Olive Plant (Olea europaea L.) Compounds for Human Nutrition and Health

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**Abstract**

The olive oil is one of the bases of the Mediterranean Diet, widely studied for its antioxidant benefit, particularly given to the large number of phenolic compounds present in the olive tree. Olive leaves contain phenolic compounds; the oleuropein, hydroxytyrosol, verbascoside, apigecin-7-glucoside and luteolin-7-glucoside are the most abundant already identified in olive leaf extracts. The large number of phenolic compounds present in olive leaves reported beneficial health effects such as the capacity of antioxidant, antihypertensive, hypoglycemic, hypcholesterolemic, cardioprotective, anti-inflammatory and as coadjuvant in the treatment of obesity. Oleuropein has an antihyperglycemic, lipid-regulating, and cardioprotective effects especially in cell culture and animal models. Olive leaf (Olea europaea L. folium) is used in many fields including pharmaceutics, cosmetics, and food industry. Olive tree includes secoiridoids, carbohydrates, sugar alcohols, and terpenoids as biochemicals. Basic components in olive leaf are secoiridoids such as oleuropein, ligstroside, 1-methyloleuropein, and oleoside; flavonoids such as apigenin, kaempferol, luteolin, and chrysoeriol; and phenolic compounds such as caffeic acid, tyrosol, and hydroxytyrosol.

Secoiridoids, chemical components of leaf, are glycosidically bound and produced by secondary metabolisms of terpenes as the pioneers of various indole alkaloids. Secoiridoids are generally derived from an oleoside type of glucoside oleosides that are characterized with the combination of elenolic acid and glucoside residues. Olive leaves extracts have health benefits, such as increasing energy levels, lowering blood pressure, and supporting the cardiovascular and immune systems. Olives contain many potentially bioactive compounds having anti-oxidant, anti-inflammatory, antiviral, and hypcholesterolemic proper-ties. Olive leaves are important for their content in secondary metabolites, in particular the secoiridoid derivatives oleacein and oleuropein, the former being responsible for the hypotensive and hypoglycemic activities.

Hydroxytyrosol and oleuropein inhibited the platelet aggregation and eicosanoid production, regulate blood flow, and reduce the coronary heart disease risks. Oleuropein has potent antiviral activities against herpes mononucleosis, hepatitis virus, rotavirus, bovine rhino virus, canine parvovirus, and feline leukaemia virus. Investigations have been also focused on anti-HIV effect of olive leaves. Oleuropein and hydroxytyrosol were the first group of small molecules capable of multiple actions against the AIDS virus, inhibiting both viral entry and integration both outside and inside of the cellular environments offering unique benefits to these small molecules against viral resistance. Phenols in olive oil have inhibitor effects on LDL (low-density lipoprotein) oxidation and it is recently known that olive leaves are the richest source of these phenols. Olive leaf extract was suggested to be protective against cardiovascular diseases due to effects on adrenaline, and arrhythmia and intestinal muscle spasms. Olive leaf extract possessed an inductive effect on mouse liver glutathione S-transferases and had a potential inhibitory effect on tumor necrosis factor, suggesting usage in allergic diseases. Olive leaf extracts and oleuropein are known to act on diabetes by at least two mechanisms: increased peripheral glucose utilization and improved glucose stimulated insulin release. Olive leaves were especially effective against Klebsiella and Pseudomonas, two bacterial genera which pose major resistance problem and had antimicrobial effect against Escherichia coli and Candida albicans.

Olive leaf extract is signified as a part of natural medicine with a wide range of health benefits. It has been used traditionally as an herbal supplement because...
it contains polyphenolic compounds with beneficial properties such as increasing energy levels, lowering blood pressure, and supporting the cardiovascular and immune systems.

**INTRODUCTION**

The olive tree (Olea europaea L.) is cultivated in many parts of the world, but the Mediterranean region is the main area of agricultural production, it represents approximately 98% of the growing around the world. Apart from the Mediterranean region, the olive tree is cultivated on a large scale in the Arabian Peninsula, India and Asia (Somova et al., 2003).

The olive oil is one of the bases of the Mediterranean Diet, widely studied for its antioxidant benefit (Japon-Lujan et al., 2006), particularly given to the large number of phenolic compounds present in the olive tree. However, the olive leaves also contain phenolic compounds; the oleuropein, hydroxytyrosol, verbascoside, apigenein-7-glucoside and luteolin-7-glucoside are the most abundant already identified in olive leaf extracts. The term “olive leaves” refers to a mixture of leaves and branches from both the pruning of olive trees and the harvesting and cleaning of olives (Molina-Alcaide and Yáñez-Ruiz, 2007).

The large number of phenolic compounds present in olive leaves aroused the interest of researchers around the world and the studies with animals and humans have reported beneficial health effects such as the capacity of antioxidant, anti-hypertensive, hypo-glicemic, antihypertensive, cardioprotective (Nekooeian et al., 2007; Al-Azzawie and Alhamdani, 2006; Rafferty et al., 2015 and El et al., 2009).

Several studies have shown that oleuropein possesses a wide range of pharmacologic and health-promoting properties including antiarrhythmic, spasmylytic, immune-stimulant, cardioprotective, hypotensive, anti-inflammatory, antioxidant, and anti-thrombic effects (Hassen et al., 2015 and El et al., 2009).

Previously, oleuropein was reported to have an antithyperglycemic, lipid-regulating, and cardioprotective effects especially in cell culture and animal models (Khan et al., 2007; Al-Azzawie and Alhamdani, 2006; Rafferty et al., 2011; Jemai et al., 2008 and Bali et al., 2014).

Olive leaf (Olea europaea L. folium) is used in many fields including phar-maceutics, cosmetics, and food industry (de Bock et al., 2013). Olive tree includes secoiridoids, carbohydrates, sugar alcohols, and terpenoids as biochemicals (Guinda et al., 2015). Basic components in olive leaf are secoiridoids such as oleuropein, ligstroside, l-methyleoleu-ropein, and oleoside; flavanoids such as apigenin, kaempferol, lu-teolin, and chrysoeriol; and phenolic compounds such as caffeic acid, tyrosol, and hydroxytyrosol (EMA, 2009).

Nowadays, there has been a considerable interest in natural antioxidants from plant materials to replace synthetic ones (Salah et al., 2017). It is well known that the activity of the olive tree by product extracts in medicine and food industry is due to the presence of some important antioxidant and phenolic components to pre-vent oxidative damage (Lins et al., 2018). The olive tree has long been recognized as having antioxidant molecules, such as oleuropein, hydroxytyrosol, and tyrosol; caffeic acid; and ligstroside associated with the prevention of certain diseases (Castellano et al., 2015 and Servili et al., 2009).

The chemical composition of olive leaves varies according to origin, proportion of branches present in the extract, storage conditions, weather conditions, moisture content and degree of soil contamination (Martín-García AI and Molina-Alcaide, 2007 and Delgado-Pertiñez et al., 2000). The nutritional composition of the extract from olive leaves is strongly influenced by processing (drying and extraction) (Ahmad-Qasem et al., 2013).

In the study, the luteolin-7-O-glucoside was the most stable phenolic compound in the in vitro simulation of the digestion process (Ahmad-Qasem et al., 2014). They are rich in amino acids such as arginine, leucine, proline, glycine, valine and alanine and poor in cysteine, methionine and lysine (Martín-García et al., 2003). The greatest proportion of hemicellulose fibers are arabino-nosa type, whereas the branches have predominantly mannose (Garcia-Maraver et al., 2013). The extra virgin olive oil is produced from the fruit of the olive tree, botanically known as Olea europaea L, rich in polyphenols and known for its antioxidant capacity (Soni et al., 2006).

The total content of flavonoids and polyphenols of olive leaves was determined as 2.058 mg GAE (gallic acid equivalent) per 100 g and 858 mg CTE (catechin equivalent) per 100 g, values similar to a red grape (Makris et al., 2007).

This cell damage is related to the increased risk of chronic diseases such as cardiovascular disease and cancer (Dimitrios, 2006).

Olive tree (Olea europaea, Oleaceae) leaves have an extensive use in traditional herbal medicine with the aim of preventing and treating several diseases particularly in Mediterranean region. The related literature aims to identify the relationship between olive cultivars and diabetes, cardiovascular disease, cancer, and a number of health problems (Boss et al., 2016 and Hassen et al., 2015).

The olives are rich in polyphenols and known for its antioxidant capacity.
glycosidically bound and produced by secondary metabolisms of terpenes as the pioneers of various indole alkaloids. Secoiridoids are generally derived from an oleoside type of glucoside oleosides that are characterized with the combination of enolic acid and glucoside residues (Soler-Rivas et al., 2000).

Olive leaves extracts have reported to have health benefits, such as increasing energy levels, lowering blood pressure, and supporting the cardiovascular and immune systems (Khayyal et al., 2002; Covas, 2007; El and Karakaya, 2009).

Olive leaves contain many potentially bioactive compounds having anti-oxidant, anti-inflammatory, antiviral, and hypocholesterolemic properties (Covas, 2007). O. europaea is widely studied in nutrition research, whereas the leaves are important for their content in secondary metabolites, in particular the secoiridoid derivatives oleacein and oleuropein, the former being responsible for the hypotensive and hypoglycemic activities.

It has been shown that the qualitative and quantitative phenolic composition of the olive tree strongly differs among cultivars, plant parts and environmental conditions (Techathivanan et al., 2014).

It can be hypothesized that the significant differences observed for total phenols and flavonoids may be related both to genetics and to the geographical origin (Kallithraka et al., 2004; Felhi et al., 2016).

The results on total phenols and flavonoids contents support the observed activity of the extracts against free radicals (Felhi et al., 2016).

In other scientific report Blasi et al. (2016) reported that the highest total phenols values were found in June for all cultivars. so we can conclude that phenol content showed marked variations with plant growth, in fact probably the phenol storage in the leaves is a time dependent regulated process, according to the life cycle of olive leaves. In addition, Özcan et al. (2019) demonstrated that fatty acid composition and phenols contents of the olive oils showed differences depending on the olive variety.

Akbas, et al. (2017) reported that The highest total phenol contents were found in olive leaves heated in microwave 540 W and atmopheric air.

Hydroxytyrosol, tyrosol, 4-hydroxybenzoic acid, rutin, luteolin-7-O-glucoside, apigenin-7-O-glucoside, oleuropein, apigenin and catechin hydrate. All these compounds were previously characterized in olive leaves (Meirinhos et al., 2005; Sahin and Bilgın, 2012).

Rocchetti et al. (2019) reported that homogenizer-assisted extraction using methanol 100% produced an extract of M. oleifera leaves with the highest amounts of phenolic compounds.

Techathivanan et al. (2014) found that Olea europaea leaf extracts have antimicrobial activities against foodborne pathogens, such as S. aureus, E. coli, Salmonella spp., and L. monocytogenes, with MIC values ranging between 1.4 and 5.2 mg/ml. These good antibacterial activity of Tunisian olive varieties could be attributed to oleuropein, which is the major compound identified in the present study or this may be due to the climatic difference between Tunisian varieties and turkish variety.

Liu et al. (2017) demonstrated that at 62.5 mg/ml, ethanolic extract of olive leaves almost completely inhibited the growth of Listeria mono-cytogenes, Escherichia coli O157:H7, and Salmonella enteritidis. In addition, they observed that ethanol extracts were able to destroy the flagella of L. monocytogenes and reduce the motility of the pathogens. Furthermore, they found that the extracts inhibit biofilm formation in L. monocytogenes and S. enteritidis. According to Masoko and Makgapeeta (2015), the methanol extract of Olea africanahave a good antibacterial activity against E. coli, P. aeruginosa, E. faecalis and S. aureus, with MIC values comprised between 0.24 and 0.63 mg/ml. The differences observed between the present study results and these findings are probably due to differences between the two olive species.

Owen et al. (2003) also reported that olive leaves have antimicrobial activity against E. coli, S. aureus, B. cereus and S. typhi. The results re-reported in the present study show similarity with previous ones (Markin et al., 2003; Pereira et al., 2007; Sudjana et al., 2009; Lee and Lee, 2010; Gökmen et al., 2014) about the antimicrobial activity of olive leaves extracts. According to Pereira et al. (2007), the antimicrobial mechanism of the extract consists in the denaturation of the proteins and increasing cell membrane permeability. Similarly, Lee and Lee (2010) reported that the combined phenols mixture prepared from an olive leaves extract showed inhibition effects against B. cereus and S. enteritidis. In addition, Gökmen et al. (2014) showed that the MICs of olive leaves extract against L. monocytogenes, E. coli O157, E. sakazakii and P. aeruginosa were 32 μg/mL, while the MIC against B. cereus, S. aureus, E. faecalis, P. vulgaris, E. coli, Salmonella typhimurium was 16 mg/mL.

In a previous study, it was shown that the olive mill waste was able to reduce biofilm formation in E. coli (Carraro et al., 2014). On the contrary, according to Liu et al. (2017), olive leaves extracts slightly inhibited the biofilm formation in L. monocytogenes at 7.8 mg/mL. In the same study, the biofilm formation in S. enteritidis, was more inhibited (74% at 15.6 mg/mL).
The observed antibiofilm activity is generally attributable to the high concentrations of phenolic compounds, such as oleuropein, which antibiofilm activity was previously tested (Carraro et al., 2014) or may be due to a synergistic effect of some phenols contained in the olive extracts.

The mechanisms of antibacterial and antibiofilm activities of oleuropein are not completely understood. However, phenolic compounds have the ability to increase the permeability of cell membranes, thus facilitating their rupture (Taweechaisupapong et al., 2012). Casas-Sanchez et al. (2007) reported the interaction of oleuropein with phosphatidylglycerol at the surface of the bacterial cell membrane, causing changes that lead to the disruption of the cell envelope.

Generally, it can be observed that all olive leaf extracts exhibited high radical scavenging activity even if it is well known that antioxidant capacity is influenced by several factors, among which harvesting period and cultivar (Yorulmaz et al., 2012; Brahmi et al., 2015). The results reported by Blasi et al. (2016) showed that the antioxidant activity of four Italian cultivars was the highest in March, when the leaves had completed their growth, while it decreased slightly until September, when started the ripening of the fruit.

The leaf is the primary site of plant metabolism at the level of both primary and secondary plant products (Antolovich et al., 2000) and can be considered as a potential source of bioactive compounds (Tsimidoua nd Papoti, 2010). Numerous studies have been focused on the composition of olive leaves based on phenolic compounds considering their richness of such valuable compounds.

Phenolic compounds in olive leaves are numerous and of diverse nature. They are grouped with regard to major molecular characteristics as simple phenols and acids, lignans, secoiridoids and flavonoids (Tsimidoua nd Papoti, 2010), including flavones (luteolin-7-glucoside, apigenin-7-glucoside, diosmetin-7-glucoside, luteolin, and diosmetin), flavonols (rutin), flavan-3-ols (catechin), substituted phenols (tyrosol, hydroxytyrosol, vanillin, vanillic acid, and caffeic acid), and oleuropein (Ela nd Karakaya, 2009). Oleuropein, related secoiridoids, and other derivatives are the principal compounds of olive leaves (Kontogianni and Gerothanass, 2012) among which the major compound frequently reported is oleuropein. Flavonoids may occur in appreciable amounts (Savournin et al., 2001).

Simple phenols and acids are present in lower amounts. However, several factors may influence the qualitative and quantitative phenolic composition of olive leaves among which we can cite date of collection (Brahmi et al., 2012), drying conditions (Silva et al., 2006), cultivation zone (Bilgin and Şahin, 2013), extraction procedure (Rafiee et al., 2011), and cultivar (Japón-Lujan et al., 2006).

The olive tree (Olea europaea) is native to the Mediterranean region, Asia and Africa. It is a small evergreen tree with 4 to 10 cm long green silvery leaves and small white flowers. Tea made with olive leaves has been in use for medicinal purposes since the Ancient Egyptians and olive oil was considered to be sacred in Ancient Greece, being used to light the lamps of temples and to fuel the flame of the ancient Olympic Games (Liu et al., 2011).

Today the olive is ever present in Mediterranean cuisine and olive oil holds the reputation of being one of the healthiest cooking oils. Let's then look at some of the best known health benefits this smooth golden tea has to offer (Peralbo-Molina and de Castro, 2013).

Tea is best known for its preventive action in these circumstances, maintaining normal DNA repair. This tea stimulates the immune system. Infusion made with olive leaves and olive tree bark can bring down fevers and fight germs. Is the cold season coming? Then it’s best to know that this tea fights colds and the flu. Many studies indicate that olive leaf herbal tea produces anti-viral action in the body, as it stops viral replication in cells. It is anti-fungal, antibacterial and anti-inflammatory, in other words, it is a natural killer of pathogens by stopping their reproduction process. Tea made from olive leaves fights yeast infections and viral infections, such as herpes. It aids in the treatment of chronic fatigue and allergies. Additional help may come for those who suffer from rheumatism or gout by drinking this herbal infusion. It may help prevent muscle spasms. And it is said to aid the prevention of shingles (Wang et al., 2008).

The major constituent of the secoiridoid family in olive leaves is oleuropein. Oleuropein is the bitter compound in fruits of olive trees and its quantity is high in young olives. But during maturation, it metabolizes to hydroxytyrosol and its amount decreases. Therefore, it is found in olives and olive oil while oleuropein is most concentrated in olive leaves (Benavente-Garcia et al., 2002).

It was specified as the heterosidic ester of elenolic acid and dihydroxyphenylethanol. It is commonly known that compounds sharing an orthophenolic (catecholic) structure possess antioxidant activity (Tuckand Hayball, 2002) and the main reason of high antioxidant capacity. Oleuropein cannot be absorbed directly in human digestion system, it is known that it cannot be found in human plasma or faeces, because oleuropein metabolizes completely to hydroxytyrosol and other degradation products (Soni et al., 2006 and Silva et al., 2006).
Hydroxytyrosol is absorbed in intestines and its transport occurs via a bidirectional passive diffusion mechanism (Manna et al., 2000).

Human absorption and excretion of olive phenols has been first reported by Visioli et al. (2000) They reported that hydroxytyrosol was dose-dependently absorbed in humans after ingestion and excreted in the urine as glucuronide conjugates. The increase in the dose of phenolics administered increased the proportion of conjugation with glucuronide (Visioli et al., 2000). Similarly, Bai et al. and Christian et al. suggested that hydroxytyrosol was rapidly absorbed and excreted (Christian et al., 2004).

Visioli et al. (2003) compared the human excretion of hydroxytyrosol by the condition of its consumption as a natural component of extra virgin olive oil or the addition to refined olive oil and yogurt (Visioli et al., 2003).

Studies showed that hydroxytyrosol and oleuropein inhibited the platelet aggregation and eicosanoid production, regulate blood flow, and reduce the coronary heart disease risks (Singh et al., 2008 and Covas, 2007).

Phenols in olive oil have inhibitory effects on LDL (low-density lipoprotein) oxidation, and it is recently known that olive leaves are the richest source of these phenols. Olive leaf extract was suggested to be protective against cardiovascular diseases due to effects on adrenaline, (Khayyal et al., 2000 and Somova et al., 2004) arrhythmia and intestinal muscle spasms (Benavente-Garcia et al., 2002).

It was reported that olive leaf extract possessed an inductive effect on mouse liver glutathione S-transferases (Han et al., 2001) and had a potential inhibitory effect on tumor necrosis factor, suggesting usage in allergic diseases (Nishibe et al., 2001).

In vivo, olive leaf extracts and oleuropein are known to act on diabetes by at least two mechanisms: increased peripheral glucose utilization and improved glucose stimulated insulin release (Sato et al., 2007).

Zaslaver et al. evaluated the modulator effect of olive leaves on the nitric oxide production and oxidative status in epithelial lung cells, and suggested that olive leaves may have a therapeutic potential in the treatment of inflammatory diseases (Zaslaver et al., 2005).

Furthermore, it was proved that olive leaves were especially effective against Klebsiella and Pseudomonas, two bacterial genera which pose major resistance problem and had antimicrobial effect against Escherichia coli and Candida albicans (Markin et al., 2003).

Recently, oleuropein has claimed in a U.S. patent to have potent antiviral activities against herpes mononucleosis, hepatit virus, rotavirus, bovine rhinovirus, canine parvovirus, and feline leukaemia virus (Micol et al., 2005). Investigations have been also focused on anti-HIV effect of olive leaves. These studies displayed that oleuropein and hydroxytyrosol were the first group of small molecules capable of multiple actions against the AIDS virus, inhibiting both viral entry and integration both outside and inside of the cellular environments offering unique benefits to these small molecules against viral resistance (Bao et al., 2007; Lee-Huang et al., 2007).

Olive leaf extract is a liquid with dark brown color and bitter in taste. Olive leaf extract is signified as a part of natural medicine with a wide range of health benefits. It has been used traditionally as an herbal supplement because it contains polyphenolic compounds with beneficial properties such as increasing energy levels, lowering blood pressure, and supporting the cardiovascular and immune systems. In addition to all beneficial effects mentioned above, olive leaf extract also has antimicrobial properties. As in the case of many natural products, the composition of the extract may vary according to different conditions, such as geographical location, cultivar, and plant nutrition (Sudjana et al., 2009).

Olive leaves could also play effective roles in health care because they contain large amounts of other valuable phytochemicals, such as triterpenes, flavonoids, and chalcones (Dekanski et al., 2009 and What Is Olive Leaf Extract, 2020).

Numerous publications on isolation of active compounds from olive leaves have appeared over the past few decades. In this article, we review and present status of the current knowledge of the methods for isolation, characterization, presence of enzymes and determination of antimicrobial potentials of compounds found in olive leaves (Pereira et al., 2007; Erdohana nd Turhan, 2012; Dekanski et al., 2011; Goreishi and Gholami Shahrestani, 2009 and Sahin and Samli, 2013).

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