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Original Contribution

Postprandial LDL phenolic content and LDL oxidation are modulated by olive oil phenolic compounds in humans

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Abstract

Olive oil phenolic compounds are potent antioxidants in vitro, but evidence for antioxidant action in vivo is controversial. We examined the role of the phenolic compounds from olive oil on postprandial oxidative stress and LDL antioxidant content. Oral fat loads of 40 mL of similar olive oils, but with high (366 mg/kg), moderate (164 mg/kg), and low (2.7 mg/kg) phenolic content, were administered to 12 healthy male volunteers in a cross-over study design after a washout period in which a strict antioxidant diet was followed. Tyrosol and hydroxytyrosol, phenolic compounds of olive oil, were dose-dependently absorbed ($p < 0.001$). Total phenolic compounds in LDL increased at postprandial state in a direct relationship with the phenolic compounds content of the olive oil ingested ($p < 0.05$). Plasma concentrations of tyrosol, hydroxytyrosol, and 3-O-methyl-hydroxytyrosol directly correlated with changes in the total phenolic compounds content of the LDL after the high phenolic compounds content olive oil ingestion. A 40 mL dose of olive oil promoted a postprandial oxidative stress, the degree of LDL oxidation being lower as the phenolic content of the olive oil administered increases. In conclusion, olive oil phenolic content seems to modulate the LDL phenolic content and the postprandial oxidative stress promoted by 40 mL olive oil ingestion in humans.
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Keywords: Olive oil; Tyrosol; Hydroxytyrosol; LDL phenolic content; LDL oxidation; Postprandial; Free radical

Introduction

There is increasing evidence that oxidative modification of low density lipoprotein (LDL) plays a key role in the development of atherosclerosis [1]. Elevated levels of oxidized LDL showed a positive correlation with the severity of acute coronary events [2] and have been considered a biochemical marker for coronary heart disease [3]. The process of LDL oxidation led to the modification of the protein moiety of LDL, directly, i.e. via myeloperoxidase-derived HOCl [4], or indirectly, i.e. via the peroxidation of the polyunsaturated fatty acids [5]. The modified apo B has immunogenic properties prompting the generation of autoantibodies against oxidized LDL [5]. Linoleic acid accounts for 90% of the polyunsaturated fatty acids (PUFA) present in LDL and is the major substrate for its oxidation [6]. Therefore, diets rich in PUFA may increase the risk of LDL oxidation. On the other hand, diets rich in oleic acid generate particles that appear to be more resistant to this process [7,8]. However, apart from its fatty acid profile, the formation of oxidized LDL depends upon its antioxidant content, such as vitamin E and phenolic compounds, present in LDL [8–10].

Besides containing high quantities of oleic acid, virgin olive oil, obtained exclusively by physical procedures, is rich in phenolic compounds. In animal and in in vitro studies, olive oil

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phenolic compounds have been shown to be strong antioxidants protecting lipids from oxidation [11–14]. The biological activities of olive oil phenolic compounds have prompted several studies on their potential activity in the prevention of cardiovascular diseases and cancer. However, controversial results have been obtained in the randomized, cross-over, controlled human in vivo studies performed on the olive oil phenolic compounds antioxidant capacity [15–18]. Tyrosol (T) and hydroxytyrosol (HT) are the main olive oil phenolic compounds which are present as free or conjugate forms as secoroids or aglycones [19].

Postprandial lipemia has been recognized as a risk factor for atherosclerosis development as it is associated with oxidative changes [20,21]. After a high-fat meal an oxidative stress occurs impairing endothelial function [22]. However, the consumption of fatty meals with suitable sources of antioxidants, such as red wine [23], vitamin C [24], or antioxidant drugs such as simvastatin [22], minimizes this postprandial oxidative stress. In this report, through a randomized, cross-over, controlled study, we describe the impact of three similar types of olive oils, but with differences in their phenolic content, on the postprandial oxidative stress and the antioxidant content of the low density lipoproteins (LDL).

Subjects and methods

Subjects and study design

Twelve healthy male volunteers were recruited, with a mean age of 21.2 years (range 20–22 years), and a mean body mass index of 22.9 (range 20.8–31.6 kg/m^2). Subjects were considered healthy on the basis of physical examination and routine biochemical and hematological laboratory determinations. The protocol was approved by the CEIC-IMAS Ethic Committee. The protocol was fully explained to the participants before they gave their written informed consent.

Each subject was tested three times in a randomized cross-over, double-blind manner with regard to the administration of 40 mL of olive oil with low (LPC, 2.7 mg/kg), medium (MPC, 164 mg/kg), and high (HPC, 366 mg/kg) phenolic compounds content. The amount of phenolic compounds administered with the 40 mL olive oil dose was: 0.097 mg, 5.92 mg, and 13.2 mg, for LPC, MPC, and HPC olive oil, respectively. Two Latin squares of 3 × 3 for the three treatments were used to randomize participants into six orders of olive oil administration. Prior to each intervention volunteers followed a 10-day washout period. During the first 7 days of the washout period participants were asked to avoid excessive antioxidant intake. During the last 3 days before the day of the intervention (days 8–10 of the washout period) they followed a strict phenolic compound-low diet (Fig. 1). A nutritionist instructed them on excluding several foods, rich in phenolic compounds, from their diet (vegetables, legumes, fruit, juice, wine, coffee, tea, caffeine-containing soft drinks, beer, cacao, marmalade, and olives). LPC olive oil was given to the participants for raw and cooking purposes (including supplies for the family) during washout periods, and for cooking purposes in the intervention day. Daily dietary records were obtained from each volunteer. At 8 a.m., after an overnight fast, volunteers were provided with 40 mL of one of the three olive oils, which was administered as a single dose accompanied by a standard piece of bread. The 40 mL olive oil dose was the sole source of olive oil or antioxidants during the intervention day. Venous blood was collected in tubes containing 1g/L EDTA at baseline of each intervention period (0 h) and at several periods after olive oil administration. Plasma was obtained by centrifugation of blood at 1500 × g at 4°C for 20 min. Aliquots of the plasma samples were mixed with 3,5-di-tert-butyl-4-hydroxytoluene 100 μM to avoid auto-oxidation and stored at −80°C until analyzed. All biochemical and analytical determinations were performed in duplicate.

Nutrient intakes were calculated from the daily dietary records of each intervention period and the three previous days of the washout periods by a nutritionist using the software MediSystem 2000 (Conaycyte S.A, Madrid, Spain).

Measurement of tyrosol, hydroxytyrosol, and 3-O-methyl-hydroxytyrosol, in plasma

Tyrosol (T), hydroxytyrosol (HT), and 3-O-methyl-hydroxytyrosol (MHT) a biological metabolite of HT, were

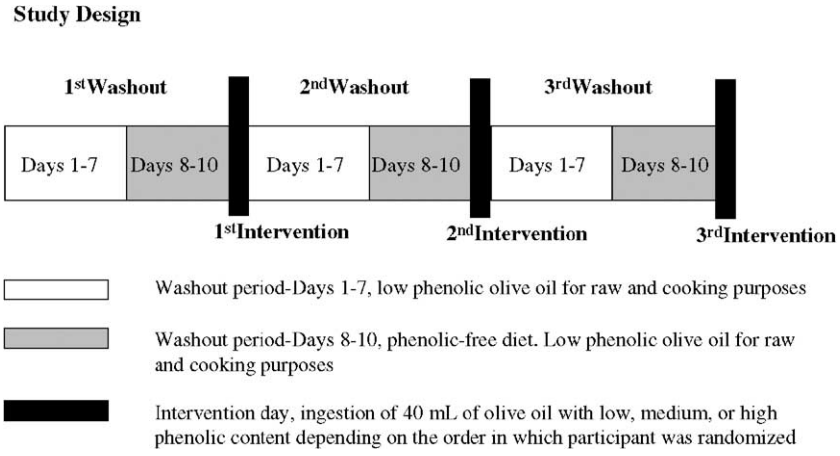

Fig. 1. Time-line showing the study design.

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