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Review Article

Is Olive Oil a Functional Food with Systemic Benefits on Pathological Conditions and Ageing by Improving Mitochondrial Functions and Antioxidant Status?

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Abstract

There are many studies examining the effect of olive oil consumption and its bioactive components on health. Experimental models and studies on volunteers, epidemiological studies, systemic reviews and metaanalyses show that olive oil consumption has a positive effect on the formation, prevention and treatment processes of many chronic diseases, mainly due to its antioxidant and anti-inflammatory effects. By preserving the mitochondrial function with its polyphenolic properties, olive oil is thought to have benefits on metabolism and maintaining the cellular structure. Similarly, it has been thought that the role of the Mediterranean diet in maintaining healthy life is based on olive oil, as an important component of the Mediterranean diet and main source of dietary fat. In this review, the systemic effects of using olive oil as a source of fat in diet or olive oil applications with experimental models have been discussed with many *in vitro*, *in vivo* and human studies.

Keywords: Antioxidant; Anti-Inflammatory; Ageing; Functional Food; Mediterranean Diet; Mitochondria; Metabolism; Olive Oil

Abbreviations

T2DM: Type 2 Diabetes Mellitus; MetS: Metabolic Syndrome; CVD: Cardio-Vascular Diseases; MD: Macular Degeneration; P1NP: Procollagen Type 1 N-Terminal Propeptide.

Introduction

Olive is a fruit which consists about 50% chemically water, 1.6% protein, 22% fat, 19% carbohydrate, 5.8% cellulose, 1.5% ash. Pectins, organic acids and phenolic glycosides are other important components. The components or some of their hydrolyzed products are present in the fruit juice of the olive and are separated into olive oil during processing [1]. Although there are many different factors affecting the quality of olive processing, it is reported that quality of olive oil is effected olive varieties (20%), fruit maturity (30%), harvest (5%), storage before transport and processing (15%) and processing (30%)[2]. Natural olive oil contains highly monounsaturated fatty acids as well as natural antioxidant compounds such as vitamins, carotenoids, aliphatic, diterpenic and triterpenic alcohols, hydrocarbons, phytosterols, flavonoids and phenolic compounds, secoiridoids [3,4]. Most of the fat composition of olive oil (98-99%) is composed of triacylglycerol and it is reported that the structure of these triacylglycerols is rich in oleic acid which is known as monounsaturated fatty acid (56-84%) [5]. In general, polyphenols in olive oil have anti-inflammatory, antiproliferative, antioxidant, antimicrobial properties and have positive effects on cancer, diabetes, skin diseases, neurological and cardiovascular diseases [6].

Antioxidant properties and regulatory pathways

Antioxidant capacity, which is mainly provided by phenolic content, can be mentioned as the starting point of many effects of olive oil and Mediterranean diet on diseases. These strong antioxidant phenolic compounds function based on their chemical structure and their hydroxyl group containing molecular oxygen scavenging capacities [7]. As part of the EUROLIVE study, a 13% reduction in DNA oxidation with olive oil supplementation was reported [8]. In postmenopausal women which were treated with 50 gram/day olive oil for 8 weeks, it was reported that DNA damage in lymphocytes obtained from peripheral blood samples decreased by 30% in olive oil consumption with high phenolic content compared to

low phenolic content [9]. The Mediterranean diet enriched with natural extra virgin olive oil after 1 year of application has been reported to increase significantly in non-enzymatic antioxidant and total radical-binding antioxidant capacities compared to the basal level [10]. In a randomized controlled study in which total antioxidant capacity was shown to be associated with natural extra virgin olive oil consumption in healthy elderly, it was observed a significant increase in erythrocyte catalase activity which is an important enzymatic endogenous antioxidant mechanisms and there were significant decreases in superoxide dismutase and glutathione peroxidase levels [11].

It's well known that increased intra-cellular or extracellular reactive oxygen radicals and reactive nitrogen specifies stimulate the inflammatory response and these have closely related with different diseases such as type 2 diabetes mellitus (T2DM), liver diseases, cardiovascular diseases, metabolic syndrome (MetS), cancer or neurodegenerative diseases. Olive oil has great importance for health care on this regard [12].

High level of phenolic content decreased NF-kB, IL-1B, IL-6 levels in patients with MetS compared to olive oil with lower level of phenolic content treatments [13]. Similarly in both obesity and ageing, when the different dietary fat sources were examined, it was observed that olive oil was decreased blood pressure and improved lipoprotein profile [14]. Again as part of the PREDIMED study, in elders, olive oil-enriched Mediterranean diet decreased the circulating monocytes and CD49d, which acts as a leukocyte-targeted adhesion molecule, and CD40, which is a proinflammatory ligand, serum IL-6 and ICAM-1 compared to the low fat diet-control group [15]. Following research of same study group, olive oil-enriched Mediterranean diet decreased TNF receptors, ICAM-1 and IL-6 level which were increased with low fat diet application with one year treatment [16]. It was stated that different formulations of olive oil may be an additional food supplement that can be used for many pathological conditions with systemic and local anti-inflammatory effect, and that both existing forms and bioactive compounds and substances which may be protective by activating the physiological repair mechanisms of the body [17].

Mitochondrial benefits and metabolic effects

Mitochondria are one of the metabolic centers where the energy needs of the cell are met and the oxidative radicals produced during energy supply are cleaned. With these features, mitochondria can be said to have a role on the mechanism of cell survival and apoptosis as the main area where metabolic events occur. Maintaining mitochondrial membrane potential is also important to provide gradients for ATP synthesis. It is well known that oxidative stress during ageing or chronical diseases is the main reason for impaired mitochondrial metabolism [18,19]. There are different studies showing the effects of olive oil on antioxidant status and mitochondrial functions. Extra virgin olive oil and sunflower olive oil have been shown to have an impact on rats in terms of life-long nutrition. Although there is no difference in survival between the two groups, the olive oil group has low aging parameters such as plasma cholesterol, triglycerides, phospholipids, total lipids, polyunsaturated fatty acids and DNA double strand breaks [20]. Following to this research, same study group showed that mitochondrial oxidative stress levels in the liver of elderly rats fed with extra virgin olive oil were lower than those fed with sunflower oil. In addition, both animal groups had increased mitochondrial DNA deletions due to aging, but were lower in the virgin olive oil group than in the sunflower group [21].

In the review of Rigacci and Stefani, the protective effects of oleuropein which is the one of the phenolic compounds in olive oil against the components of the metabolic syndrome, are mentioned as reduction of intracellular TG deposition, prevention of oxidative damage in pancreatic B cells and liver, reduction of visceral adipocyte. The beneficial effects of hydroxytyrosol are stated as increasing mitochondrial biogenesis and function [6]. 191 volunteers with a high cardiovascular risk between the ages of 55-80 were included in the study which examined the effects of olive oil consumption on Type 2 DM under PREDIMED study. HOMA-IR, adiponectin/leptin and adiponectin/HOMA-IR indices were measured 1 year after dietary interventions. Adiponectin/HOMA-IR ratio and body weight loss were reported to be significantly higher in the olive oil group compared to the other groups[22]. 59,930 women from the NHS study in the United States and 85,157 women from the NHS-II study were evaluated every 22 years for eating habits (especially olive oil consumption). It was observed that with every 8 grams of olive oil adding to the diet, the incidence of Type 2 DM decreased by 6% [23]. Mediterranean diet has positive effects on T2DM and MetS. According to the data collected from many studies, it is thought to have a more positive effect on T2DM and MetS compared to low fat diets due to the presence of olive oil in the Mediterranean diet [24]. Olive oil polyphenols have been suggested in different studies that it may reduce the risk of central obesity by reducing adipocyte differentiation and lipogenesis and inducing lipolysis and adiponectin secretion, hyperglycemia by increasing insulin secretion and sensitivity, hypertension by regulating lipid profile and increasing nitric oxide release. Furthermore, it may decrease hyperlipidemia by increasing plasma HDL concentration and by decreasing plasma total cholesterol-LDL-TG and also lipid peroxidation by showing antioxidant activity [25-28]. In another study, it was explained that the positive effect of hydroxytyrysol which is the major phenolic compound of olive oil. Endothelial dysfunction which was created with inflammatory stimulation by phorbol myristate acetate were treated with hydroxytyrosol. Hydroxytyrosol reversed the harmful effects on inflammed cell by reducing mitochondrial superoxide production, oxidation of lipids and elevating superoxide dismutase levels. Also, it was observed that hydroxytyrosol improved on mito-

chondrial membrane potentials, ATP synthesis and ATP5B expressions [29].

Anti-aging properties, bone metabolism and skin health

Due to the increasing elderly population in the world, the prevention and treatment of common diseases in old age have started to attract more attention. Hypertension, Type 2 Diabetes, heart failure, dementia, osteoporosis, respiratory problems, cataract, macular degeneration and infection are some of the common diseases. It is thought that the studies examined in the review published in 2015 reveal that elders consuming olive oil are healthier and have a longer life [30]. In the study which included 654 participants, regular consumption of olive oil significantly reduced the risk of late macular degeneration (MD). However, regular olive oil consumption was not significantly associated with the risk of early MD [31].

In a review by Garcia-Martinez., *et al*. It is stated that olive oil reduces oxidative stress that plays a role in the pathogenesis of osteoporosis, contributes to the maintenance of DNA repair mechanism, and may have an impact on bone health as it increases proliferative capacity [32]. In the cohort study of the PREDIMED project investigating the effect of extra virgin olive oil on the incidence of osteoporotic fractures, the feeding habits of 870 individuals were questioned and followed for 8.9 years. The risk of occurrence of osteoporotic fracture in the highest consumption of natural extra virgin olive oil (55.5 ± 4.62 g/day) was 51% lower comparing to the lowest consumption (28.77 ± 10.27 g/day) [33]. Also, in another study, Osteocalcin and P1NP (Procollagen Type 1 N-terminal propeptide) levels of the individuals in the natural extra virgin olive oil group increased significantly compared to the control group [34]. The 8-year follow-up study of 4421 participants with a mean age of 60 in North America by Veronese., *et al*. showed that the incidence of fragility was significantly lower in individuals with the highest compliance with the Mediterranean diet [35]. However, in France with 1,482 individuals aged 67+, it was shown that there was no evidence that compliance with the Mediterranean diet could reduce the risk of hip, vertebral and wrist fractures[36]. Total bone density, trabecular bone density and cortical bone density of female individuals with high olive oil consumption (> 18.32 g/day) were found to be significantly higher than those of the groups with low olive oil consumption [37]. Studies have shown that olive oil consumption reduces osteoporosis and osteoporosis-related fractures, especially in postmenopausal women.

Skin is a tissue that sensitive to oxidative stress, atmospheric pollution, ultraviolet rays and diseases. Depending on all these negative factors; it has been thought that skin is under the high risk of impaired structure-function, aging and cancer [38]. It is possible to see studies on the effects of olive oil on skin aging besides cognitive effects in aging. In the study, which included 2919 individuals, it was found that individuals with high consumption of monounsaturated fatty acids had lower level of skin aging [39]. It was found that increased ROS and inflammatory response due to pressure ulcers were decreased by the antioxidant effect of olive oil and recovery was accelerated by increasing collagen deposition and re-epithelialization in ulcers. Local application of olive oil has been shown to have positive effects in many wound models, diabetic foot treatment and pressure ulcers [40-42].

Conclusion

Oxidative damage is a major contributor to the development of chronical diseases and ageing. In healthy individuals, the generation of reactive oxygen species is balanced by the counterbalancing act of antioxidant defenses. Olive oil is one of the important dietary and functional source to the balance of oxidative status. Olive oil's beneficial effects are not only related to its high content of oleic acid, but also to the antioxidant potential of its polyphenols. The free radical theory of ageing and chronical diseases argues that free radicals produced in the mitochondria are responsible for the damage that affects systematically. It was concluded with this literature review that olive oil intake is related to lower mitochondrial oxidative stress and improvement of antioxidant capacity which leads to healthier metabolic pathways.

Conflict of Interest

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version. Additionally, there are no conflicts of interest in connection with this paper, and the material described is not under publication or consideration for publication elsewhere.

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