Bioavailability and metabolism aspects of natural products: the case of olive bioactives

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Nature still comprises an untapped source of bioactive compounds and a driving force in drug discovery. Especially after the disclosure of the decisive role of gut microbiome in disease onset, prevention, and health maintenance, active compounds found in food products, beyond any nutritional value or food bioactives (FBs), have been repositioned as a unique class of natural compounds with high impact to human health[1]. It is evident that gut microbiome is one of the major factors affecting the metabolic fate and therefore bioavailability of orally administered compounds. On the other hand, scientific dialogs globally over-comments the correlation of biological and/or pharmacological functions of natural products and FBs' with their *in vivo* bioavailability and metabolism, as well as highlight the lack of relevant information and solid data. This is particularly true for the FBs found in olive and olive products such as olive oil and table olives despite their central role in Mediterranean regime[2].

Amongst the most characteristic chemical classes of olive oil are phenylalcohols and secoiridoids (olive biophenols-OBs) widely known for their significant health beneficial effects[3]. As expected, their bioactivity is directly related to their metabolism and biotransformations in human organism demonstrating their mechanism of action, efficacy and safety. However, there are limited and scattered data related to the metabolism of OBs. LC-MS-based metabolite profiling approaches and dereplication methods have been proven as powerful tools offering a systematic mining and identification of biomarkers and/or biosynthetic pathways for the investigation of relevant metabolic patterns[3].

Aiming towards the exploration of OBs bioavailability aspects, a multi-arm workflow is establishing involving metabolite profiling of olive products and characterization of OBs; targeted isolation of pure compounds i.e. hydroxytyrosol, tyrosol, oleacein, oleocanthal and oleuropein; *in vitro* investigation of their metabolism using a continues GastroIntestinal Dialysis Model with colon phase (GIDM-colon)[4]; animal experiments as well as human studies[5]. Finally, an attempt for the procurement of relevant metabolites biotechnologically is under progress. All the analyses of diverse samples are performed using LC-HRMS & HRMS/MS platforms, statistical tools and databases (public and in house) following a holistic and interactive cross-talk.

Keywords: Olive biophenols, food bioactives, secoiridoids, GastroIntestinal Dialysis Model, human studies, metabolomics

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