

## A Potential Role of Sulfite Oxidase Deficiency in Xenobiotics Metabolism

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Sulfite oxidase (SOX) is an essential enzyme in the pathway of the oxidative degradation of sulfur containing amino acids. It protects cells from toxicity of sulfite which has both endogenous and exogenous provenances. SOX deficiency is an inborn error of the metabolism of sulfated amino acids. Individuals affected with SOX deficiency most commonly present in the neonatal period with intractable seizures, characteristic dysmorphic features, and profound mental retardation. Xenobiotic metabolism is carried out by large groups of xenobiotic metabolizing enzymes (XME) that include the phase I cytochromes P450s and phase II enzymes including various transferases. XME play a dual role in xenobiotics metabolism. On one hand, they transform compounds to more water soluble metabolites and thus enhance their excretion. On the other hand, some of the intermediates arising during this process become more toxic. Some factors like species, sex, age, diet and genetic polymorphism alter XME levels and causes considerable differences in biotransformation ability of individuals, which is a problem faced by drug researchers interpreting toxicological results to humans. The present project investigates the role of SOX deficiency on xenobiotic metabolism, which is the first report on changes of XME in SOX deficiency. In this study, male Wistar albino rats, aged 3 months, were used. Three experimental groups, each consisting of 16 rats, were formed; control group, SOX deficient group, and the SOX deficient group treated with sulfite. Animals were housed in groups of four to five rats in stainless steel cages at standard conditions ( $24 \pm 2$  °C and  $50 \pm 5\%$  humidity) with a 12 h light–dark cycle and fed ad libitum with standard rat chow and tap water. SOX deficiency was produced in rats by the administration of a low molybdenum diets (AIN 76a, Research Diets Inc, USA) with concurrent addition of 200 ppm tungsten to their drinking water. At the end of the experimental period (6 weeks), livers were taken and cytosolic and microsomal fractions were prepared. First, hepatic SOX activity in deficient groups was measured to confirm SOX deficiency. Then, cytochrome b5 reductase (b5 RED), ethoxyresorufin O-deethylase (EROD), erythromycin N-demethylase (END), glutathione S-transferase (GST), N-nitrosodimethylamine N-demethylase (NDMA-ND) and penthoxyresorufin O-deethylase (PROD) activities were determined to monitor XME activity changes in SOX deficiency. Our results clearly demonstrated that SOX deficiency significantly elevated END and NDMA-ND activities while decreasing EROD and GST activities. No significant changes were observed with b5 RED and PROD activities. These alterations in XME can contribute to the varying susceptibility and response of these individuals to different drugs and/or therapeutics used for treatments.

Keywords: Sulfite oxidase deficiency, xenobiotic metabolizing enzymes, drugs

Category: Molecular Basis of Diseases (or Enzymes)