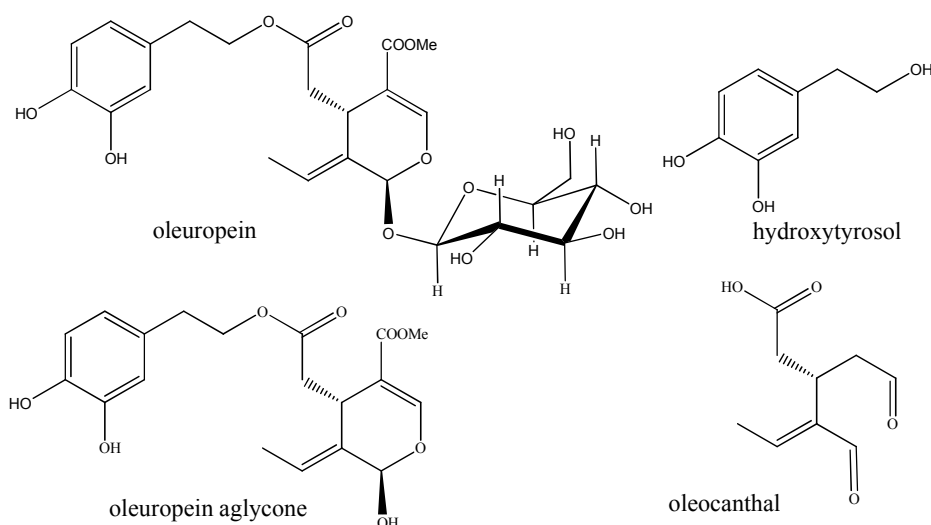


Subject proposal for Erasmus student in Chemistry

Tackle the Alzheimer's disease: Synthesis of inhibitors of the protein Tau aggregation.

Neurodegenerative diseases and particularly tauopathies are a major public health problem in Europe and USA that will be amplified with the ageing of the society. To date, no drug that delays or halts the progression of these diseases is available. The largest component of the neurofibrillary tangle (NFT) observed in senile plaques in the brain of the patients was identified in the 1980s as the tau protein. There are several therapeutic strategies to reduce tau-mediated neuropathology and neurodegeneration. A number of approaches are being pursued to reduce the consequences of pathological Tau: microtubule-stabilizing agents, inhibitors of tau kinases, inhibition of β -N-acetylglucosaminidase (*O*-GlcNAcase), Heat shock protein 90 (HSP90) inhibitors and Tau fibrillization inhibitors.

Epidemiologic studies have shown that Mediterranean diet has a positive impact on the cognitive disease and olive oil has been identified to contribute to these properties. We had identified the molecules that could confer these properties to olive oil. We have shown that oleuropein, oleuropein aglycone and hydroxytyrosol are able to inhibit the fibrillization of protein Tau. More recently it has been shown that (-)-oleocanthal, a new phenol isolated from freshly-pressed extra virgin olive oil abrogates fibrillization of tau.



In this context a programme devoted to the design of inhibitors of the aggregation of the protein Tau has been initiated in our lab. The project will consist in develop and optimise the synthesis of (-)-oleocanthal derivatives and synthesize a series of hydroxytyrosol metabolites in collaboration with biologists and biophysics.

The candidate will be learnt in organic synthesis in liquid phase and practical multinuclear 1 and 2D NMR to be able to realize his own experiments.

Keywords: Polyphenols, olive oil, protein Tau, Alzheimer disease

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