Superoxide dismutase: an antireductant enzyme?

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Superoxide dismutase (SOD) catalyzes the dismutation of superoxide to hydrogen peroxide and oxygen. Some form of SOD has been discovered in almost all aerobic organisms studied.(1) On the one hand superoxide is a potent reducing agent as it will readily reduce transition metals.(2) On the other hand superoxide, while acting as a reducing agent in the formation of hydroxyl radical, produces a potent oxidant (Haber-Weiss reaction). In vivo, production of hydroxyl radical is minimized by rapid destruction of the hydrogen peroxide needed for the Haber-Weiss reaction by catalase and glutathione peroxidase. Overall, superoxide is usually thought of as an oxidant.

It has been suggested that ionic channels and some enzymes may be regulated by changes in reduction or oxidation status (redox). We have recently shown that a K+ channel is susceptible to redox control (3), opening in response to diamide, a known sulphydryl oxidizing agent. Local redox status can also regulate intracellular enzymes, such as adenylate cyclase.(4) Iron is readily reduced by superoxide. Redox status is determined in part by disulfide exchange involving various proteins, following the initial reduction of a metal, such as iron.(5,6) Reduction of the metal may lead to reduction of disulfide groups associated with ionic channels or enzymes. Reduction under uncontrolled conditions of these channels could lead to inappropriate ion flux and cell damage. It is possible that, by eliminating superoxide, superoxide dismutase is an important antireductant enzyme, preventing uncontrolled reduction of ionic channels and enzymes.

Superoxide is known to leak from the mitochondrial electron transport chain. This leakage is mostly in the ubiquinone-cytochrome b area.(7) There is also considerable leakage at the NADH dehydrogenase point which becomes more significant during reoxygenation following ischemia.(8) Superoxide is part of a complex postulated to transfer electrons along the mitochondrial chain. This complex which also contains an unsaturated fatty acid and iron, could be a potential site of superoxide leakage.(9)

Quinones are ubiquitous electron carriers found in cell membranes. This study examines the concept that electrons from superoxide can be shuttled through a quinone to reduce ferric cytochrome C.

Methods and Results: We observed the effect of duroquinone on the reduction of ferric cytochrome C by a superoxide generating system (xanthine-xanthine oxidase). The reduction of cytochrome C (25 nM) in 50 mM Pi buffer by superoxide (generated by 5 uM xanthine-xanthine oxidase 9x10^3 M^-1) was significantly enhanced by 40uM duroquinone. The reagents were combined in a cuvette, the xanthine oxidase added and the reactants mixed. A baseline absorbance was taken 30 sec after mixing and then readings were taken every 15 sec at 550nm.

Conclusion: Superoxide may supply electrons, shuttled by substances such as quinones, thereby altering the redox status of ion channels, pumps and enzymes. Thus an important role for superoxide dismutase may be the destruction of superoxide leaking from enzyme transfer systems.

SOD may have a direct protective antireductant role as well as an indirect antioxidant role.

References