NARINGENIN PROTECTS MYOCARDIUM AGAINST AGEING-RELATED INJURY

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Ageing represents an important health issue for modern society. Ageing enhances the vulnerability of several tissue, such as brain, liver and heart, against ischemia/reperfusion (I/R) injury. In this context, sirtuin 1 enzyme (SIRT1) plays a pivotal role, since it is involved in the regulation of many physiological functions and its expression decreases with age [1]. Therefore, an effective strategy to prolong the life-span and to improve tolerance to I/R damage is focused on improving the expression/activity of SIRT1 by pharmacological approaches, in order to modulate different intracellular downstream pathways strictly related with ageing. The polyphenol resveratrol represents the lead compound of SIRT1-activators but other natural compounds have been reported in the literature, including naringenin (NAR), a flavonoid typical of Citrus genus [1,2].

Interestingly, NAR confers cardioprotection in rat myocardium submitted to I/R injury, through the activation of mitochondrial big conductance calcium-activated potassium (mitoBK) channels [3]. Unfortunately, besides SIRT1, an ageing-dependent decline of the mitoBK expression has been observed by us and others [4] and it is major cause of reduced tolerance of myocardium to I/R injury.

This study aims to evaluate the possible anti-ageing effects of NAR, firstly on cardiac cell senescence induced by treatment with doxorubicin and then in 6 months old male mice, chronically treated with flavanone (100mg/Kg), 3 months (group 1) or 6 (group 2) months.

On cell senescence model, NAR significantly reduced typical markers of ageing, such as X-gal staining.

As regards in vivo protocol, at the end of treatments, in mice of both group 1 (9 months old) and group 2 (12 months old), an improvement of the cardiac mitoBK channel expression was observed. Moreover, as concerns SIRT1 enzyme and its downstream pathways, enhanced expression of cardiac SIRT1 and marked reduction of the oxidative stress have been shown.

The effects of NAR-treatment on other ageing markers correlated with SIRT1 have been also evaluated in order to define the machinery regulated by the Citrus flavonoid.

These preliminary results suggest that a nutraceutical approach with NAR may have a positive impact on critical markers of ageing, and that the use of Citrus flavanones may be suitable for improving the tolerance of myocardium against I/R damage.

Funding: Progetti di Ricerca di Ateneo 2017 (PRA2017).

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[3] Testai et al., Biochem Pharmacol. 2013 Jun 1;85(11):1634-43.

[4] Testai et al., Front Pharmacol. 2017 Feb 27;8:71.