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Summary: Acetaminophen (APAP) overdose is one of the predominant causes of drug induced acute liver injury in the U.S and U.K. Clinical 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 when APAP is ingested even shortly after alcohol is cleared from the body. However, clinical reports also suggest that acute alcohol consumption may have a protective effect against hepatotoxicity by inhibiting microsomal acetaminophen oxidation and thereby reducing N-acetyl-p-benzoquinone imine (NAPQI) production. The aim of this study is to model this dual role of alcohol to determine how the timing of alcohol ingestion affects APAP metabolism and resulting liver injury and identify mechanisms of APAP induced liver injury. The mathematical model is developed to capture condition of a patient of single time APAP overdose who may be an acute or chronic alcohol user. The analysis suggests that the risk of APAP-induced hepatotoxicity is increased if APAP is ingested shortly after alcohol is cleared from the body in chronic alcohol users. A protective effect of acute consumption of alcohol is also observed in patients with APAP overdose. For example, simultaneous ingestion of alcohol and APAP overdose or alcohol intake after or before few hours of APAP overdose may result in less APAP-induced hepatotoxicity when compared to a single time APAP overdose. The rate of hepatocyte damage in APAP overdose patients depends on trade-off between induction and inhibition of CYP enzyme.

MSC:
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acetaminophen; alcohol; overdose; hepatotoxicity; chronic liver injury; acute liver injury

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