

ETHANOL, TRACE ELEMENTS AND SUPEROXIDE DISMUTASE IN RATS

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Both manganese superoxide dismutase (Mn-SOD) and cupro-zinc superoxide dismutase (Cu, Zn-SOD) are important in protecting cellular membranes against oxidative damage by superoxide radicals (O_2^-). Both enzymes appear to be induced by increased levels of O_2^- , but little is known concerning the relative response of the two enzymes, or of conditions which might favour the synthesis of one particular metalloenzyme form. Superoxide is generated within the cell by a number of mechanisms, including the metabolism of ethanol by microsomal NADPH - cytochrome P450 reductase. Indeed, increased SOD activity was first reported in the livers of fetal rats following maternal intoxication during pregnancy (Dreosti and Record 1979) and subsequently in adult rat livers (Valenzuela et al. 1980) and in erythrocytes from human alcoholics (Del Villano et al. 1979).

The present study undertook to examine the effect of extended alcoholism (20% aqueous ethanol for 24 and 32 weeks) in adult rats on the activity of both forms of SOD in a variety of organs, as well as on the distribution of Cu, Mn and Zn in these tissues. In addition, the increased activity of fetal SOD following maternal alcoholism (20%) during pregnancy was studied in greater details, in order to establish the form of SOD principally involved.

Both total-SOD and the activity of Mn-SOD were significantly increased in the livers and kidneys of ethanol-treated adult rats and in livers taken from fetuses, carried by alcohol-dosed dams. Hepatic Mn levels were significantly higher and the concentrations of Cu and Zn were lower in the adult, alcoholic animals. Separation of fetal liver homogenates into mitochondrial and cytosolic fractions revealed that most of the increased SOD activity was located in the cytosol and that Mn was also accumulated in this fraction.

The data suggest that, in rats, exposure to ethanol leads to enhanced activity of Mn-SOD which occurs predominantly in the cell cytosol. In turn this raises the question whether the response represents a protective mechanism against O_2^- produced from the metabolism of ethanol, the points to a degree of metabolism of alcohol by the fetus. In addition, the subcellular distribution of induced Mn-SOD suggests an extra-mitochondrial location and points to a less rigid compartmentation of this enzyme than generally recognised.

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