

Hydroxytyrosol derivatives prevent apoptosis and autophagy

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Hydroxytyrosol (HT) is released primarily in olive mill wastewater and in olive oil (Fabiani et al., 2008).

In animal and cellular model studies, HT and its metabolites show strong antioxidant and antimicrobial properties, as well as beneficial effects on the cardio-vascular system and in several human diseases (Goya et al., 2007). Differently, many reports in tumor cells (Han et al., 2009) suggested that HT down-regulates cell viability and proliferation, and induces apoptosis.

Nevertheless, little is known about its effect on normal cell apoptosis. Previous biochemical studies suggested that HT and HT derivatives, in particular the HT-Laurate (Laur-HT), show antioxidant effects on human erythrocytes (Manna et al., 1999).

In this study, we have investigated the effect of 20 μ M HT and 5 μ M Laur-HT in C2C12 myoblasts, a murine proliferating cell model, and U937 cells, a human monocytoic tumor cell line. H₂O₂, at the concentrations (0.5 and 1 mM) known to induce apoptotic death (Salucci et al., 2010), was utilized as cell death trigger.

Cell response was analysed by reverted (RM), light (LM) and transmission electron microscopy (TEM). Both cell lines observed at RM and LM showed a good morphology, in control condition. On the other hand, HT and Laur-HT, added to the control cells, did not influence cell viability.

After H₂O₂-treatment, the characteristic apoptotic features (D'Emilio et al., 2010) appeared at ultrastructural analysis in both cell models. Nevertheless, myoblasts exposed to 0.5 mM H₂O₂ presented a scarce response. For this reason, skeletal muscle apoptosis was investigated using H₂O₂ at major concentration (1mM) that evidenced an apoptotic cell number increase, as well as a relevant presence of autophagic vacuoles (Zhang et al., 2009).

Their pre-incubation with HT and Laur-HT prevented, in general, cell death and both apoptotic and autophagic patterns (Feng et al., 2011), as furtherly demonstrated by statistical analysis.

The anti-apoptotic and anti-autophagic action of these compounds, both on normal myoblasts and on tumor cells could represent an interesting property with potential biological and clinical applications.

Further studies are in progress in other cell models.

Keywords: apoptosis, autophagy, C2C12 and U937 cells, H₂O₂, HT, Laur-HT.