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(-)-Oleacein and (-)-oleocanthal, two phenolic compounds present in Extra Virgin Olive Oil, inhibit angiogenesis

Ana Dacil Marrero^{1,3,4}, Juan Ortega Vidal², Sofia Salido², Joaquin Altarejos², Ana R. Quesada^{1,3,4}, Beatriz Martinez Poveda^{1,3,5}, Miguel Angel Medina Torres^{1,3,4}

1) Department of Molecular Biology and Biochemistry, University of Malaga, Spain

2) Department of Organic and Inorganic Chemistry, University of Jaen, Spain

3) Institute of Biomedicine of Malaga (Ibima)-Plataforma BIONAND, Malaga, Spain

4) CIBER de Enfermedades Raras (CIBERER), Spain

5) CIBER de Enfermedades Cardiovasculares (CIBERCV), Spain

Phenolic compounds in the Mediterranean diet contribute to many of the health-related benefits accounted in this dietary choice. (-)-Oleocanthal and the less studied (-)-oleacein, are two phenolic compounds present in the Extra Virgin Olive Oil that have shown anti-tumoural effects both in vitro and in vivo. Among their effects on cancer, they could inhibit tumour cell migration and invasion, key processes also in angiogenesis, the process by which de novo blood vessels are formed. Herein, we explored the anti-angiogenic potential of (-)-oleocanthal and (-)-oleacein in a comparative study in in vitro experiments on endothelial cells, and in two in vivo models. (-)-Oleocanthal and (-)-oleacein affected endothelial viability in the micromolar range, as well as the formation of tubule-like structures by these cells, and their migration. Interestingly, only oleacein inhibited cell migration and induced apoptosis significantly. Regarding cellular signalling, both compounds were able to reduce the activation of the AKT and ERK1/2 pathways, which are related to survival and proliferation, respectively. Finally, both compounds showed anti-angiogenic activity in a zebrafish model of regeneration and in the chicken chorioallantoic membrane. Altogether, these results support the anti-angiogenic potential of (-)-oleocanthal and (-)-oleacein, and suggest that (-)-oleacein exerts more potent effects on endothelial cell migration and induction of apoptosis. Thus, we propose these two phenolic compounds, with a special focus on (-)-oleacein, as new candidates for clinical use as anti-cancer and anti-angiogenic agents. [Grants: PID2019-105010RB-I00 and RTI2018-098560-BC22 (Spanish Government), UMA18-FEDERJA-220, and PY20_00257 (Andalusian Government and FEDER). Funds from BIO 267 (Andalusian Government). CIBERER, CIBERCV].

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