Abstract

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Olive leaf extract effects on Female Reproductive Cancers

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Modifications in dietary intake and benefits of the Mediterranean diet can importantly increase life expectancy, reduce the risk of developing cancer and related chronic diseases and improve the quality of life. Indeed, there is an increased interest in the study of the antitumor properties of different food components. Some recent researches have demonstrated the effective antiproliferative and antiangiogenic activity of natural comestibles such as mangos teen, grapes, tomato or chestnut extracts in cancer.

Olea europaea leaves, oil and fruits have been shown to inhibit proliferation and induce apoptosis in different cancer cell lines, throughout anti-inflammatory actions related to their ability to scavenge free radicals and prevent cellular injury. Among these compounds, polyphenols have been reported to interfere with the initiation, promotion and progression of cancer by affecting tumorigenic cell transformation. Nevertheless, Olive leaves still remain a non-edible source rich in polyphenols that can play an interesting role in cancer.

Breast and ovarian cancer are two of the most frequently diagnosed cancer and the main and fifth reason of tumour death among females, respectively. In this respect, our research is focused on the analysis of an Olive Leaf Extract -OLE- rich in Oleuropein (~50% of its content) as a potential antitumor agent on a malignant TNBC cell line, MDA-MB-231, and OVCAR-3 ovarian cancer cells that overexpress stem cell-enriched genes and has a natural tendency to metastasize to brain and lungs.

Cell proliferation assay was determined with colorimetric MTS after 24-72h of treatment with different concentrations of OLE (100-400 µg/mL). Cell cycle was then analyzed at 250-200 µg/mL of OLE (IC_{50} of MDA-MB-231 and OVCAR-3 cells, respectively) by FACS after 24 and 72h. Same experimental conditions were used to prepare the whole cell lysates (treated and not), analyzed then by Western blot. Immunofluorescence (IF) was also performed and cellular staining with MitoTracker was observed by laser confocal microscopy

Results: Cell viability decreases up to 95% vs control at high OLE concentrations (>300 µg/mL). Cytofluorimetric analysis showed a block in the cell cycle S phase, confirmed later by the decrease of Cyclins (B2, D1) and the increase of caspases and Cyclin E analyzed by WB. Apoptotic marker p27 is also

overexpressed in MDA-treated cells. IF assay revealed an increased PPAR-γ nuclear localization and a marked reduction in mitochondrial number and function

Conclusions: OLE induces MDA-MB-231 cell cycle arrest at the S phase, caspase-dependent apoptosis and mitochondrial damage. Polyphenols present in OLE may modulate PPAR-γ transcriptional activity -strongly involved in mitochondrial biogenesis- which could represent e a potential target of the OLE pathway that will be explored soon through PPAR-γ silencing experiments. The obtained results suggest that OLE exerts antitumor activity in two different cellular models of female reproductive system cancer.

Keywords: OLE, Mediterranean diet, MDA-MB-231, TNBC, Ovarian cancer, OVCAR-3

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