Oleuropein and its semisynthetic peracetylated derivative prevent hepatic steatosis and hyperinsulinemia in high fat fed C57BL/6 mice

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The high consumption of olive tree products in the Mediterranean diet has been associated to a lower incidence of metabolic disorders and cardiovascular diseases. In particular, the protective effects of olive oil have been attributed to the presence of polyphenols such as oleuropein (Ole) and its derivatives. In our laboratory, we have synthesized a peracetylated derivative of Ole (Ac-Ole) which has shown *in vitro* antioxidant and growth-inhibitory activity higher than the natural molecule.

This study aimed to evaluate the effects of Ole and its semi-synthetic peracetylated derivative Ac-Ole in mice fed with a high fat cafeteria diet (caf). Male C57BL/6JOlaHsd mice were fed with a standard diet, caf and caf supplemented with 20 mg/kg/day of Ole or Ac-Ole. After 15 weeks, we observed that supplementation of caf with Ole or its derivative significantly reduced the caf-induced increase of body weight, due to minor accumulation of fat in the adipose tissue. Moreover, Ole and Ac-Ole prevented the development of hepatic steatosis and the liver weight increase in high fat fed mice. Finally, Ole and Ac-Ole supplementation of caf determined a lower increase of plasma total, HDL and LDL cholesterol levels, and correction of caf-induced elevation of glucose plasmatic levels without increase of insulin levels. Hematologic analysis and histological examination of liver, kidney and lung did not reveal any toxic effects in mice treated with these compounds.

These findings demonstrate that oral subchronic administration of Ole and Ac-Ole are able to prevent body weight increase, hepatic steatosis and hyperinsulinemia in this model of high fat fed mice, suggesting a potential pharmaceutic use of these compounds in metabolic disorders.