

Evaluation of Olive Oil Polyphenols' Properties on *Ex Vivo* Models: future perspectives on senolytic and senomorphic studies

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Keywords: Aging, Hydroxytyrosol, Inflammation, Oleuropein, SASP: Senescence-Associated Secretory Phenotype, SCAP: Senescence Cell Anti-apoptotic Pathway, Senolytic, Senomorphic, Senotherapeutic drugs.

Abstract

Senescence is a physiological process that occurs since embryogenesis, in case of tissue damage, and during aging. Its persistence can trigger an inflammatory process which is harmful [1], causing a phenomena called senescence-associated secretory phenotype (SASP). The paracrine activity of SASPs in the microenvironment contributes to the dysfunction of the organism's tissues. This process determines an inflammation state activated by the transcription factor NF- κ B, and consequently the production of proinflammatory chemokines and cytokines with increased expression of antiapoptotic genes. In this regard, senotherapeutic drugs are substances able to block the SASP and, therefore, slow down the aging process. These drugs are differentiated on the basis of their natural or synthetic origin and by their senolytic or senomorphic effect. The senolytic effect induces apoptosis and eliminates the senescent cells (SC). Instead, drugs with a senomorphic effect hinder the transition of young cells in SC within tissues or acts on molecules produced by these cells. Recent researches focused on olive oil polyphenols and their possible use as senotherapeutic drugs thanks to their anti-inflammatory properties that reduce the oxidative stress, inhibit NF- κ B and the consequent transition to the SASP [2]. Among the natural compounds, it is known the proapoptotic activity of the phenolic compound Oleuropein (OLE) and its derivative Hydroxytyrosol (HT) extracted from fruits and leaves of *Olea europaea*. Future studies should be concentrated on the possible senotherapeutic effects of OLE and HT to enrich our knowledge of phenolic compounds. Since fibroblast are involved in the cell damage repair process, they could be used as cellular model in culture to achieve senescence. Thus, fibroblasts should be stimulated with the olive oil polyphenols and after that qPCR or ELISA test could evaluate the effect of OLE and HT on the senescence cell antiapoptotic pathways (SCAPs), on the gene expression of proinflammatory chemokines and cytokines produced by SASPs and on senescence markers such as SA- β -gal, p16, p21 and p53.

References

- [1] Chaib S., Tchkonina T., Kirkland J.L., "Cellular senescence and senolytics: the path to the clinic", *Nature Medicine*, 28, 1556–1568, (2022).
- [2] Calabrò A., Accardi G., Aiello A., Caruso C., Galimberti D., Candore G., "Senotherapeutics to Counteract Senescent Cells Are Prominent Topics in the Context of Anti-Ageing Strategies", *International Journal of Molecular Sciences*, 25,1792, (2024).