# Vanadium in Biological Systems

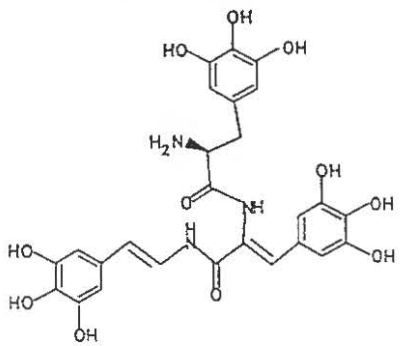
Shawne Van Deusen Literature Seminar March 2, 1989

Vanadium is a trace element present in all known living systems. In humans it inhibits a wide range of enzymes, including ATPases which synthesize ATP and generate in ionic gradient, and acts as an insulin mimic [1]. During the early 1970's several studies were done which supported the proposition that vanadium is an essential element; yet, no specific function for vanadium in any living system could be determined [2].

Currently, three biological systems in which vanadium is important are being studied — tunicates, which concentrate vanadium from sea water; vanadium containing bromoperoxidases; and vanadium nitrogenases.

Tunicates are marine invertebrates which have been known to sequester vanadium. The vanadium is stored in the vacuoles of blood cells known as vanadocytes. The vanadium in these organisms was originally thought to be protein bound and to serve as an oxygen carrier analogous to hemoglobin. This premise has been shown to be untrue [3]. The vanadium in vanadocytes is stored as vanadium(III) [4] and is not protein bound [4b,c]. XAS and EXAFS data show that only a small fraction (< 10%) of vanadium in the cells is vanadium(IV) and this amount does not change significantly upon aerobic cell lysis [4b]. If the vanadium in the cells is in the +3 oxidation state, the questions arise as to how it is transported into the cell and how the high concentration gradient (1.1M versus $5 \times 10^{-8}$M) is maintained. Vanadium is present in seawater as orthovanadate. This is taken into the cells through specific anion channels and is reduced in a two-step process to vanadium(III). As a V(III) cation it is unable to leave the cell [5]. Nakanishi and coworkers have recently isolated and characterized a compound known as tunichrome which may be complexed to the vanadium and may reduce the vanadium(V) as it enters the vacuoles [5c,6]

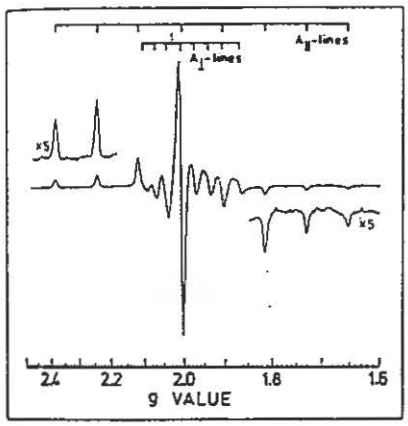
Tunichrome from *Ascidia ceratodes*




Most bromoperoxidases are iron(III) heme proteins [7]; however, bromoperoxidases recently isolated from several species of algae and one type of lichen were found to lack the Soret band characteristic of heme proteins and to be inactivated upon addition of EDTA to a solution of the enzyme [8]. Subsequently, it was determined using atomic absorption spectroscopy that these bromoperoxidases contained vanadium. EPR studies of the native enzyme showed no signal, while the EPR

of the reduced enzyme showed the eight-line signal of vanadium(IV) [8c,d]. Reconstitution experiments show that only vanadium(V) restores activity to the enzyme and maximum activity is achieved at concentrations of vanadate equivalent to 2 V atoms per mole of enzyme [8d] $^{51}V$ NMR studies show that the vanadium is protein-bound and in the +5 oxidation state [9].

***Ascophyllum nodosum***




**Bromoperoxidase + $Na_2S_2O_6$**

For heme containing haloperoxidases the mechanism of halogenation is the subject of some controversy. The mechanism of halogenation of substrates by V-bromoperoxidases is thought to be formation of $BrO^-$ followed by subsequent substrate halogenation because these enzymes will not oxidize substrates without a halide present.

Nitrogen fixation by species of Azotobacter has been known for some time [10]. During genetic studies on these bacteria, it was found that mutants which lacked the genes coding for both nitrogenase proteins could still reduce nitrogen to ammonia [11]. This system has been studied and found to contain vanadium in an analogous fashion to molybdenum in "regular" nitrogenase [12]. The V-nitrogenase has two protein components, one of which is an Fe-S protein like the Fe-protein of nitrogenase and the other contains both [4Fe-4S] clusters and an isolatable iron-vanadium cofactor [12b,e,f]. EXAFS studies indicate that the vanadium has 4 oxygens, 2 sulfurs, and 3 iron atoms in its coordination sphere [12c]. This is analogous to what has been found for molybdenum in Mo-nitrogenase [10,12d]. V-nitrogenase exhibits slightly different activities toward substrates than Mo-nitrogenase [12b,13].

True biological roles of vanadium have now been found but much work remains to elicite the structures of the active sites of the two enzymes discussed and to determine the function of vanadium in tunicates.

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