

Sulfite Reduction by an Iron-Containing Metalloenzyme

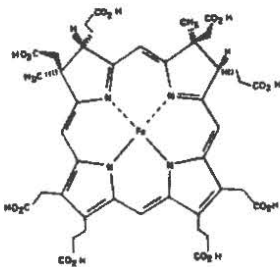
Cristi L. Hamilton

Literature Seminar

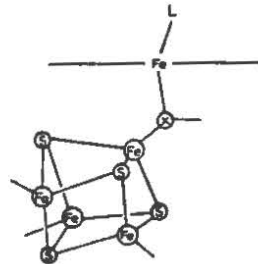
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A key step in the biosynthesis of sulfur-containing compounds in plants and microorganisms is the six-electron reduction of sulfite to sulfide. This reaction is catalyzed by sulfite reductase, one of the few enzymes capable of transferring more than two electrons without the release of species intermediate in oxidation state between substrate and product [1].

Sulfite reductase in *E. coli* is a complex hemoflavoprotein of molecular weight 685,000 [2]. It is composed of two different polypeptide chains in an $\alpha_8\beta_4$ structure [3]. Treatment of the enzyme with 4 M urea allows each subunit to be isolated. The α subunit, or flavoprotein, contains two prosthetic groups, FAD and FMN. The β subunit, or hemoprotein, is also associated with two prosthetic groups: an iron isobacteriochlorin termed siroheme [4] and an [4Fe-4S] cluster [3]. The hemoprotein can reduce sulfite if supplied with a suitable electron donor [3]. The electron flow from NADPH, the biological electron donor, to sulfite follows the sequence: NADPH \rightarrow FAD \rightarrow FMN \rightarrow siroheme \rightarrow sulfite, with the role of the [4Fe-4S] cluster still unclear [5].



Structure of Siroheme

Hypothetical Arrangement
of the Metal Centers

Ligand binding studies on extracted siroheme have established it to be the sulfite binding site on the enzyme [2,6]. The [4Fe-4S]₀ cluster cannot be extracted from the hemoprotein for characterization, but ^{57}Fe Mössbauer studies have revealed that two different types of iron sites exist, one being ferrous in nature while the other is ferric. Two iron atoms are associated with each site [7].

Extensive ^{57}Fe Mössbauer and Electron Paramagnetic Resonance (EPR) studies have been done on the hemoprotein in order to characterize the electronic nature of the siroheme and [4Fe-4S] cluster. These experiments suggest that the two iron centers are exchange coupled [8].

The enzyme can be reduced by two electrons. Optical, EPR, and Mössbauer studies have shown the first electron to be accommodated by the siroheme and the second by the [4Fe-4S] cluster. The coupling is maintained in these two reduced states [8,9].

The exchange coupling has been postulated to occur via an endogenous ligand. While the nature of this ligand is unknown, X-ray crystallography suggests that either a cysteine sulfur or a similar-sized ligand could serve as the bridge. Larger amino acid side chains would be difficult to fit to the electron density [10].

Further studies need to be done to clarify the exact nature of the coupling ligand. It is important to establish whether the sulfite binds trans to this ligand or whether it displaces it to form a new bridge between the two iron centers.

References

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