

Mathematical Modeling of Acetaminophen-Induced Liver Injury and the Effect of Alcohol.

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Acetaminophen (APAP) overdose is one of the predominant causes of drug induced acute liver injury in the U.S and U.K. We test the Mathematical Model of Acetaminophen-Induced-Liver-Damage (MALD) using a large multicentre dataset maintained by the Acute Liver Failure Study Group (ALFSG) to predict the extent of liver injury. We then extend the model to include the effect of alcohol. Case studies show that ingestion of alcohol may increase the risk of APAP induced liver injury. Chronic alcoholism may potentiate APAP hepatotoxicity and this increased risk of APAP toxicity is observed even when APAP is ingested shortly after ethanol is cleared from the body. However, clinical studies also suggest that acute alcohol consumption may also have a significant protective effect against hepatotoxicity by inhibiting microsomal acetaminophen oxidation and thereby reducing N-acetyl-p-benzoquinone imine (NAPQI) production. This study models the dual role of alcohol to determine how it effects APAP metabolism and resulting injury. The mathematical model is based on a single time APAP overdose and considers both acute and chronic alcohol ingestion with varying amounts and timing which is very crucial in predicting liver injury.