

EVOO polyphenols can relieve autophagy dysregulation in Alzheimer's disease

P-02.2-07

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Autophagy is a key process involved in the control of cell proteostasis, in the regulation of lipid metabolism and organelle turnover and in the clearance of materials of endogenous or exogenous origin. Autophagy efficiency declines with age, leading to accumulation of harmful protein aggregates and damaged mitochondria, with increased ROS production. These modifications contribute to several pathophysiological conditions, including Alzheimer's disease (AD). Indeed, several studies have reported that the maturation of autophagolysosomes and the inhibition of their retrograde transport creates favourable conditions for the accumulation of the A β peptide, whose aggregation into extracellular plaques is considered a key responsible of neuronal damage in AD. Recent data have shown that oleuropein aglycone (OleA), a key component of olive oil, interferes with A β aggregation, stimulates cell defences against plaque-induced neurodegeneration and triggers autophagy. After ingestion, OleA is metabolized to hydroxytyrosol (HT), the most powerful antioxidant compound in the olive tree. Based on these premises, we aimed to investigate the molecular mechanisms involved in autophagy activation by a mixture of OleA and HT. Therefore, we performed a set of *in vitro* experiments to extend and to deepen the knowledge on the molecular determinants of the beneficial properties of olive polyphenols. Our results show that a mix of OleA/HT activates the autophagic pathway more than the same amounts (in molar terms) of OleA or HT taken alone. Moreover, a reduction of ROS production with a significant recovery of cell viability was observed in cells exposed to toxic A β oligomers following treatment with the mixture. These studies extend previous data and provide the rationale to consider these molecules as promising candidates for prevention and long-term nutraceutical treatment of neurodegeneration or as molecular scaffolds for further pharmacological development.