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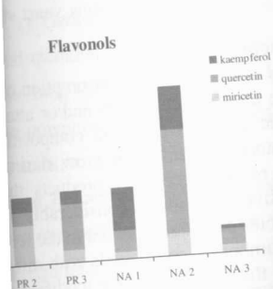
rol	Methanol	Tartaric A.	Citric A.
7	0,08	2,45	0,21
6	0,1	3,33	0,3
1	0,02	3,95	0,28
4	0	2,5	0,32
2	0,03	2,23	0,13
9	0,1	2	0,25



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In vitro effects of extracts of Extra Virgin Olive Oil on Human Colon Cancer Cells

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Olives and olive oil are a major components of the traditional Mediterranean diet. They represent a source of polyunsaturated fatty acids and their consumption has been associated with a low incidence of atherosclerosis, cardiovascular diseases, and certain types of cancer. Both *in vivo* and *in vitro* studies have shown that olive oil components have positive effects on metabolic parameters, such as plasma lipoproteins, oxidative damage, inflammatory markers, platelet function, and antimicrobial activity. A recent *in vitro* study demonstrated that olive oil extracts induced both cell apoptosis and cell differentiation in colon cancer derived cells. These findings suggest that the consumption of olive oil may contribute to a chemo-protective effects against colon carcinogenesis.

The interest of the scientific community has focused on phenolic components present in virgin olive oils, and in particular to the role that they play in tumor progression. The phenolic compounds present in the olive oil belong to three categories: simple phenols (tyrosol and hydroxytyrosol), secoiridoid (oleuropein, the aglycone of ligstroside) and lignans [(+)-1-acetoxypinoresinol and pinoresinol]. Hydroxytyrosol and secoiridoids with hydroxytyrosol have potent antioxidant properties. Olive oils rich in hydroxytyrosol have been demonstrated to inhibit cell proliferation, induce apoptosis in human promyelocytic leukemia and in colorectal cancer (CRC) cell lines. Lignans were reported as low antioxidants, capable to inhibit estrogen synthesis and cancer cell proliferation.

Many epidemiological and experimental studies suggest a protective role of estrogens against colorectal tumorigenesis. Experimental data have demonstrated that CRC express an elevated number of estrogen receptors (ERs), estrogen receptors alpha (ERα) and beta (ERβ) are the 2 known subtypes of ERs, the so-called ligand-activated transcriptional factors through which estrogens exert their effects on various tissues. Most of the phenolic compounds show a chemical structure similar to the 17β-estradiol (17β-E2).This common structure can lead to suppose a possible mechanism of action of these compound related to their capability to compete with estrogens at ER binding site.

Antiproliferative activity on colon cancer cell lines, of two extra virgin olive oils (EVOO), M and T, kindly supplied respectively by Tuscan and Ligurian enterprises (Italy), were evaluated. Oil sample preparation and extraction, as well as identification, characterization and quantification of single polar compounds were carried out as reported in Romani *et al.* (1). The two EVOO extracts were tested on the colon cancer cells line HCT8-β8 engineered to overexpress ERβ.

Characterization of EVOO-M extract showed the presence of hydroxytyrosol, oleocanthal, deacetoxy-oleuropein aglycone and secoiridoid that are the main components (all>12%), followed by elenolic acid (11%) and tyrosol, 5-hydroxytyrosol, deacetoxy-oleuropein aglycone and oleuropein aglycone. In addition it was rich in secoridoids and had a relatively low amount of lignan derivatives. In the EVOO-T extract lignan derivatives are the main components (54%), followed by elenolic acid and elenolic acid derivatives (>15%); it contained a high percentage of lignan derivatives (54.5%) and no 5-hydroxytyrosol, deacetoxy-oleuropein aglycone or oleuropein aglycone.

The cells HCT8-β8 were stimulated with 50 μM of M and T-EVOOs extracts and with 10 nM 17β-E2 as a control. Cells growth was evaluated and Lucyferase assay test was performed to study the possible interaction between EVOOs and estrogen receptor β (ERβ).

The results showed an anti-proliferative activity of the EVOO-M and -T at the concentration of 50 μM (Fig 1). HCT8 β8 cell growth was significantly inhibited by both extracts during the experimental period of observation. EVOOs extracts are able to interact with the estrogen receptor ERβ promoting the ligand-dependent response cascade. At 50 μM the two olive oil extracts were able to activate ERβ in a similar manner to that observed for 10 nM 17β-E2, in physiological condition (Fig. 2).

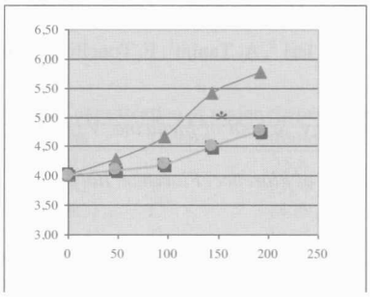

Fig. 1 Effects of the EVOOs (50μM) in comparison to the control (▲) on the cellular lines HCT8-β8 treat with EVOO M (■) and T (●). * p< 0,05 vs control

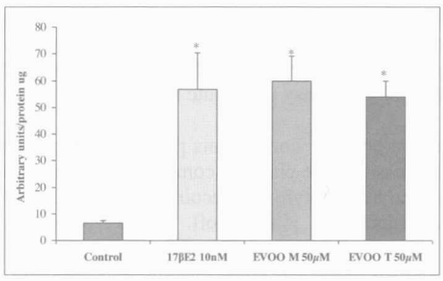

Fig. 2 Effects of EVOO T and M on transactivation in HCT8-β8 cells. The 17βE2 was used for positive control. * p<0.05 vs untreated cells, p<0.05 vs 17βE2-treated cells.

In conclusion our study shows that the two extra-virgin olive oil defatted extracts, EVOOs M and T, are able to induce a significant inhibition of colon cancer cell proliferation, probably due to a mixture of phenolic compounds with estrogenic activity present in the extracts. Inhibition of proliferation may be through a series of events, encompassing transactivation of the ER β. In effect EVOO-M and-T extracts reveal the ability to interact with estrogen receptor ERβ similar to 17β-E2, also if their effect results evident at more elevated concentration compared to 17β-E2.

1. Romani A. et al. HPLC and HRGC analyses of polyphenols and secoiridoids in olive oil. Chromatographia 2001, 53, 279-284.