Induction Of Oxidative Stress By Phytanic Acid In Heart Of Young Rats

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Phytanic acid (Phyt) is a branched-chain fatty acid that accumulates in tissues and biological fluids of patients affected by Refsum disease. Refsum disease is caused by the deficiency of the enzyme phytanoyl-CoA-hydroxylase, which catalyzes the first step of peroxisomal α-oxidation pathway. Clinically, patients present predominantly neurological symptoms, and cardiomyopathy, which is a major cause of death of these individuals. Since the mechanisms of heart damage found in this disease are poorly known, we investigated the in vitro effects of Phyt on important parameters of oxidative stress in heart of young rats. Supernatants and slices from heart of 30-day-old Wistar rats were incubated for 1 h at 37°C in the absence (control) or presence of Phyt (test) (1-500 μM). Our results show that Phyt significantly increased the thiobarbituric acid-reactive substances levels, an indicator of lipid peroxidation, and this effect was attenuated by trolox and melatonin (MEL). We also observed that Phyt provoked protein oxidative damage, as evidenced by increased formation of carbonyl groups, and decreased reduced glutathione (GSH) concentrations, an important non-enzymatic antioxidant defense. The decrease of GSH was completely prevented by MEL. In addition, Phyt increased the production of reactive species, as verified by the increase in the oxidation of 2′, 7′-dichlorofluorescin. Therefore, oxidative stress induced by Phyt may be involved, at least in part, in the pathogenesis of cardiomyopathy found in patients affected by Refsum disease.

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