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Lysosomal membrane leakiness and metabolic biomethylation play key roles in methyl tertiary butyl ether-induced toxicity and detoxification

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Methyl tertiary butyl ether (MTBE) is the most widely used motor vehicle fuel oxygenate since it reduces automobile emissions of carbon monoxide and compounds involved in photochemical smog formation. The increasing use of MTBE raised concern over its health safety. The cytotoxic mechanism of MTBE was investigated in freshly isolated rat hepatocytes. MTBE cytotoxicity was associated with reactive oxygen species (ROS) formation and glutathione (GSH) depletion suggesting that oxidative stress contributes to the MTBE cytotoxic mechanism. In this study the hepatocyte mitochondrial membrane potential was rapidly decreased by MTBE which was prevented by antioxidants and ROS scavenger, suggesting that mitochondrial membrane damage was a consequence of ROS formation. MTBE cytotoxicity was also associated with lysosomal membrane leakiness. Data showed that in the addition to CYP2E1, GSH is also involved in metabolic activation of MTBE. MTBE-mediated oxidative stress cytotoxicity and subsequent methylation is the unique pathway for detoxification.

Keywords: Methyl tertiary butyl ether; Glutathione; Oxidative stress; methylation; Mitochondria; Lysosomes