

# What is the role of reactive oxygen species in ethanol-mediated cell death of polarized hepatic cells?

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Liver disease that results as a consequence of alcohol abuse is a major medical problem worldwide. Ethanol consumption leads to a variety of liver alterations including the accumulation of fat, inflammation of the liver, as well as the presence of scar tissue. However, how these events happen after drinking alcohol are not well understood. It is known that ethanol-related liver alterations involve impairments to the hepatocyte cell in the liver that includes the induction of cell death mechanisms. It has also been shown that as a consequence of ethanol metabolism, oxidative stress is induced in hepatocytes through the generation of reactive oxygen species (ROS). However, the relationship between hepatocellular oxidative stress and the promotion of cell injury is not completely understood.

Recently, research published by B.L. McVicker and colleagues from The University of Nebraska Medical Center in *World Journal of Gastroenterology* discussed the relationship that exists between alcohol-induced hepatocellular oxidative stress and the promotion of [cell death](#) mechanisms. The aim of the study was to evaluate alcohol-mediated cellular alterations associated with apoptosis, a regulated mode of cell death which is characterized by specific biochemical and morphological changes in the cell. Using a polarized hepatic cell line (WIF-B cultures), an emerging model for studying the effects of ethanol on cellular processes, the investigators demonstrated that apoptosis induced as a consequence of ethanol metabolism was not completely dependent upon

oxidative stress mechanisms and was related to sustained cellular glutathione levels. Specifically, it was shown that ethanol treatment resulted in corresponding elevations in caspase-3 activity (an enzyme involved in apoptosis) and reactive oxygen species that were generated following ethanol metabolism. However, when the activity of cytochrome P450 2E1 (an enzyme known to oxidize ethanol to reactive metabolites) was induced in the cells, the level of ROS products in the cells doubled yet the amount of apoptotic cell death did not change. Also, when the level of the antioxidant glutathione was depleted in the cells, the ethanol-mediated induction of apoptotic cell death was abrogated, an effect that was related to the diminished activity of an upstream protease, caspase-8.

The researchers concluded that ethanol administration not only results in the trigger of signals associated with apoptosis, but that ethanol also primes hepatocytes making them more susceptible to apoptotic damage. Also, the study demonstrated that apoptosis induced as a consequence of ethanol metabolism in the hepatoma cultures was not completely dependent upon oxidative stress mechanisms and was related to sustained cellular glutathione levels.

Source: World Journal of Gastroenterology ([news](#) : [web](#))

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