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Ethylene glycol monomethyl ether metabolism and aldehyde dehydrogenase 2

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Ethylene glycol monomethyl ether (EGME), or 2-Methoxyethanol (ME), is a water-miscible solvent used extensively in the chemical industry. Encephalopathy, central nervous system symptoms, erythropenia and granulocytopenia has been reported in workers exposed to ME. Moreover, human reproductive toxicity including oligospermia, azoospermia, sperm count reduction and ovarian luteal cell toxicity, also has been reported.

The biotransformation of ME plays an important role on the appearance of its toxicity. It has been speculated that the main pathway of ME metabolism is the oxidization to methoxyacetaldehyde (MALD) by alcohol dehydrogenase (ADH), and the successive oxidation of MALD to methoxyacetic acid (MAA) by ALDH. It is suspected that MALD besides MAA has a toxic function, but its details are still unclear. ALDH comprises more than nine families in humans, however, it has not been determined which has a key function for MALD metabolism. It is considered ALDH2 as a candidate enzyme because it metabolizes shorter chain aliphatic aldehydes. The genetic polymorphism of *ALDH2* has been characterized as *ALDH2*2* which loses the enzymatic activity. In addition, ALDH2*2 phenotype is dominant over the wild type, ALDH2* 1. To assess the role of ALDH2 in MALD metabolism, liver subcellular fractions were prepared from Japanese who carried three different *ALDH2* genotypes and *Aldh2* knockout mice, and examined *in vitro* MALD oxidization activity.

The activity was distributed in mitochondrial fractions of *ALDH2 *1/*1* and wild (*Aldh2*+/+) mice, but not *ALDH2 *1/*2*, **2/*2* subjects or *Aldh2* homozygous mutant (*Aldh2*-/-) mice. These results suggest that ALDH2 is a key enzyme for MALD oxidization and ME susceptibility may be influenced by *ALDH2* genotype.