Abstract

Green tea based dietary supplements containing high levels of (-)-epigallocatechin-3-gallate (EGCG) have become popular for weight management. Case-studies have reported hepatotoxicity associated with consumption of green tea-based supplements and laboratory studies have demonstrated the potential hepatotoxicity of oral EGCG. We previously found that EGCG induced hepatotoxicity (increased plasma alanine aminotransferase and hepatic necrosis). Hepatic histone 2AX phosphorylation was increased and levels of reduced and total glutathione were decreased in mice treated with EGCG compared to vehicle-treated controls. Based on these results and those of other studies, it has been proposed that EGCG exerts pro-oxidant effects in the liver and induces hepatotoxicity. The exact mechanism by which EGCG induces oxidative stress is unclear. **We hypothesize that EGCG mediates oxidative stress and hepatotoxicity by inducing mitochondrial dysfunction.** The mitochondria are a major source of endogenous reactive oxygen species in cells, and mitochondrial dysfunction has been shown to increase cellular oxidative stress and cell death. Here, we will investigate the effect of EGCG on mitochondrial function in primary mouse hepatocytes. We will further determine the impact of obesity on the susceptibility of cells to EGCG mediated hepatotoxicity, as obesity has been shown to increase instances of drug induced liver injury.