ALTERATIONS ON THE HEPATIC METABOLOME IN RESPONSE TO OLIVE OIL COMPOUNDS ADMINISTRATION ON METABOLIC SYNDROME.

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Olive oil, the gold standard of Mediterrannean diet has proved to play a protective role on Metabolic Syndrome (MetS), reducing the risk of Cardiovascular Disease and Type II Diabetes. The purpose of this study is to investigate the potential health benefits of four olive-derived compounds, namely Oleuropein (OL), Hydroxytyrosol (HT), Oleocanthal (OC), and Oleanolic Acid (OA), focusing on the hepatic metabolic profile in a MetS mouse model.
Metabolic Syndrome was induced to C57Bl6 mice (N=34) fed with Western type, rich in fat, diet for 14 weeks. On the 8th week, animals were randomized into the following 6 groups: OL (n=5, 20.6 mg/kg), HT (n=5, 5.9 mg/kg) and the corresponding Control group of normal saline (NS, n=6), OC (n=6, 11.6 mg/kg), OA (n=6, 17.4 mg/kg) with Control group DMSO 5% (DMSO, n=6). Mice were treated daily by oral gavage for the last 6 weeks. On the 14th week, mice were sacrificed, and liver tissues were serially extracted to obtain polar metabolites.
Liver tissue metabolomics were performed by means of 1H 1D Nuclear Magnetic Resonance (NMR) Spectroscopy, on a Bruker Avance III 600 MHz spectrometer. Acquired spectral data were subjected to statistical analysis, applying both untargeted multivariate (PCA, PLS-DA, OPLS-DA) and univariate methods with the aim to reveal an insight on potential alterations in hepatic metabolome between the groups.
Fasting blood glucose and total cholesterol levels, were significantly increased in the control group confirming the development of MetS in the animal model, while OL treatment reduced fasting glucose and OA restored total cholesterol to the baseline levels. According to our results, pairwise supervised multivariate analysis (OPLS-DA) revealed that OA administration is characterized by increased levels of taurine, alanine ($p<0.05$, t-test), succinate and 3-hydroxybutyrate ($p<0.01$, t-test). Additionally, choline and o-phosphocholine metabolites were also elevated suggesting alterations on hepatic lipid metabolism. In contrast to OA beneficial administration, the rest of the examined olive compounds do not result any observed statistically significant modifications on the liver metabolome.
In conclusion, our findings demonstrate that OA induces modifications in the hepatic metabolome, related with the induction of fatty acid β-oxidation and the citric cycle. These molecular mechanisms are probably correlated with the limited levels of plasma total cholesterol, even though further investigation of the underlying molecular mechanism is required.