Protective Effects of a Standardized Onion Peel–Derived Bioactive Ingredient Against Palmitate-Induced Steatosis and Oxidative Stress in HepG2 Cells

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Onion peel is a valuable agri-food by-product rich in phenolic compounds with potential health-promoting properties. Based on previous phytochemical investigations, a standardized extract from the *Rossa di Tropea* variety was developed as a bioactive ingredient (OPI-T). An extract from the *Ramata di Montoro* variety (M) was included as a natural reference to account for compositional variability. This study aimed to evaluate the antioxidant and antisteatotic effects of these extracts in HepG2 cells, a widely used *in vitro* model of hepatic steatosis. Steatosis is closely associated with oxidative stress and mitochondrial dysfunction, which are regulated by mitochondrial dynamics, including fusion and fission processes. While mitochondrial fusion supports functional recovery under stress conditions, excessive fission is linked to mitochondrial impairment. Steatosis was induced by palmitate (500 µM), and cells were co-treated with OPI-T or M (25–50 µg/mL). Lipid accumulation and oxidative stress were assessed by Oil Red O and BODIPY staining and DCF assay, respectively. Mitochondrial dynamics and autophagy were investigated by evaluating the expression of key markers, including MFN2 and DRP1 (fusion/fission balance), and LC3 II/I and SQSTM1/p62 (autophagic flux), through western blot .The results highlighted that OPI-T significantly reduced palmitate-induced lipid accumulation and ROS production, promoting a shift toward mitochondrial fusion and restoring autophagic flux. In contrast, the *Ramata di Montoro* extract exhibited weaker protective effects under the same conditions. Overall, these findings support the functional validation of a standardized onion peel–derived ingredient and highlight its potential application in functional foods or nutraceuticals targeting hepatic steatosis and oxidative stress. Further studies are needed to elucidate the underlying molecular mechanisms and identify the bioactive compounds responsible for these effects.

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