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Randomized Controlled Trial

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Human Absorption and Metabolism of Oleuropein and Hydroxytyrosol Ingested as Olive (*Olea Europaea* L.) Leaf Extract

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Abstract

Phenolic compounds derived from the olive plant (*Olea europaea* L.), particularly hydroxytyrosol and oleuropein, have many beneficial effects *in vitro*. Olive leaves are the richest source of olive phenolic compounds, and olive leaf extract (OLE) is now a popular nutraceutical taken either as liquid or capsules. To quantify the bioavailability and metabolism of oleuropein and hydroxytyrosol when taken as OLE, nine volunteers (five males) aged 42.8 ± 7.4 years were randomized to receive either capsulated or liquid OLE as a single lower (51.1 mg oleuropein, 9.7 mg hydroxytyrosol) or higher (76.6 mg oleuropein, 14.5 mg hydroxytyrosol) dose, and then the opposite strength (but same formulation) a week later. Plasma and urine samples were collected at fixed intervals for 24 h post-ingestion. Phenolic content was analyzed by LC-ESI-MS/MS. Conjugated metabolites of hydroxytyrosol were the primary metabolites recovered in plasma and urine after OLE ingestion. Peak oleuropein concentrations in plasma were greater following ingestion of liquid than capsule preparations (0.47 versus 2.74 ng/mL; $p = 0.004$), but no such effect was observed for peak concentrations of conjugated (sulfated and glucuronidated) hydroxytyrosol ($p = 0.94$). However, the latter peak was reached earlier with liquid preparation (93 versus 64 min; $p = 0.031$). There was a gender effect on the bioavailability of phenolic compounds, with males displaying greater plasma area under the curve for conjugated hydroxytyrosol (11,600 versus 2550 ng/mL; $p = 0.048$). All conjugated hydroxytyrosol metabolites were recovered in the urine within 8 h. There was wide inter-individual variation. OLE effectively delivers oleuropein and hydroxytyrosol metabolites to plasma in humans.

Keywords: Bioavailability; Hydroxytyrosol; Oleuropein; Olive leaf extract; Phenols.

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