans (include: cosmetic, food, agriculture, and chemical industries) and drug applications in animals [1,17,18].

A marine enzyme may be a unique protein molecule not found in any terrestrial organism or it may be a known enzyme from a terrestrial source but with novel properties. This review is intended to start from a thorough analysis of habitat-related properties presenting marine SODs with novel chemical biodiversity. Additionally this paper describes the different bioprocess engineering approaches adopted for the production of marine SODs derived mainly from all of kingdom (e.g. Bacteria, Chromista, Plantas, fungi and Animalia). We insert each organism in kingdoms by information of site *World Register of Marine Species* [19].

## 2. Superoxide dismutases in marine bacteria

Marine bacteria are abundant and play critical roles in the ocean environment. As the technology that allows us to study these microscopic organisms evolves, so does our understanding of who they are and what they do [20]. SODs have been identified in a number of marine bacteria (Table 1). Except for one case, all of marine bioluminescent bacteria contain a ferri protein enzyme. The Fe-SODs from *Photobacterium leiognathi* (symbiont) and from *Photobacterium sepia* (free living) have been purified. Although the two enzymes are closely similar, various differences exist. The isoelectric point found for SODs from *P. sepia* and SODs from *P. leiognathi* were 4.1 and 4.4, respectively. Both SODs showed a high thermal stability and contains 1.6 g atoms of iron/molecule [21]. The SODs enzyme from *P. leiognathi* assumed that is a dimer containing one iron atom/subunit. In the Fe-SOD from *P. leiognathi* histidine and tryptophan residues are probably involved in the catalytic activity and that one tyrosine and one tryptophan residue/subunit may be metal ligands. Neither carboxyl groups nor tyrosine residues seem to be involved in the catalytic site [22].

**Table 1**
Superoxide dismutases (SODs) from marine bacteria sources.

| Source | Important properties | Reference |
|---|---|---|
| *Photobacterium leiognathi* | p*I* 4.4<br>A high thermostable enzyme<br>Histidine and tryptophan residues involved in the catalytic activity<br>Tyrosine and one tryptophan residue/subunit may be metal ligands | [21,22] |
| *Photobacterium sepia* | p*I* 4.1<br>A high thermostable enzyme | [22] |
| *Cyanobacterium Synechococcus* | N-terminal similarity to both the Fe-SODs and the Mn-SODs of *Escherichia coli* | [23] |
| *Nodularia Aphanizomenon Anabaena* | May have a role in the photoadaptation of diazotrophic cyanobacteria and help to protect them from light injury | [24] |
| *Geobacillus* sp. | Molecular mass 50.23 kDa<br>p*I* 4.65<br>The recombinant enzyme had high thermostability at 50 °C<br>The enzyme also showed striking stability over a wide range of pH 5.0–11.0<br>Good tolerance to some inhibitors, detergents, and denaturants | [17] |

Three constitutive forms of SODs activity have been demonstrated in the cyanobacterial marine picoplankter *Synechococcus* sp. WH 7803. Three distinct SODs activities were observed, an Fe-SODs, a Cu/Zn-SODs and a third form which has not been identified. All three types appear to be located in both the soluble cytoplasmic and membrane fractions. Growth of *Synechococcus* cells in artificial sea water (ASW) medium containing no added iron resulted in no alteration in the activity of the Fe-SODs. Growth of cultures in the absence of copper or zinc resulted in differential changes in the activities of the Cu/Zn-SODs and the unidentified SODs [23].

The abundance and cellular location of Fe-SOD in trichomes of *Nodularia*, *Aphanizomenon* and *Anabaena*, and in trichomes of a cultured *Nodularia* strain. For trichomes collected from natural populations the areal concentration of Fe-SOD labeling decreased with depth. An increase in the Fe-SOD content, particularly evident in scum samples that are continuously exposed to high irradiances, may have a role in the photo adaptation of diazotrophic cyanobacteria and help to protect them from light injury in the Baltic Sea [24]. A new gene encoding a SODs was identified from a thermophile *Geobacillus* sp. EPT3 isolated from a deep-sea hydrothermal field in east Pacific. The open reading frame of this gene encoded 437 amino acid residues. The recombinant SODs were determined to be a homodimer with monomeric molecular mass of 59.0 kDa. In comparison with other Mn–SODs, the manganese-binding sites are conserved in the sequence (His260, His308, Asp392, His396). The recombinant enzyme had high thermostability at 50 °C. The enzyme also showed striking stability