

Pharmacokinetics and metabolism of food bioactives. The case of oleocanthal, a natural anti-inflammatory agent of olive oil

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Olive oil (OO) has been established in public consciousness as a superior edible oil, due to its exceptional nutritional value and sensory properties¹. Many studies have shown that OO consumption has been associated with diverse health-promoting and disease-preventing properties, mainly attributed to its chemical composition². Apart from fatty acids, OO also contains a highly complex and variable mixture of polar compounds, known as OO biophenols³. The most distinctive and predominant chemical class of compounds found in the majority of OO, is secoiridoids. Secoiridoids have been extensively studied for their biological and pharmacological properties. However, limited data exist for their metabolic fate *in vivo*, a commonly underestimated aspect in natural products and food bioactives research. Oleocanthal (Oleo) is one of these OO secoiridoids, acting as a strong anti-inflammatory agent, while studies have also shown its antioxidant and antimicrobial properties^{4,5}. Though, along the same lines, its pharmacokinetic properties (PK) have never been described so far. Towards the investigation of Oleo metabolism and PK characteristics, Oleo was isolated from OO in high amount and purity and administered to a mouse-model. For the selection of the most appropriate OO sample, rich in Oleo, more than 200 OO samples were analyzed via LC-HRMS and subjected to untargeted metabolomics. After multivariate data analysis and biomarkers identification, an integrated orthogonal methodology was applied for the targeted isolation of Oleo in high amount and purity. A pharmacokinetic experiment was designed and Oleo was supplemented in the dose of 5 mg/kg in a mice model. Plasma samples were collected in ten time points and analyzed via LC-HRMS/MS. The PK characteristics of Oleo and its metabolic derivatives were determined in time, along with their relative content. Novel biomarker compounds were revealed and associated for the time with Oleo administration.

References

¹ Edwin N. Frankel. *J. Agric. Food Chem.* 2011, 59, 3: 785–792

² Visioli F. *et.al. J. Pharmacol.* 2020, 177: 1316–1330

³ Apostolis A. *et al. J. Chromatogr. A.* 2017, 149: 126-136

⁵ Beauchamp, GK *et.al. Nature.* 2005, 437(7055): 45-6.

⁶ Kok-Lun P., Kok-Yong C. *Nutrients.* 2018, 10(5): 570

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