Resveratrol Alters Mitochondrial Dynamics mRNA Expression and increases mtDNA Stimulating Organelle Fission, Fusion and Biogenesis

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INTRODUCTION Mitochondrial dynamics is characterized by mitochondria movement within cells and by regulation of these organelles morphology mediated by fusion/fission events during cell development or in response to cytotoxicity. We previously showed that treatment with 1 to 50µM of Resveratrol, a phytoalexin related to the beneficial effects of red wines, induced mitochondrial movement/morphology changes and mitophagy in GRX, a hepatic stellate cell line. Here, we measured the mtDNA content and mRNA expression of mitochondrial dynamics proteins in GRX. We also evaluated the organelle function and ultrastructural feature. MATERIALS AND METHODS GRX were treated for 24h with Resveratrol diluted in medium (1, 10 and 50µM). The mtDNA (mitochondrial NADH dehydrogenase subunit-1) and the mitochondrial dynamics-related mRNA expression (mitofusin-1, MFN1; mitofusin-2, MFN2; optic atrophy protein-1, OPA1; and dynamin-related protein-1, DRP1) were analysed through real-time PCR. Mitochondrial mass and function were analysed by staining samples with MitoTracker™ green and red before measuring fluorescence through flow cytometry. Mitochondria ultrastructure was analysed through transmission electron microscopy and the organelles area were quantified through ImageJ in samples randomly-selected images. RESULTS AND DISCUSSION Lower doses of Resveratrol increased mtDNA content, while 50µM did not alter this parameter. It was found similar alterations in the MFN1, MFN2, OPA1 and DRP1 mRNA expression. The MTG and MTR ratio showed that besides the increase of mitochondrial mass there was a decrease in the organelle function. The images showed that treatment with 10µM of RSV induced mitochondrial clustering while 50µM of RSV promoted mitochondria swelling. Lower Resveratrol doses affected mitochondrial dynamics, which may be related to the organelle function impairment. However, this decreased mitochondrial function could be compensated by mitochondrial biogenesis. The mitochondrial swelling and diminished molecular activity found in the highest dose could be related to toxic effect of RSV. CONCLUSION Further studies are necessary to better understand these finds.

Keywords: Hepatic stellate cells, mitochondrial biogenesis, mitochondrial fission/fusion, resveratrol.

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