Evaluating Urolithins for Ability to Protect Against Oxidative Stress

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Oxidative stress plays an important role in the pathogenesis of many diseases, including cancer. The anti-oxidative stress response in cells is mediated through the activation of the transcription factor NRF2. Thus, compounds able to activate this pathway may have great potential for cancer chemoprevention. The purpose of this study is to examine the chemopreventive properties of Urolithin A (UroA; a microbial metabolite for plant phytochemicals such as ellagic acid in the gut) through induction of the NRF2 pathway and its downstream detoxifying genes. HepG2-C8-ARE-luciferase cells were maintained in Dulbecco's Modified Eagle's Medium (DMEM) with 10% fetal bovine serum (FBS) at 37°C in a humidified 5% CO_2 incubator. An MTS assay was used to determine cell viability at different concentrations of UroA. Different concentrations for treatment were determined based on the results of the MTS assay. The cells were treated for 24 hours with UroA, which was dissolved in dimethyl sulfoxide (DMSO) and diluted in cell culture media with 1% FBS, at concentrations of 25, 50, 100, and 200 µM. Luciferase assays using these concentrations of UroA demonstrated its dose-dependent ability to increase ARE activity. UroA was also able to induce an increase in levels of NRF2 protein, as quantified by Western Blotting. Results from qPCR assays were inconclusive thus far, leaving UroA's ability to upregulate NRF2 and downstream target genes of NRF2, NQO1 and HO1, somewhat unclear. UroA may serve in the future as a key agent for cancer prevention and mediating oxidative stress related diseases.

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