

A comparison of melatonin and α -lipoic acid in the reduction of oxidative stress in L6 rat skeletal muscle cells

Gaia Favero¹, Stefania Castrezzati¹, Vitor Antunes De Oliveira¹, Lorenzo Nardo², Claudio Lonati¹, Russel J. Reiter³, Rita Rezzani¹

¹ Section of Anatomy and Physiopathology, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy - ² Department of Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, California, USA - ³ Department of Cellular and Structural Biology, University of Texas Health Science Center, San Antonio, Texas, USA

Aging is an universal, inevitable and multifactorial biological process, which causes progressive loss of function and an increased risk of death. Free radicals have been implicated in aging process, causing cumulative oxidative damage to crucial macromolecules and are responsible for failure of multiple physiological mechanisms [1]. Muscle mass and function are gradually lost during aging leading to neuromuscular disorders (such as fibromyalgia, sarcopenia, etc.). The indoleamine melatonin is able to prevent oxidative stress both through its free radical scavenging effect and by increasing endogenous antioxidant activity and so protecting against oxidative damage induced by drugs, toxins and different diseases [2].

Herein, we evaluated the susceptibility of rat L6 skeletal muscle cells to induced oxidative stress due to the exposure of cells to hydrogen peroxide and the potential protective effects of the pre-treatment with melatonin (Melapure™ by Flamma S.p.A.), compared to the known beneficial effect of alpha-lipoic acid. Our results showed that hydrogen peroxide-induced obvious oxidative stress, increasing the expression of tumour necrosis-alpha and in turn of nuclear factor kappa-B, overriding the endogenous defence mechanisms and altering the mitochondrial structure. In contrast, the pre-treatment with melatonin of the hydrogen peroxide-exposed cells increased endogenous antioxidant enzymes, including superoxide dismutase-2 and heme oxygenase-1, and ameliorated significantly both the oxidative stress damage and the mitochondrial alterations, that are known to be involved in aging and aging related diseases. In conclusion, melatonin had important anti-oxidant and anti-aging effects at the level of skeletal muscle *in vitro*.

Sincere thanks to Flamma S.p.A.-Italy (www.flammagroup.com) for courteously providing the melatonin and for the precious economic support to this study.

References

- [1] Ramis MR et al. (2015) Caloric restriction, resveratrol and melatonin: Role of SIRT1 and implications for aging and related-diseases. *Mech Ageing Dev* 146-148C:28-41; doi: 10.1016/j.mad.2015.03.008.
- [2] Espino et al. (2011) Melatonin is able to delay endoplasmic reticulum stress-induced apoptosis in leukocytes from elderly humans. *Age (Dordr)* 33:497-507; doi: 10.1007/s11357-010-9194-0.

Keywords

Alfa-lipoic acid; hydrogen peroxide; melatonin; oxidative stress; skeletal muscle cell.