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Superoxide Dismutase

I.U.B.: 1.15.1.1

Superoxide: superoxide oxidoreductase

Superoxide dismutase (SOD) catalyzes the destruction of the O^{2-} free radical.

$$2O^{2-} + 2H^{+} \longrightarrow O_2 + H_2O_2$$

It protects oxygen-metabolizing cells against harmful effects of superoxide free-radicals (Petkau *et al*. 1975; Fridovich 1972, 1973; Lavelle *et al*. 1973; Paschen and Weser 1973). It has been reviewed by Malmström *et al*. (1975).

McCord (1974) found that SOD protects hyaluronate against depolymerization by free-radicals and indicated that exogenous SOD might have an anti-inflammatory effect (Salin and McCord 1975). The O^{2-} ion, which has been considered important in aging, lipid peroxidation and the peroxidative hemolysis of red blood cells (Fee and Teitelbaum 1972), is formed by the univalent reduction of O_2 during various enzymatic reactions or by ionizing radiation. (See also Fee *et al*. 1975). There is also superoxide radical formation during leukocyte phagocytosis (Allen *et al*. 1974; DeChatelet *et al*. 1974). See also Dionisi *et al*. (1975). Winterbourn *et al*. (1975) indicate that SOD deficiency might lead to Heinz body hemolytic anemia. Fridovich (1986) reports on the biological effects of the superoxide radical.

Superoxide dismutase is widespread in nature. Gregory *et al*. (1974) indicate it to be present in all oxygen-metabolizing cells. Hewitt and Morris (1975) have found it in anaerobic bacteria. It has been purified from diverse sources such as: fungi (Rapp *et al*. 1973); green pea (Sawda *et al*. 1972); *Streptococcus mutans* (Vance *et al*. 1972); wheat germ (Beauchamp and Fridovich 1973); *E. coli* (Gregory *et al*. 1973); *Saccharomyces cerevisiae* (Goscin and Fridovich 1972) and *Neurospora crassa* (Misra and Fridovich 1972).

Three superoxide dismutases are characterized by different metal content. A blue-green Cu(II)-Zn(II) enzyme comes from human and bovine erythrocytes, a wine-red Mn(III) protein is found in *E. coli,* and in chicken, and rat (Peeters-Joris *et al*. 1975) liver mitochondria (Tyler 1975) and a yellow Fe(III) enzyme from *E. coli* (Villafranca *et al*. 1974). It is of interest that the chicken liver cytosomal enzyme is the copper-zinc type (Weisiger and Fridovich 1973). Peeters-Joris *et al*. (1975) show SOD activity in many organs of the rat. Gregory *et al*. (1973) have reported on intra-cellular sites and functions.

Bovine erythrocyte SOD, to which the following data apply, has been extensively studied. It is identical to the enzyme from human erythrocytes and from beef heart (Bannister *et al*. 1971; Keele *et al*. 1971 and Nyman 1960).

Characteristics of Superoxide Dismutase from Bovine Erythrocytes:

Molecular weight: 32,500 (Keele *et al*. 1971).

Composition: Superoxide dismutase consists of two subunits of

Superoxide Dismutase

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identical molecular weight joined by a disulfide bond. The molecular weight is 32,500 (Keele *et al*. 1971). There are two Cu(II) and two Zn(II) atoms per molecule (Bannister *et al*. 1971). Crystal studies have been reported by Richardson *et al*. (1972) and Lieberman and Fee (1973). The amino acid sequence was determined by Steinman, Naik, Abernethy and Hill (1974), Abernethy *et al*. (1974) and Evans *et al*. (1974); the subunit tertiary structure by Richardson *et al*. (1975). Rotilio *et al*. (1972, 1973, 1974) have reported on the roles of copper and zinc. According to Forman and Fridovich (1973) zinc has a structural, stabilizing role, while Cu^{2+} is directly involved in the catalytic activity. See also Calabrese *et al*. (1991). Both zinc and copper have been removed to yield the apoenzyme (Carrico and Deutsch 1970). Fee and co-workers have published studies on the metal binding sites (Fee 1973; Fee and DiCorleto 1973; Fee and Gaber 1972). and enzymatic activity (Fee *et al*. 1973). Beem *et al*. (1974) report on the replacement of zinc by cobalt, mercury, and cadmium. Forman *et al*. (1973) and Rigo *et al*. (1975) indicate histidine to be involved at the active site. Nuclear magnetic resonance studies have been reported by Stokes *et al*. (1973), Lieberman and Fee (1973) and Villafranca *et al*. (1974). Superoxide dismutase activity and kinetics have been reported by Halliwell (1975), Rigo *et al*. (1975), Fielden *et al*. (1974), Goda *et al*. (1974), Michelson (1974), Hodgeson and Fridovich (1973), Rotilio (1973), and Grunow and Schöpp (1989).

Extinction coefficient: The protein is peculiar in that it does not show an absorption maximum at 280 nm (McCord and Fridovich 1969; Bannister *et al*. 1971). According to Symonyan and Nalbandyan (1972) A_{259}/A_{680} = 30.

Isoelectric point: 4.95 (Bannister *et al*. 1971).

Inhibitors: Cyanide inhibits cupro-zinc SOD but has no effect on the mangano enzyme of chicken liver mitochondria (Beauchamp , in Weisiger and Fridovich 1973). SOD is inactivated by H_2O_2 (Symonyan and Nalbandyan 1972, Fielden *et al*. 1973) and may be protected by catalase (Bray *et al*. 1974) with which it is usually associated. Hartz *et al*. (1973) found that in some tissue including cerebral cortex and thyroid, SOD is present but not catalase.

Stability: SOD is an unusually stable enzyme although its apoenzyme is very unstable. (Forman and Fridovich 1973). Worthington SOD retains its activity for up to a year at 5°C.

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