Hepatoprotective Effects of Fermented *Curcuma longa* L. against Ethanol-induced Oxidative Stress *in vitro* and *in vivo*

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The long-term heavy consumption of alcohol results in the development of alcohol-related liver disease, which is the second leading cause of death among all liver diseases. Oxidative stress is considered as one of the key mechanisms responsible for alcoholic liver damage. In the present study, the protective effects of fermented *Curcuma longa* L. (FC) and partially-purified fractions from its cold water extract against alcoholic liver damage were investigated in male C57BL/6 mice and HepG2 cells transfected with human CYP2E1 (HepG2/2E1). Mice (n=8 per group), which received FC (100 mg/kg b.w./day and 300 mg/kg b.w./day) with ethanol revealed the prevention of alcohol-induced hepatotoxicity as evidenced by the significant reductions of serum alanine aminotransferase activities compared to ethanol-alone administered mice (5 g/kg b.w./day of ethanol). The protective effects of partially-purified fractions from the cold water extract of FC against ethanol-induced hepatotoxicity was investigated in HepG2/2E1. Four fractions, FCC-25M, -50M, -75M, and -100M were obtained by Amberlite XAD-2 column chromatography, eluting with 25%, 50%, 75%, and 100% methanol, respectively. After the cytotoxicities of fractions on HepG2/2E1 were evaluated using an XTT assay, concentrations of 50 ug/mL, 12.5 ug/mL, 6.25 ug/mL, and 6.25 ug/mL were chosen as the non-cytotoxic level to carry out the subsequent studies for FCC-25M, -50M, -75M, and -100M, respectively. The oxidative stress induced by ethanol caused a drastic decrease in cell viability with approximately 60%. This ethanol-induced cellular toxicity, however, was significantly reduced when the HepG2/2E1 cells were pretreated with FCC-25M (100% of cell viability). On the other hand, the treatment of other fractions did not prevent cell death by oxidative stress in comparison to the ethanol-alone treated group. These results suggest that FC supplementation antagonizes the ethanol-induced hepatic injury and FCC-25M is largely responsible for its protective action.