Effects of Probucol in an Experimental Model of Huntington’s Disease In Vitro

Hartwig, J. M., Colle, D., Santos, D. B., Godoi, M., Leal, R. B., Farina, M.

Departamento de Bioquímica, Centro de Ciências Biológicas, Universidade Federal de Santa Catarina, Florianópolis, Santa Catarina, Brazil

Departamento de Química, Universidade Federal de Santa Catarina, Florianópolis, Santa Catarina, Brazil.

Huntington’s disease (HD) is a progressive neurodegenerative disorder characterized by symptoms attributable to the death of striatal and cortical neurons. Neurodegeneration and cell death in HD have been related with mitochondrial dysfunction and oxidative damage. 3-Nitropropionic acid (3NP), an inhibitor of the mitochondrial enzyme succinate dehydrogenase, has been found to effectively produce HD like symptoms. Probucol (PB) is a phenolic lipid-lowering agent with powerful antioxidant properties, clinically used during the past for the treatment and prevention of cardiovascular diseases; especially due to its hypocholesterolemic and anti-inflammatory properties. This study evaluated the potential protective effects of probucol on oxidative stress and mitochondrial dysfunction induced by 3-nitropropionic acid in rat brain mitochondria-enriched preparation. 3-NP (2 mM) caused significant inhibition of mitochondrial complex II activity induced mitochondrial dysfunction and increased reactive oxygen species (ROS) generation, as well as significantly increased lipid peroxidation in mitochondria. Probucol (1, 3 and 10 μM) did not prevent 3-NP-induced complex II inhibition and mitochondrial dysfunction. On the other hand, this compound prevented ROS formation and lipid peroxidation. Thus, the present results indicate that probucol is able to counteract the oxidative stress induced by 3-NP. These results contribute to better understand the process of neurodegeneration caused by oxidative stress and mitochondrial dysfunction.

Keywords: Huntington’s disease, 3-nitropropionic acid, probucol, mitochondrial dysfunction, oxidative stress.

Supported by: CNPq, CAPES and UFSC.