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Vascular oxidative stress-induced senescence is minimized by melatonin intake in ApoE-deficient mice

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Aging is a natural process that produces deleterious changes in all tissues of the organism. One leading theory about the cause of aging suggest that oxidative stress play a fundamental role in pathogenesis. Oxidative stress induces intracellular damage that affects all biological components, including, DNA, lipids, sugars and proteins. Therefore, the imbalance between intracellular reactive oxygen species (ROS) and antioxidant defence mechanisms results in harmful oxidative stress. One of the most widely considered strategies for preventing aging and for treating age-related disease is the use of natural anti-oxidant agents, such as melatonin and resveratrol.

Melatonin is a potent endogenous anti-oxidant neurohormone, which acts through various mechanisms to ameliorate the toxic effects of ROS. However, little is known about the mechanisms of signalling pathways through which melatonin acts to reverse the effects of ROS.

In the present study we treated ApoE-deficient mice, a well-known senescence model, from 6th week to 15th week of life, with a specific melatonin formulation: Armonia Retard (kindly provided by Nathura s.r.l, Reggio Emilia, Italy), with an extended-release pharmacokinetic, at different progressive doses 0.04, 0.1, 10 mg/kg/day. We used the same treatment in C57BL6 mice, as control group. Vascular alterations were evaluated in aorta by morphology and immunofluorescence analysis was focused on pleiotropic inflammatory markers, such as interleukins (IL) 6 and 10, inducible nitric oxide synthase (iNOS), tumor necrosis factor-alpha (TNF-α). We observed in ApoE-deficient mice endothelial cell detachment and IL-6, IL-10, iNOS and TNF-α overexpression. Melatonin treatment improved not only the endothelial damage, but also the overall vascular cytoarchitecture and reduced inflammation and macrophages infiltration. In particular, melatonin Retard at the highest dose, recovered all the above markers to the levels of C57BL6 mice.

These results outline the anti-inflammatory and anti-oxidant properties of melatonin and its beneficial anti-aging and anti-atherosclerotic effects, especially in extended-release formulation.

Keywords: Oxidative stress, Melatonin, Senescence, Vessels