

Synthetic Models for the Active Site of the Nickel Superoxide Dismutase Enzyme (NiSOD)

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The superoxide molecule is an inevitable byproduct of aerobic respiration, which is the process by which nutrients are converted into useful energy in cells. If not regulated, superoxide causes significant cellular damage, leading to various diseases such as cancers, rheumatoid arthritis, osteoporosis and some neurological diseases such as Alzheimer's and Parkinson's disease. Superoxide dismutases (SODs) are enzymes which are responsible for detoxifying superoxide by helping to convert it into molecular oxygen and hydrogen peroxide, thereby protecting biological systems from oxidative damage. Among the four different SODs known, nickel-containing superoxide dismutase (NiSOD) has been discovered recently in *Streptomyces* species and cyanobacteria. NiSOD has a strikingly different geometry from other SODs and the relationship between the structure of NiSOD and its function is still not fully understood. We have been making two kinds of synthetic models for the NiSOD active site, which is the part of the enzyme responsible for its function. All these models have been characterized by various physical methods, including single-crystal X-ray crystallography. The ability of the model compounds to perform the enzymatic function will also be assessed. Using the information gained from this study, we hope to understand how the NiSOD enzyme works and suggest a new direction for the development of a new class of drugs to treat SOD deficiency and related diseases.