Chapter

Olive Phenomenon from the Mediterranean Diet: Health Promotion via Phytochemicals

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Abstract

The Mediterranean Diet contains fruits, vegetables, nuts, whole grains, fish and virgin olive oil (VOO) as a key component. It is well explained that those consumption has a number of positive health effects. It has been accepted for a long time that the leading compound in olive was oleic acid as a monounsaturated fatty acid. However, the latter researches were figured out that VOO rich in natural phenolics have multifaceted influence on major diseases including cancer, diabetes, cardiovascular diseases, neurodegenerative disease, and metabolic disorders. Recent medical studies proved that oleocanthal and oleacein, characteristic bioactive biophenol-secoiridoids in VOO, success in the anti-inflammatory and in the antioxidant properties, respectively. It has more recently investigated that oleocanthal and hydroxytyrosol (HT) kills cancer cells (CCs). HT and oleuropein reduces breast cancer and cutaneous melanoma cancer cells both in number and aggressiveness, and inhibits CCs multiplying. It has been declared too many times that nutrition type is the strongest factor can be caused acute and chronic diseases. However, at the same time, nutrition can also prevent some of those heavy symptoms. The main purpose of presented chapter is to meet olive's bioactive molecules and to examine how to improve our health with diet.

Keywords: phytochemicals, health, olive, virgin olive oil, bioactive compounds

1. Introduction

Olea europaea is naturally cultivated in Mediterranean region. It's drupe fruit (olive), flowers & leaves, seeds, fibers and some of by-products (liquid and solid wastes) are used technologically by humans live in there, and also, this is an agricultural & economic culture of Mediterranean populations (Spain, Turkey, Greece, Italy, Morocco, Tunisia, in particular). However, olive oil is also produced in Australia and the USA and basically [1] consumed European Union Countries, United States, Turkey and China (**Figure 1**). The olive oil is the best demonstrated product that examined both its nutritional and medicinal properties. Ancient historical evidence recommended using VOO for stomach health and against to dermatological ulcer.

Nutritional quality of olives depends on various factors. Cultivar, genetic and biologic factors, soil structure, climatic conditions, harvest time, agricultural applications and extraction type are the most effective parameters [2]. These are

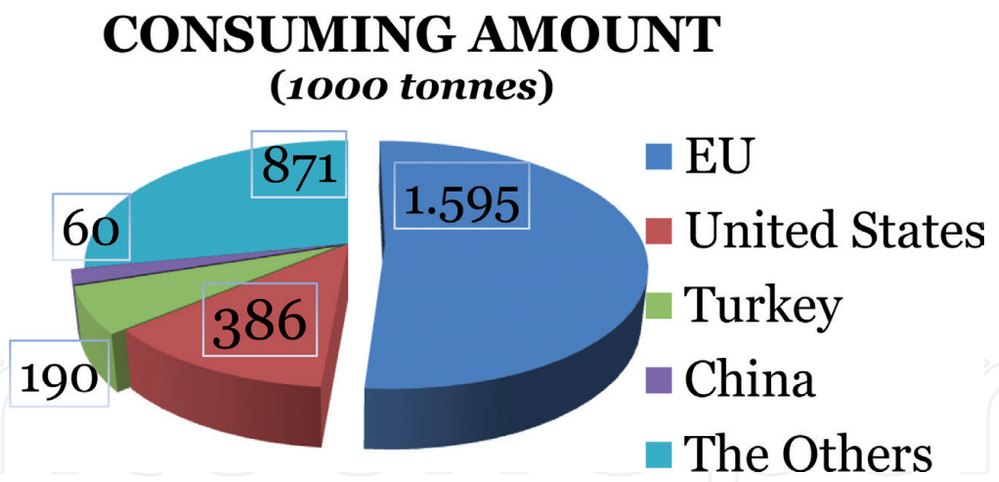


Figure 1.
Leading consumers of olive oil worldwide from in 2020/2021.

also influence on the olive oil quality and its chemical composition. Free acidity determines chemical subtype of olive oils such as lampante, virgin, extra virgin, etc.

The edible oils are commonly well-known due to their unsaturated fatty acids and phenolic profiles. In particular, olive oil is rich in both monounsaturated fatty acids and polyphenols. These attributes basically related to consumption of the Mediterranean Diet. One tablespoon of olive oil contains approximately 120 kcal composed of 10 g monounsaturated lipid. The most important of polyphenols are phenolic acids such as ferulic and vanillic acids, phenolic alcohols like hydroxytyrosol and tyrosol, flavonoids and secoiridoids such as oleuropein [3].

Olive oil is contains triacylglycerols as major components (98–99%) and contains small quantities of free fatty acids, glycerol, phosphatides, pigments, flavor compounds, and sterols as minor components (1–2%). Approximate fatty acid composition of olive oil as fallows: 14–15% saturated fats (13% palmitic acid-C16:0 and 1–2% stearic acid-C18:0) and 85% unsaturated fats (60–70% oleic acid-C18:1, also known as ω-9 and 12–15% linoleic acid-C18:2, also known as ω-6 fatty acid, and 3% palmitoleic acid). This profile shows us olive oil composed of more monounsaturated than polyunsaturated fatty acids and it is free of trans (E-) form of fatty acids. Previous researches indicated that a higher proportion of monounsaturated fatty acids in diet cause a strong reduction in the cardiovascular disease (CVD) risks.

The polyphenols are natural antioxidants that link oil's bitter taste and astringency. Moreover, they raise the resistance capacity against to oxidation. The bioactive compounds namely phenolic antioxidants (oleic acid, squalene, terpenoids), simple phenols (hydroxytyrosol, tyrosol), secoiridoids (oleuropein, aglycone of ligstroside, and their respective decarboxylated dialdehyde derivatives, oleacein, oleochantal) and lignin, vitamin E contribute to oil different biologic character such as antitumor, antimicrobial and antioxidant effects via possible pathophysiological pathways generally associated with a decreased risk in breast, colon and skin cancer. It needs to be noted that the quantity of these bioactive molecules depends on many factors such as olive variety, environmental factors (altitude, cultivation practices), harvest time (unripe, semi, ripe olives the extraction and storage conditions [4].

Here, in this chapter, phytoactive compounds found in olive are determined chemically and then biologic mechanisms are described how they prevent us some chronic diseases.

2. Phytochemicals

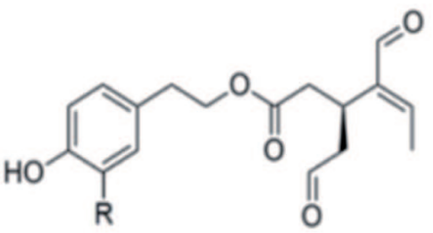
2.1 Phenolics and tocopherols

The presences of phenolics and tocopherols affect radical scavenging activity and so, antioxidant capacity of olive oil. These chemicals also considered as a functional food component, contains different classes of phenols: simple phenols, phenolic acids, phenolic alcohols, secoiridoids, lignans, and flavonoids. According to EFSA [5], molecules from olive (hydroxytyrosyl and oleuropein complex) have beneficial effects on human health. The consumption of this complex approximately 2–15 mg/day is essential. The vitamin E is a fat-soluble vitamin and is composed by α-, β-, γ and δ-tocopherols and α-, β-, γ- and δ-tocotrienol isomers. α-tocopherol has the highest antioxidant activity in fat-riched foods. Moreover, vitamin E and phenol mixtures are very promising oil stabilizing agent during frying, thanks to its capacity to reduce acrolein and acrylamide production. According to EFSA's current scientific opinion [6] an average requirements of α-tocopherol could be 11–13 mg/day for adults. Extra virgin olive oil contains 100–760 mg/kg α-tocopherol [7, 8].

Mediterranean country peoples demonstrate a long life and lower case of the age-related diseases due to their food habits. Thus, the consumption of extra virgin olive oil has been clinically and experimentally associated with the health promoting properties of the Mediterranean diet. Extra virgin olive oil is characterized by a high amount of polyphenols as miracle pharmanutritional properties against to the development of several chronic diseases such as cardiovascular diseases, diabetes, obesity, metabolic syndrome and cancer. Squalene is a hydrocarbon composed in olive oil and acts as a weak antioxidant affect. Especially, its importance comes from the protective effect under heating against to the oxidative stress. Besides, the squalene quantity varies between 2 and 7 g/kg of olive oil. Scientific papers prove us the health benefits of squalene and its influence capability on cancer cells [9–11]. Meanwhile, tocopherols have attracted tremendous attentions because of their potential roles in preventing aging-associated diseases such as cardiovascular and Alzheimer's disease [12–14]. Oleacein and oleochantal (**Figure 2**) are among the major phenolics determined in virgin olive oil. These are the dialdehydic forms of the elenolic acid deriving from oleuropein and ligstroside, respectively. They have positive role in the treatment of cardiovascular pathologies, certain types of cancers, chronic inflammatory diseases, Alzheimer's disease, Helicobacter pylori infection [14]. Cutaneous melanoma is a type of cancer that is spreading in Europe. The relation between melanoma risk and consumption of olive oil has been recently studied. Oleuropein, the main secoiridoid glucoside present in the *Olea europaea* leaves have already been investigated in melanoma *in vitro* and *in vivo* models revealing their cytotoxic activity and anticarcinogenic action. Oleacein, another abundant secoiridoid in olive and leaves show antitumor activity via controlling the altered pattern of gene expression (transcripts and miRNAs) related to mTOR and BCL2 pathways in melanoma cells. Hydroxytyrosol, the most representative simple phenol of *Olea europaea* L. leaves and virgin oils, causes inhibition of melanoma cell proliferation activating caspase-3-dependent apoptosis [15, 16].

2.2 Phytosterols

Phytosterols, in other words plant sterols, are bioactive compounds of seeds, fruits, cereals, and nuts. They can be found in free form, esterified with fatty acids or conjugated with glycosides. Campesterol, β-sitosterol and stigmasterol are the most common phytosterols. Phytosterols are by-products of isoprenoid biosynthesis



R: -OH

Oleacein

Synonyms:

3,4-DHPEA-EDA,

Dialdehydic form of decarboxymethyl oleuropein aglycone,

Dialdehydic form of elenolic acid linked to hydoxytyrosol

R: -H

Oleochantal

Synonyms:

p-HPEA-EDA,

Dialdehydic form of decarboxymethyl ligstroside aglycone,

Dialdehydic form of elenolic acid linked tyrosol

Figure 2.
Chemical structure of Oleacein and Oleochantal.

pathway via squalene from acetyl coenzyme A. Its generation cascade involving more than 30 enzymes catalyzed reactions in similar cholesterol biosynthesis within cell membranes. All phytosterols contain one double bond at carbon-5 position and saturation of this double bond occurs either enzymatically in vivo or through hydrogenation. Both β-sitostanol and campestanol are the two most common stanols. In olive oil, they are esterified with fatty acids like esters of sitostanol (sitostanyl oleate) and esters of campestanol (campesteryl oleate). Human cells cannot synthesize those endogenously, so we have to obtain them from our diet. The daily intake of plant stanols (saturated sterols) is about 25 mg/day compared to sterols ranging from 150 to 400 mg/day which include 65% of intake as β-sitosterol, 30% as campesterol and 5% as stigmasterol. The maximum values of campesterol, stigmasterol and β-sitosterol were found in different types of olive oil 34.46 mg, 29.56 mg and 259.46 mg/100 g oil, respectively. Serum phytosterol level in humans should range from between 2.9 and 17.0 mg/L. Phytosterols are alcohols for organic chemistry, resemblance to cholesterol both in structure and in function. Their function in plant cells is to regulate the fluidity and permeability of cell membranes in a way similar to cholesterol in cell membranes of mammals. They can inhibit the absorption of cholesterol by its direct displacement from micelles. This reported as the cholesterol-lowering effect of phytosterols in humans. Additionally, phytosterols and their derivatives have high health benefits related to antiinflammatory, antiulcerative, antitumor, antibacterial, and cardioprotective properties [17–23].

2.3 Chlorophyll and carotenoids

The minor contents in olive oil give to its characteristic organoleptic and nutritional features. Among them, color pigments play an important role in oxidative stability during storage and in the preservation of its quality because of their antioxidant characteristics and prooxidant roles under light. The pigments used as indicators to indicate olive oil freshness or storing conditions. For example, low amount of pheophytins show a fresh, well-stored olive oil, while high presence of those indicate an old, bad-stored oil [24, 25]. Pigments are divided into two main

groups in foods namely carotenoids and chlorophylls. Chlorophylls are responsible for the greenish color of extra virgin olive oil. On the other side, β-carotene, lutein, zeaxanthin and xanthophylls called carotenoids are natural antioxidants found in various amount in olive oil. They have beneficial properties for human health. β-carotene appears to lower the risk of heart diseases, while lutein protects the eye retina from oxidative damage. Some other studies were showed that carotenoids exhibit bioactivities in photosynthesis, special antioxidant properties and produce improvements in cognitive function and cardiovascular health [26–30].

3. Clinical and experimental studies on chronic diseases

The potential health advantages caused by olive oil consumption, particularly within the context of the Mediterranean diet, have been extensively investigated. As mentioned before, olive oil consumption was found to be beneficial for some of chronic non communicable diseases [31]. Below-explained clinical results are also given in **Table 1** with references.

Scope	Outcomes	References
Olive oil consumption and cancer risk	It can decrease the risk of upper digestive and respiratory tract neoplasms, breast and colorectal cancer sites	Pelluchi et al. [32]
Whether olive oil or MUFA intake was associated with the development of cancer	Olive oil intake has a protective role on cancer risk. But, it was not clear which component is responsible for the beneficial effects	Psaltopoulou et al. [33]
MUFA effect on CVD and mortality	VOO reduced risk of all-cause mortality, CV mortality, stroke	Schwingshackl Hoffman [34]
VOO intake and CHD & stroke risks correlation	VOO intake had a significant protective effect	Martinez-Gonzalez et al. [35]
Determine inflammation or endothelial effect of olive oil	Olive oil might be exert benefical effects on endothelial function and markers of inflammation and endothelial function	Schwingshackl et al. [36]
VOO with high phenolic content, CVD effect and Nutraceutical prevention	Provides small benefical effect on systolic blood pressure and serum oxidative status. Considered as nutraceutical in CV prevention	Hohmann et al. [37]
Breast cancer risk and dose–response	Olive oil might be a protective factor for the cancer occurrence among case–control studies	Xin et al. [38]
To compare olive and other edible oils effects on blood lipid level	VOO intake decreased serum total cholesterol, LDL and triglycerides less but increased HDL more than other plant oils	Ghobadi et al. [39]
High versus low polyphenol content on CVD risk factors	olive oils contains high polyphenol show some CVD risk reductions	George et al. [40]
To illustrate the impact of olive oil on type II diabetes	Olive oil intake could be benefical for the prevention and management of type II diabetes	Schwingshackl et al. [41]
to investigate effects of 2 oil blends phytonutrient concentrations on blood lipid profile, compared with refined olive oil as a control	borderline hypercholesterolemia extent as refined olive oil	Haldar et al., [42]

Table 1.
Experimental and clinical studies about olive, nutrition and health [32–42].

3.1 Cardiovascular diseases (CVD)

A comprehensive work included 101,460 cases of Coronary Heart Disease (CHD) and 38,673 cases of stroke participants revealed that after every 25 g increase in olive oil consumption, the risk of CHD was reduced by approximately 4%, while the risk stroke was decrease by 26%. Another research aimed to assess the consumption of monounsaturated fatty acids and olive oil intake on human mortality was applied 32 sample group contains total 841,211 cases. Overall, higher oil intakes lead to a lower risk for all-cause mortality, cardiovascular mortality, cardiovascular events and stroke. On the other hands, the other lipid origin such from animal had no significant positive effect on morbidity and mortality in this work. A research including 3106 individuals search try to detect the potential mediators of the olive oil/CVD relationship. The daily consumption between 1 mg and 50 mg resulted in a significantly more pronounced decrease in C-reactive protein and interleukin-6. The other study examined the effect of high versus low concentration of polyphenol in olive oil on CVD risk factors in clinical trials. It was found that high polyphenol olive oil has beneficial effects on malondialdehyde, oxidized-LDL, total cholesterol and HDL cholesterol, suggesting that olive oil may have cardioprotective properties. A comparative research, which aimed to explain the effects of olive oil or some of other edible oils consumption on blood lipids, showed that olive oil intake significantly diminish total cholesterol, LDL and triglyceride less, but increased HDL more than the others. Chronic kidney disease (CKD) is one of the most common chronic degenerative diseases and it carries a considerable risk factor for CV disorders and mortality. Noce et al., [43] study shows that daily use of high phenolic contents from extra virgin olive oil contributes anti-inflammatory and antioxidant action in nephropathic patients. Consequently, the essential role has been highlighted again here that a well-balanced nutritional-diet therapy plays in the clinical management of CKD cases and the eventual improvements in patient's life style, performing positive effects on CKD symptoms.

3.2 Cancer

There are too actual clinical meta-analysis researches. They are mainly focused between olive oil consumption and various cancer types. 37,140 participants from 19 case–control studies were revealed that extra virgin olive oil intake was associated with low probability to have any type of cancer, compared with the lowest quality of olive oil intake. The other study evaluated the effect of olive oil consumption on breast cancer risk. The results stated that olive oil can decrease the risk of breast cancer as well as other types of cancer. Another comprehensive research, included 150,000 females from 5 cohort and 11 retrospective case control studies, demonstrated that higher olive oils consumption showed a protective effect against breast cancer. Some clinical studies show that the mixtures of phytosterols have inhibitory effect on 5α-reductase, give rise to apoptosis, alter testosterone metabolism, change urine flow and prostate volume. On the other hand some other experimental studies explain that phytosterols prevent lipoprotein oxidation, inhibit cell growth and the expression of caveolin-1, decrease cell proliferation, reduce or inhibit hyper proliferation of colonocytes, reduce in tumor size. These are the various mechanisms to express anticancer features from phytosterols of olives and olive oils [19, 44]. More recently, Bartolomei [45] provides a huge dataset to characterize of olive oils antioxidant properties, both in vitro by Trolox equivalent antioxidant capacity, oxygen radical absorbance capacity (ORAC value), ferric reducing antioxidant power (FRAP value), and 2,2-diphenyl-1-picrylhydrazyl assays, and at the cellular level in hepatic (HepG2) and intestinal (Caco-2) cells. One of the highlighted results of this

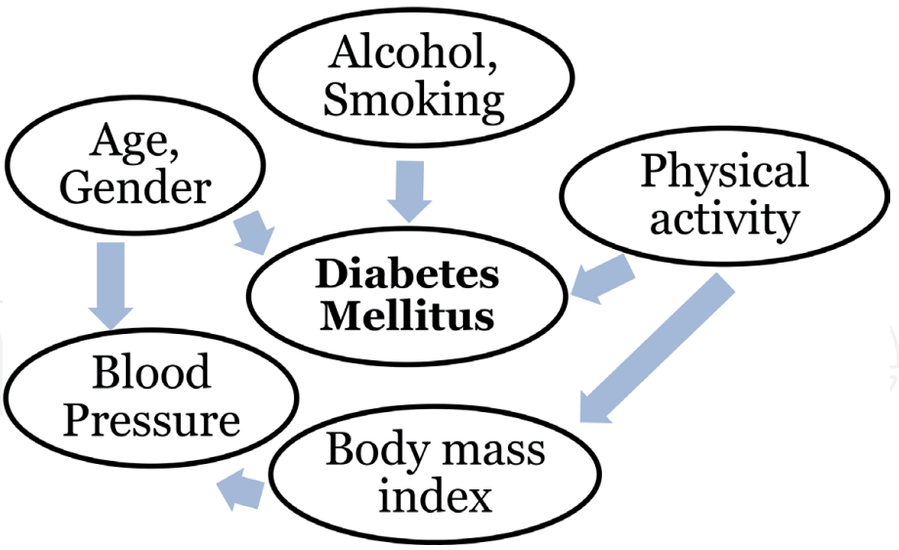


Figure 3.
Risk factors in diabetes mellitus.

study was to determine the antioxidant effects of phenolic compounds in an extra virgin olive oil (EVOO) extract, using either in vitro assays or liver and intestinal cell models, rather than the effects of single phenols, such as hydroxytyrosol or oleuropein. The selective trans-epithelial transport of some oleuropein derivatives was observed for the first time in differentiated Caco-2 cells in this research.

3.3 Type II diabetes

Risked factors for diabetes Mellitus (DM) has been described [46] as fallows: physical inactivity, first degree relative with DM, members of high-risk ethnic populations (such as African Americans, Latinos, Native Americans, Asian American and Pacific Islanders), women who delivered baby, hypertension, HDL cholesterol <35 mg/dL, triglycerides >250 mg/dL, women with polycystic ovary sendrome, HbA1C ≥ 5.7%, impaired glucose tolerance, ımpaired fasting glucose, obesity, insulin resistance and finally history of CVD (**Figure 3**). It was proved that 10 g daily increasing intake of olive oil was caused 9% reduced risk of type-II diabetes, while when the highest quality olive oil intake category was compared to the lowest quality intake category, it was revealed a 16% reduced risk of diabetes. This meta-analysis collected data from 187,068 individuals, participating in 4 cohort studies and 29 trials. Therefore, this meta-analysis provides beneficial evidence concerning the risk of type II diabetes consuming olive oil [42].

4. Conclusion

In biological systems, free radical reactions are associated with aging, cancer, cardiovascular disease, optical disease, and neurodegenerative disease. Antioxidants are used to prevent such reactions and are therefore supporting health. Regular consumption of olive oil has a strong correlation with prevention of cardiovascular disease, immune function, and gastrointestinal (GI) disease. Olive oil improves the curing of mortal diseases like cancer and liver disease. Dietary use of olive oil is therefore helpful in maintaining good health. The present chapter evaluating the effect of olive oil consumption on human health, identified the protective effects

of olive oil on all-cause and cardiovascular mortality, as well as on cardiovascular events. Olive oil consumption exhibits a protective role against overall and particularly breast cancer occurrence, as well as diabetes mellitus type 2. In general, benefits which have been recorded from the intake of pure olive oil have also been recorded from the adoption of a health-promoting lifestyle, based on the principles of the Mediterranean diet. Diets including plants foods, fish, and seafood and preferably including plant oils and low-fat dairy products are associated with a lower risk of most chronic diseases. In conclusion, the aggregated evidence corroborates that the specific impact of olive oil consumption is beneficial for human health, and particularly for the prevention of cardiovascular diseases, several cancers, and diabetes mellitus.

Conflict of interest

The author declares no conflict of interest.

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