# Investigating Cyproheptadine as an NRF2 Activator in Human Liver Cancer Cells

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The buildup of free radicals due to UV radiation and the body's metabolism can cause damage and mutations in DNA, leading to the formation of tumors and cancers. The NRF2-ARE pathway has been studied and is identified as a pathway against oxidative stress. Cyproheptadine (CPH), an FDA-approved allergy medication, has reported its effects on histamine and serotonin. We sought to investigate the antioxidant properties of Cyproheptadine and its mechanism by studying the NRF2-ARE pathway in HepG2 cells. The cytotoxicity of CPH was first tested by treating the cells with different concentrations (0- 30 uM) of CPH for 24h using the MTS assay. The influence of CPH on the NRF2-ARE pathway was investigated by ARE-Luciferase assay and qPCR assay. The cytotoxic result indicated CPH exhibited above 70% cell viability at 20 uM. At 15 uM of CPH, it was observed to have an activity fold change 3 times higher than the control group ($p < 0.01$) in the ARE-Luciferase assay, suggesting CPH is a potential Nrf2 activator. Therefore, we next examined the expression of Nrf2-related genes (HO-1, NQO1) using qPCR. These genes (NRF2, HO-1, NQO1) were more expressed with higher concentrations of CPH (15 - 20 uM) than the control. In this study, CPH plays an activator of the NRF2-ARE pathway, indicating its potential role against cancer. Supported by R25ES020721.