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Editorial Open Access

Olive Oil Phenolic Compounds: May Prevent Cancer in Human?

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Editorial

The most distinctive feature of the Mediterranean diet is the presence of olive oil as the main source of fat. Olive oil is widely used in the Mediterranean regions as a dressing and for the preparation of all foods. In particular "extra virgin" olive oil, contains among the others, some peculiar phenolic compounds (PC) which are not present in other oils and in other vegetable foods. These include the phenolic alcohols hydroxytyrosol (3,4-dihydroxyphenyl-ethanol: 3,4-DHPEA) and tyrosol (*p*-hydroxyphenyl-ethanol: *p*-HPEA) which are present in the olive oil as such or are combined with either the elenolic acid (EA) or the dialdehydic form of EA (EDA) giving rise to the so called secoiridoid derivatives (3,4-DHPEA-EA "oleuropein aglycon"; 3,4-DHPEA-EDA; *p*-HPEA-EA "ligstroside aglycon"; *p*-HPEA-EDA) [1]. In olive fruit and leaf the glycosilated secoiridoid precursors oleuropein and ligstroside are mainly present. The concentration of these PC in olive oil is extremely variable from a few mg/kg up to 800 mg/kg and depend upon different agronomic and technological aspects of olive oil production [1]. Recently, numerous different biological effects of olive oil PC have been deeply investigated both "*in vivo*" and "*in vitro*" systems. They have shown anti-oxidant and anti-inflammatory activities associated to beneficial effects against cardiovascular, metabolic and neurological diseases, and cancer (for recent reviews [2-4]).

From the epidemiological point of view, several studies have suggested that uptake of olive oil is associated to a reduced risk of cancer in different organs. A meta-analysis published in 2011 summarized the results of 19 observational studies and showed that high olive oil consumption was associated with lower risk of developing cancer in breast (-36%) and in the digestive system (-30%) [5]. It must be noted, however, that so far the epidemiological studies have considered the olive oil consumption itself, regardless of which type of olive oil was used (virgin or refined) or of the amount of phenols it contained (rich or poor). In addition, a few human intervention trials have investigated the effect of olive oil phenols on DNA damage with contrasting results [6]. Therefore, actually, direct evidences for the cancer chemopreventive properties of olive oil PC came from studies *in vitro* on cell systems and *in vivo* on animal models of carcinogenesis. Olive oil phenols have been shown to inhibit both initiation and promotion/progression phases of cancer development. At low doses (<10 μM) both 3,4-DHPEA and complex phenol extracts obtained from olive oil or olive mill wastewater prevented the DNA damage induced in human peripheral blood mononuclear cells exposure "*ex vivo*" to H_2O_2 and to alkene epoxides [7,8]. On the other hand, the inhibitory effect on proliferation, and the enhancement of apoptosis and differentiation on tumor cells, was observed only at higher concentrations of 3,4-DHPEA (50-100 μM) [9]. These effects were associated with a block of the cell cycle in the G_0/G_1 phase, a reduced the level of cyclin-dependent kinase 6 (CDK6) and with an increment of cyclin D3. At the same time there was an evident increase of the expression of CDK inhibitors $p21^{WAF1/Cip1}$ and $p27^{Kip1}$ at both protein and mRNA levels [9]. Further studies have demonstrated that these chemopreventive properties of 3,4-DHPEA were mediated by a pro-oxidant effect consisting in the increment of hydrogen peroxide in the culture medium [10,11]. Therefore, we suggest that at low doses 3,4-DHPEA prevents the cancer initiation by protecting DNA damage induced by oxidizing agents and xenobiotics, while anti-promotion/progression effects were observed at higher doses to which it acts with pro-oxidant mechanisms. In the last few years, many studies have supported these *in vitro* data and have further investigated the molecular mechanisms involved. These results have been effectively summarized in a recent review [12]. Animal studies also support the anti-cancer ability of olive oil PC. Among other studies, we have recently demonstrated that oleuropein was capable to inhibit tumor growth and metastases dissemination in nude mice transplanted with human cancer breast xenografts [13]. In addition, we showed that this compound prevented the azoxymethane-induced colon carcinogenesis in A/J mouse [14]. Oleuropein enriched diet reduced both the pre-neoplastic lesions in different colon segments and tumor incidence in the medial segment. Interestingly, oleuropein significantly prevented also the azoxymethane-induced DNA damage in peripheral leucocytes [14].

The above reported evidences, supporting the chemo preventive potential of olive oil PC should promote further research in this field by carrying out human intervention studies. This possibility is offered by olive phenols enriched dietary supplements which are actually available on the market. In addition, these compounds may represent new class of phytochemicals for the discovery of previously unrecognized antitumor molecules which could be used for the design of functional foods.

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