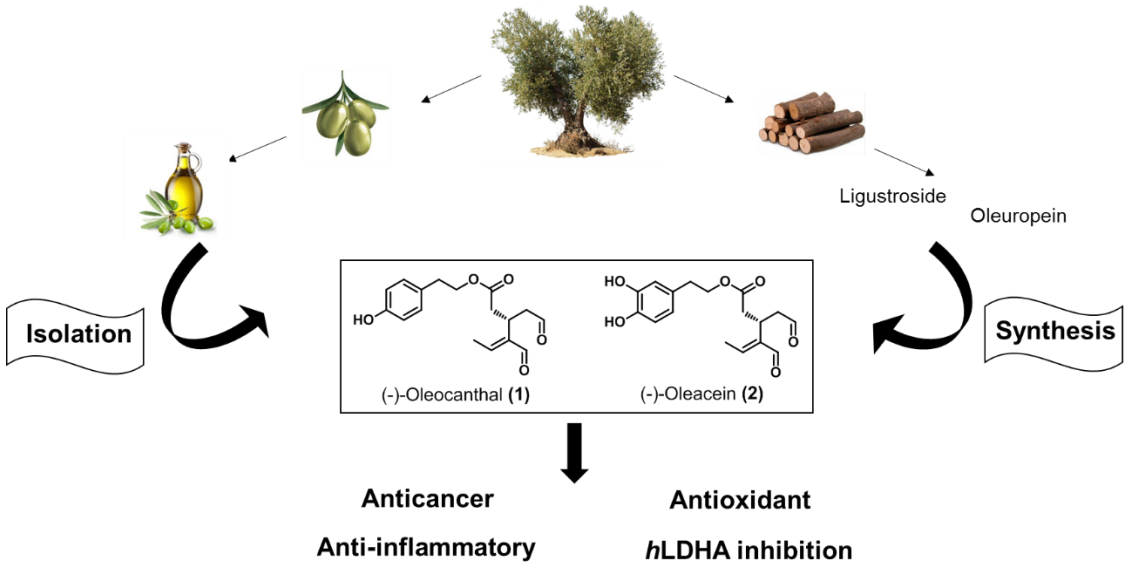
Isolation of (–)-oleocanthal and (–)-oleacein from olive oil and their synthesis from secoiridoids (–)-ligustroside and (–)-oleuropein. A case of potential new hit compounds?

Juan Ortega-Vidal*, Sofía Salido, Joaquín Altarejos

Departament of Inorganic and Organic Chemistry, Faculty of Experimental Sciences,
University of Jaén, 23071 Jaén, Spain *e-mail: jov00007@red.ujaen.es

Olive oil is the principal source of fat of the Mediterranean diet.[1] The intake of this vegetable fat is attributed beneficial properties on human diseases, such as cardiovascular, neurodegenerative and certain types of cancer.[2] Many research studies have linked these healthy effects with the presence of several phenolic compounds in the oil, such as oleocanthal (**1**) and oleacein (**2**).[3,4] These phenols are generated through an enzymatic process from ligustroside and oleuropein, respectively, during the production process of olive oil. Compounds **1** and **2** have aroused the interest of a large number of scientific due to their relevant pharmacological properties and their involvement in pathogenic processes, such as oxidative stress, inflammation, neurodegenerative, and cardiovascular diseases.[5]

Our research group has some experience in the isolation of natural products from plant sources (olive, cherry, plum and laurel woods, among others)[6–9] and in the synthesis of bioactive molecules.[10] Firstly, the aim of our work was the isolation of both compounds (**1** and **2**) from a phenolic extract of olive oil. For that purpose, a Fast Centrifugal Partition Chromatography (FCPC®) instrument was used. This chromatographic technique uses two liquid phases, stationary and mobile, and not a solid-support stationary phase as silica gel, used in conventional column chromatographies. The technique was very useful since those molecules are sensitive to decomposition in contact with solid stationary phases.[11] It allowed us to isolate small amounts of both compounds in order to evaluate their biological activity by *in vitro* assays. Due to the interesting results obtained from these assays, our second effort was focused on the development of an efficient synthetic procedure in order to prepare compounds **1** and **2** in large-scale to carry out *in vivo* assays. The procedure developed allowed us to obtain oleocanthal (**1**) and oleacein (**2**) from ligustroside and oleuropein, respectively, in good yield. In addition, the anti-inflammatory, anti-cancer and antioxidant properties of these compounds have been evaluated, with remarkable results, through collaborations with research groups from the Universities of Sevilla, Extremadura and Granada (Spain).[12–15] Furthermore, the inhibitory activity of the enzyme *h*LDHA has been evaluated in our research group within a project aimed at obtaining new therapies to treat patients of primary hyperoxaluria.[16]



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