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Differential protective effects of flavonols towards mitochondrial stress

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Plant bioactive compounds, such as flavonoids, have been shown to inhibit cellular oxidative stress in many cell types including skin cells. In particular, quercetin, a member of the flavonol subgroup demonstrates high potency in a range of biological test systems and may be a promising candidate for therapeutic applications. Prediction of biological activity based on molecule structure is commonly attempted; however, small structural differences may have a large impact on bioactivity and not many studies have linked the physical properties of flavonol compounds with biological effects. We are investigating the impact of three flavonols with similar structure, quercetin, isorhamnetin and kaempferol, on markers of oxidative stress in mitochondria and in human skin fibroblasts in relation to their membrane interaction properties.

Mitochondria isolated from rat liver tissue were incubated with quercetin, isorhamnetin and kaempferol to determine the potential of the selected flavonols to inhibit hydrogen peroxide and lipid peroxide production under baseline and stressed conditions. Furthermore, mitochondrial DNA damage, a sensitive biomarker of oxidative stress, was measured in human skin fibroblast cells, HDFn, after flavonol and hydrogen peroxide exposure. In isolated mitochondria, all compounds lowered dose dependently mitochondria lipid peroxidation (2.5-10 μ M) with quercetin and isorhamnetin being the most effective. In contrast, the specific production of hydrogen peroxide in mitochondria was largely inhibited by isorhamnetin, yet to a much lesser extent by quercetin and kaempferol. In HDFn cells, mitochondrial DNA damage was markedly inhibited by both, quercetin and isorhamnetin, but not by kaempferol. We used small angle X-ray scattering (SAXS) methodology to compare the interactions of individual flavonols with a lipid model mitochondria membrane, as an indicator of bioactivity. Based on the X-ray scattering data, all flavonols interact differently with the membrane, with isorhamnetin and quercetin representing the strongest and weakest interactions, respectively.

Although there are differences in the bioactivity of individual flavonoids, predictions of biological activity based on flavonoid-membrane interactions require further investigation and may have to consider cellular factors such as differences in uptake, metabolism and degradation of flavonol compounds.