# Hepatocyte Viability after Treatment of Weight Loss Drugs

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Glucagon-like peptide-1 (GLP-1) receptor agonists such as Tirzepatide and Semaglutide are commonly prescribed for treating type 2 diabetes mellitus and obesity. These agonists mimic the effects of endogenous GLP-1, an incretin hormone that enhances glucose-dependent insulin secretion, inhibits glucagon release, delays gastric emptying, and promotes satiety. While GLP-1 receptor agonists have demonstrated hepatoprotective effects, there are around 140 cases of drug-induced liver injury among patients taking these medications. This study aims to evaluate the cytotoxic effects of Tirzepatide and Semaglutide in a dose-dependent manner using HepG2 cells, a well-differentiated hepatocellular carcinoma, and an established in vitro model for assessing hepatotoxicity. HepG2 cells were treated with clinically relevant increasing concentrations of Tirzepatide and Semaglutide for 24, 48, 72, and 96 hours. Cell viability was assessed using Cell Counting Kit-8 (CCK-8) assays. Sorafenib, a known hepatotoxic agent, was used as a positive control, while HepG2 media was the negative control. We report no impairment in HepG2 cell viability with concentrations of the Tirzepatide and Semaglutide treatment groups up to 25 uM and 2.5 uM, respectively. In future studies, we aim to evaluate the effects of Tirzepatide and Semaglutide on a cholangiocyte cell line, given that cholangiocytes express GLP-1 receptors and GLP-1 receptor agonists have been implicated in the development of cholestasis. Supported by NJ ACTS NIH R25TR004777 CREST Program.