MYOCARDIAL ANTI-AGEING EFFECTS OF THE CITRUS FLAVONOID NARINGENIN

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Ageing represents one of the main health issues in modern societies. As regards the cardiovascular system, many studies have shown a significant increase of the vulnerability of heart against ischemia/reperfusion (I/R) injury with ageing [1]. In this context, sirtuin 1 enzyme (SIRT1) seems to play a key role because of its involvment in the regulation of many physiological functions and its decreased expression with age. In particular, a critical role of SIRT1 in cardioprotection has been reported using SIRT1-deficient and SIRT1-overexpressing mice; therefore, the cardioprotective role of SIRT1 suggests that the improvement in the expression/activity of SIRT1 with exogenous agents could be an effective strategy to extend the life-span and to improve the resistance against I/R damage [2].

Some natural compounds, such as the polyphenol resveratrol, have shown SIRT1-stimulating activity, along with cardioprotective properties, in different experimental models. Even the Citrus flavonoid naringenin (NAR) is a SIRT1 activator [3]. In addition, NAR conferred cardioprotection in rat myocardium submitted to I/R injury through the activation of mitochondrial big conductance calcium-activated potassium (mitoBK) channels [4]. Unfortunately, ageing-dependent decline of the mitoBK expression has been observed by us and others [5] and it is probably responsible for lower tolerance of myocardium to I/R injury.

This study investigated the potential anti-ageing effects of NAR, chronically administered to 6 months old male mice. In particular, animals were divided into two groups: one of these has received NAR for 3 months while the other one was treated with NAR for 6 months. At the end of the treatments, both in 9 months old mice (first group) and in 12 months old mice (second group), an improvement of the mitoBK channel expression was observed. Moreover, an enhanced expression of SIRT1 accompanied by a significant reduction of the reactive oxygen species (ROS) production have been shown. The effects of NAR-treatment on other ageing markers correlated with SIRT1, have been also evaluated in order to better investigate the mechanism of action of this Citrus flavonoid.

In conclusion, these preliminary results suggest that a nutraceutical approach with NAR may play positive effects on critical markers of ageing, and that the use of Citrus flavanone may improve the tolerance of myocardium to I/R damage.

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