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Olive: Native of Mediterranean region and Health benefits

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ABSTRACT

The Olive tree (Olea europaea) is native to the Mediterranean region, tropical & central Asia and various parts of Africa. It is an integral ingredient of the diet in the form of whole fruit or oil in the countries surrounding the Mediterranean Sea. The constituents of olive categorized into major and minor components. Major component of olive oil consist of oleic acid (Triglycerides) and a large number of minor components includes phenolic constituents, squalene, α-tocopherol and sterols having great importance and beneficial to human health. The main phenolics include hydroxytyrosol, tyrosol, and oleuropein, which occur in highest levels in virgin olive oil and have demonstrated antioxidant activity. Many studies have been conducted to prove its potential through oil, whole fruit and leaf extract as cardiovascular disorders and anti-oxidant, gastroprotective effect, osteoprotective effect, endocrine effect, immunomodulatory effect, anti-cancer, anti-viral and anti-microbial effects.

KEY WORDS: Olive, Mediterranean diet, cardiovascular disorder, anti-cancer, antimicrobial.

INTRODUCTION AND HISTORY

Olive (Olea europaea) belongs to family Oleacea, have been used widely in folk medicine in European Mediterranean area, Arabia peninsula, India and other tropical and subtropical regions, as diuretic, hypotensive, emollient and for urinary and bladder infections (1). The olive can be consumed whole as either the fully ripe black fruit or as the unripe green fruit. Archeological evidence suggests that olives were being grown in Crete as long ago as 2,500 B.C. From Crete and Syria olives spread to Greece, Rome and other parts of the Mediterranean area and component of Mediterranean diet (2). Olives are also grown commercially in California, Australia and South Africa. There is some disagreement over when the trees first appeared in California. Some say they were introduced in 1769 when seeds brought from Mexico were planted. Others site the date 1785 when trees were brought in to make olive oil. Edible olive was grown on the island of Crete around 3500 BC and may have been the source of the wealth of the Minoan kingdom. The Phoenicians spread the olive to the Mediterranean shores of Africa and southern Europe. Olives have been found in Egyptian tombs from 2000 years BC. Olive culture spread first to the early Greeks, then to the Romans. As the Romans extended their domain, they brought the olive with them. Some 1,400 years ago the Prophet of Islam, Muhammad (SAW), advised his followers to apply olive oil to their bodies; he himself used olive oil on his head. The use of oil is found in many religions and cultures. It has been used during special ceremonies and also as a general health measure. It is also known as the symbol for peace, wisdom and victory. In the early Olympic Games the winners were crowned with wreaths made of olive branches. Holy people were anointed with olive oil, and Moses exempted men who would grow olives from military service.

Most plant oils of commercial value are accumulated in seeds (3). However, olive (*Olea europaea* L.) oil produced from fruit (4). Olive is one of the most significant oil crops in Mediterranean region and ranks sixth in the world production of vegetable oils (5). Olive oil, the major source of dietary fat in the countries where olives are grown (2, 6), constitutes part the commonly referred to "Mediterranean diet" of countries that surround the Mediterranean Sea and tend to have a low incidence of chronic degenerative disease (7), particularly coronary heart disease (CHD) and cancers of the breast, skin, and colon (8, 9). This review will focus on the chemical constituents and health benefits of olive as olive oil, whole olive fruit and olive leaf extract.

CHEMICAL CONSTITUENTS

The composition of olive oil is complex; the major and minor group of compounds thought to contribute to its observed health benefits includes small amounts of palmitate but is particularly by oleic acid as monoenoic acid oleate (5), phenolics, squalene (10), sterols about 0.2% phytosterol, tocosterols, caffeic acid and Vitamin E (α-tocopherol) (11).

Oleic acid

Olive oil is a triacylgylceride: three fatty acids attached to a glycerol backbone. Chemically it is a type of glycerolipid. Triacylglycerols (Triglycerides or Fats) are the major energy reserve for plants and animals. Olive oil contains approximately 72% oleic acid (Fig. 1), a monounsaturated fatty acid (12). Llor and Pons (13) conducted in vitro experiments on the effect of olive oil or isolated oleic acid on colorectal neoplasia. They concluded olive oil induces apoptosis and cell differentiation and down-regulates the expression of cyclooxygenase-2 (COX_2) and Bcl-2. COX_2 is believed to play an important role in colorectal cancer development, while Bcl-2 is an intracellular protein that inhibits apoptosis. Oleic acid alone exhibited cell-line specific apoptotic induction, since HT-29 cells were affected but not Caco-2 cells. Menendez et al (14) examined the effect of oleic acid on breast cancer cell lines. Oleic acid down-regulates the over-expression of Her-2/neu, an oncogene over-expressed in approximately 20% of breast carcinomas. The gene, also know as erb-B2, encodes for the p185Her-2/neu oncoprotein, a transmembrane tyrosine kinase orphan receptor that, under normal cellular conditions, is highly regulated because it controls many cell functions, such as

differentiation, proliferation, and apoptosis.

Phenols

A Mediterranean diet rich in olive oil supplies ~10-20mg of phenols per day (15). Virgin olive oil is one of the few edible vegetable oils that is consumed unrefined, which implies that it contains a significant amount of minor bioactive substances. Among them, phenolic compounds have received a great deal of attention over recent years because of the beneficial properties attributed to human health (16, 17, 18). Levels of phenolic compounds in olive oil vary widely; one consistent conclusion is that extra virgin olive oil has a higher phenolic content than refined virgin olive oil (10, 17). Olive oil phenols can be categorized into: simple phenols, secoiridoids and lignans, all of which inhibit auto-oxidation. Major phenols include hydroxytyrosol, tyrosol, oleuropein (19), and ligstroside (10) (Figure 2). Percentages of individual phenolic compounds present in the olive oils were ~6.5% hydroxytyrosol, 5.5% tyrosol, 40% oleuropein aglycones, 26% ligstrosids aglycones, 12% lutein, and 3% apigenine (20). Hydroxytyrosol and tyrosol are simple phenols and oleuropein is a secoiridoid. The simple phenols hydroxytyrosol and tyrosol are formed from the hydrolysis of the secoiridoid aglycones of oleuropein and ligstroside. Hydrolysis of oleuropein, which occurs during olive oil storage (21), results in the formation of hydroxytyrosol, tyrosol, and ethanol (22) (Figure. 3). A human study showed that tyrosol and hydroxytyrosol are excreted in urine (23).

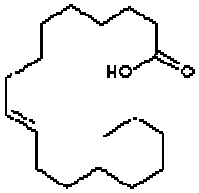

Figure 1. Structure of oleic acid

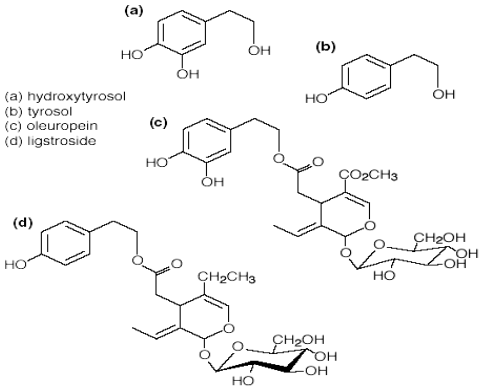

Figure 2. Olive oil phenols

Squalene

Kiritsakis (24) reported that olive oil contained the highest amounts of squalene among a range of seasoning oils. Squalene, found in high amounts in the Mediterranean diet, is believed to be responsible for the chemoprotective effect (12) and lower incidence of skin cancer seen in epidemiological studies of populations consuming this diet. Olive oil contains very small amount approximately 0.7% of sqalene (12). There is a slight difference observed between the level of squalene in extra virgin and refined virgin olive oils (extra virgin having higher levels) (10).

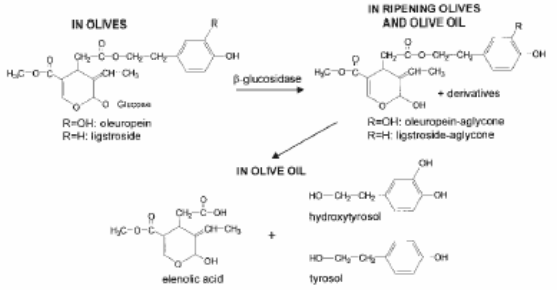

Figure 3. Phenols present in olive oil, their degradation into aglycones during ripening, and hydrolysis of aglycones into tyrosol and hydroxytyrosol.

APPLICATION AND HEALTH BENEFITS

Cardiovascular effect

Coronary heart disease (CHD) is the leading cause of death in the United States as well as in many developing and developed countries (25). Research has shown a strong connection between Mediterranean diets and lower rates of heart disease (26-29). Most researchers believe that the most important health-promoting substance in olive oil is oleic acid, which is a monounsaturated fatty acid. The natural antioxidants, including oleuropein, from the olive tree may play a role in the prevention of cardiovascular diseases through a decreased formation of atherosclerotic plaques by inhibiting LDL oxidation (30). An olive leaf extract was reported in a laboratory study to have vasodilating effects, seemingly independent of vascular endothelial integrity (31). Traditional uses support olive leaf and olive oil in cardiovascular disease prevention (32, 33). Animal experiments in rabbit and rat preparations found a hypotensive effect of oleuropein, possibly via direct action on smooth muscle. Oleuropeoside also may exert vasodilator activity. Additionally, olive leaf extracts may possess antispasmodic, vasodilator, and anti-arrhythmic properties (31, 34).

Hypolipidemic and Anti-oxidant effect

Oxidation of LDL cholesterol has been identified as one of the first steps in the development of atherosclerotic lesions by promoting injury to the arterial wall through several mechanisms, including growth factor and chemotactic protein expression, inflammation, and increased local macrophages. Macrophages bind to and engulf oxidized LDL -an innate immune response to tissue damage. This engulfment produces a fatty foam cell, which, when combined with other cells, produces a fatty streak in the blood vessel (35). Oxidized LDL can also be taken up directly by endothelial and smooth muscles cells, leading to formation of fatty streaks, which is the first sign of atherosclerosis. The lesions forming atherosclerotic plaques are made up of lipids, endothelial and smooth muscle cells, and extracellular matrix. The plaque environment is proinflammatory (7). Inflammation occurring

prior to the formation of fatty streaks and atherosclerotic lesions causes alterations to the endothelial cell wall, which increases the adhesion of leukocytes, LDL cholesterol, and platelets. This contributes to the development of atherosclerosis and cardiovascular disease (35).

Olive leaf has been reported to inhibit platelet aggregation and production of thromboxane A_2 (a stimulator of platelet aggregation with vasodilatory effects) (36). Also of interest, is a recent study reporting that olive leaf extract inhibited both angiotensin converting enzymes (37). In vitro studies have demonstrated hydroxytyrosol and oleuropein are capable of inhibiting production of isoprostanes, a marker of LDL oxidation (38). It has been suggested that phenols present in olive oil may act synergistically with these constituents to prevent LDL oxidation.

Studies in laboratory animals have reported hypoglycemic and hypolipidemic activity of olive leaf (39, 40). The active constituent was reported to be oleuropein, with a proposed mechanism of action of potentiation of glucose-induced insulin release, and an increase in peripheral blood glucose uptake.

Antioxidant activity of olive has been attributed by phenols content particularly to hydroxytyrosol, oleuropein and caffeic acid. Caffeic acid was also reported to have antioxidant activity through the scavenging of superoxide anion (41). Olive leaf has been reported to have anti-complement in vitro, and is a proposed mechanism for its anti-inflammatory effects (42). In-vitro and animal experiments have been conducted to demonstrate the antioxidant activity of olive leaf extracts. In rat epithelial cells stimulated with cytokines, a concentrated polyphenol extract reduced nitrite concentration and free radical production (43). Rabbits with induced diabetes showed a decrease in oxidative stress markers when treated with oleuropein (44). Other experiments support the antioxidant activity of the phenols oleuropein and hydroxytyrosol (6, 45, 46, 47).

Anti-hypertensive effect

As with other aspects of cardiovascular diseases, there is a reduced incidence of hypertension in populations that consume the Mediterranean diet (19, 48) and adherence to the Mediterranean diet is inversely related to systolic and diastolic blood pressure (49). Several studies have demonstrated the antihypertensive properties of olive oil (8, 50-53). Gilani et al found intravenous administration of olive oil extract reduced systolic, diastolic, and mean arterial blood pressures in normotensive rats (50). Epidemiological data from studies in three Mediterranean countries-Italy, Greece and Spain as well as non-Mediterranean countries, suggest a protective effect for monounsaturated fatty acids or olive oil, while non-Mediterranean countries show little or no positive effects (52). Ferrara et al (53) compared a diet rich in polyunsaturated fatty acids (from sunflower oil) with a diet high in monounsaturated fatty acids (from olive oil) in patients taking antihypertensive medications and found individuals who consumed an olive oil-rich diet were able to reduce the dosage of antihypertensive medication. Olive oil's precise mechanism of action for blood pressure reduction is unknown, although several theories have been proposed. Giliani et al (50) concluded that olive oil is a calcium channel antagonist, closely mimicking the effects of the calcium channel blocker drug verapamil. Another suggested mechanism is via improved endothelial function (19, 52, 54). Phenols and oleic acid may contribute to improved endothelial function by reducing ROS (19). Other potential mechanisms have been suggested, including decreasing vascular tone and changes to the fatty acid and phospholipid composition of the aorta (53).

Gastro-intestinal protective effect

An early study detected that the substitution of animal fat for olive oil in the diet produced a significant reduction in the size of ulcers in patients (55) and another work related the consumption of olive oil with a reduction in gastric acid secretion (56).

Osteoprotective effect

Ageing and oestrogen deficiency induce inflammatory and oxidant conditions that are involved in the development of bone loss, osteoporosis and a higher likelihood of low-energy fractures. In this context, a sufficient load of antioxidants supplied by a diet rich in olive oil may prevent bone loss through the scavenging of free radicals. The anti-inflammatory components present in olive oil may also act by averting the increased plasma concentration of pro-inflammatory cytokines (interleukin-6, tumour necrosis factor-α) involved in bone resorption among postmenopausal women (57).

A Mediterranean-type monounsaturated fatty acid MUFA-rich diet can also affect bone metabolism because a MUFA-rich diet might interfere with the actions of prostaglandins. Prostaglandins, especially PGE_2, stimulate bone resorption by increasing the number and activity of osteoclasts (58). Most of the potent stimulators of bone resorption increase prostaglandin production in bone by induction of COX_2, and the ability of polyphenols present in olive oil to exert a dose-dependent inhibition of the enzyme COX_2 has been recently shown (59). In addition, oleic acid is an inhibitor of prostaglandin PGE_2 synthesis, the major prostaglandin involved in bone metabolism (60). Normal or moderate levels of PGE_2 support bone formation, whereas greater quantities promote bone resorption (61).

Puel et al (62) showed that olive oil consumption had had no effect on plasma osteocalcin concentrations (marker of bone formation) or on urinary deoxypyridinoline excretion (marker of bone resorption) its feeding can prevent inflammation induced osteopenia in ovariectomised rats. His study (63) showed that every dose of oleuropein elicited protective effects on bone mass in this model of ovariectomy associated with inflammation, probably by modulating inflammatory parameters. Black olives are able to prevent bone loss in an experimental model of senile osteoporosis (oestrogen-deficient rats in which a low-grade inflammation was induced by talc injection) (64).

Endocrine effect

Anti-diabetic effect

An early study, using ethanol leaf extracts (defatted with petrol ether) given by gastric incubation to the rabbit (dose not specified), showed a 17-23% decrease in blood sugar

levels which reached a minimum within 6 hours and rose to normal after 48 hours (65). Aqueous extracts of dried leaf from Italy, administered intragastrically (IG) to male rats in a dosage of 500mg/kg, reduced the blood glucose levels of normal or alloxan induced diabetic rats (66). Aqueous decoctions of Spanish leaf, administered IG to the rat at a dose of 32.0mg/kg, showed activity against alloxan-induced hyperglycaemia (40). The hypoglycemic activity of olive leaf has been demonstrated in animals. In rabbits with induced diabetes, an ethanol extract of olive leaf decreased blood glucose. Suggested mechanisms include potentiation of glucose induced insulin release and increased peripheral uptake of glucose (40, 44).

Thyroid inducers

An aqueous extract of olive leaf administered to rats for 14 days increased T_3 levels and reduced circulating thyroid stimulating hormone levels, possibly via a feedback mechanism (67).

Immunomodulatory effect

Olive oil intake also has been shown to modulate immune function, particularly the inflammatory processes (10, 68, 69). Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic joint inflammation and damage. The initiation of RA is believed to result in an increase in the concentration of macrophages and neutrophils in the synovial fluid and free-radical-producing enzymes. This leads to high levels of ROS in the joints, which increases and prolongs inflammation and damage (70). The antioxidant effect of olive oil has been found to reduce inflammation. In addition, dietary omega-9 monounsaturated fatty acids, such as oleic acid, have been found to replace omega-6 polyunsaturated fatty acids (PUFAs) in several aspects of cell metabolism. Reducing the competition between omega-6 and omega-3-PUFAs can lead to an increased use and incorporation of omega-3-PUFAs (70). A number of studies that examined the benefits of fish oils in RA used an olive oil placebo for the control groups (71-73). Although results highlighted the benefits of fish oils, unexpected significant improvements were also seen in the control groups. Benefits including pain reduction, reduced morning stiffness, and improved patient evaluation of global disease were reported by patients receiving olive oil only. No explanation of the improvements shown by the olive oil groups were proposed, although changes in immune function may be responsible (73). As a result of these data, Berbert et al (74) conducted research to establish whether olive oil improved RA symptoms in patients already receiving fish oil. Olive oil appears to act synergistically with omega-3 fish oils to improve the symptoms of RA; the benefits are thought to be exerted through the oleic acid component. Oleic acid is converted to eicosatrienoic acid (ETA) and then leukotriene A_3 (LTA_3). LTA_3 is a potent inhibitor of proinflammatory leukotriene B_4 synthesis (74). It has also been shown that olive oil consumption decreases the risk of developing RA (75).

Anti-Cancer effect

Epidemiological evidence suggested that people who consume the Mediterranean diet have a lower incidence of certain cancers, including breast, skin, and colon (7, 10), research has focused on possible mechanisms to explain this phenomenon. Oxidation of proteins, DNA, and lipids has been shown to contribute to cancer development, and consumption of antioxidants is believed to reduce the risk of mutagenesis and carcinogenesis (76). Antioxidants are present in olive oil, fruits, and vegetables that constitute a large part of the Mediterranean diet. Owen et al (9) showed that anti cancer activity of olive oil because of its high content of antioxidants (such as hydroxytyrosol, tyrosol, secoiridoids and lignans) and compounds deemed to be anticancer agents (such as squalene and terpenoids). The exact contribution olive oil makes to the apparent dietary chemoprotection is debatable; in vitro studies have found olive oil phenols are potent antioxidants, which may provide potential chemoprotective properties, although in vivo data are lacking. Research examining individual phenolic compounds has found hydroxytyrosol is capable of protecting cells from hydrogen peroxide damage and DNA from peroxynitrite-induced damage, blocking cell cycle progression at the G_1 phase, and inducing apoptosis (77). In vivo and in vitro studies on the activity of oleuropein have found, in addition to antioxidant properties, it has antiangiogenic action and inhibits cell growth, motility, and invasiveness (78). Oleuropein has also been found to cause cell rounding, which disrupts the cell actin cytoskeleton.

Oleuropein also affects and disrupts purified actin filaments, providing direct antitumor effects due to cell disruption (78). In in-vivo animal studies, rapid tumor regression was observed when mice were given one-percent oleuropein in drinking water (78). Saturated animal fats and polyunsaturated plant fats in the diet have been implicated in colon, breast, prostate, and ovarian cancers (79). The substitution of olive oil in the Mediterranean diet may explain its apparent cancer-protective effect and accentuate the importance of the type, rather than the amount, of fat consumed.

Colon Cancer

The HCAs produced when protein-containing food is fried have been found to induce breast, colon, and pancreatic cancer in rats (80). Based on this evidence, Galeone et al (81) used data from a multinational, case control study to examine the relationship between fried foods and colorectal cancer. When olive oil was compared to other oils, it was found that fried olive oil has a protective effect against colon cancer. This agrees with data that unheated olive oil is beneficial in protecting against colon cancer (80). As described previously, when olive oil is used for frying, fewer HCAs are produced than when oils high in polyunsaturated fatty acids are used. Later in vitro research by Gill et al (82) looked at the effect of virgin olive oil phenols on colorectal carcinogenesis. Using specific cell lines, they investigated processes involved in cancer initiation, promotion, and metastasis-the three main stages in cancer development and concluded olive oil phenols exert beneficial effects in all three stages. The oil extract was shown to reduce DNA damage (initiation), increase barrier function (promotion), and reduce cell invasion of surrounding tissue (metastasis) (82).

Breast Cancer

Most of the active compounds in olive oil are lipid soluble; however, even though the phenolic glycosides are less so,

they are likely to be stored in fat tissue. This may explain the chemoprotective effect against breast cancer and the low incidence of breast cancer in Mediterranean countries. In addition, oleic acid is incorporated into the phospholipid membrane of breast tissue cells, resulting in a reduction in lipid peroxidation (82). Although in developed countries breast cancer is the most common cancer seen in women, there is vastgeographical variation in its incidence (82, 83). Epidemiological data show women in the Mediterranean basin have a lower incidence of breast cancer than women in other "Western" countries (8, 10). Case control studies that looked at women in several Mediterranean countries have shown an inverse correlation between olive oil consumption and the incidence of breast cancer (83, 84). High mammographic breast density (H-MBD) is associated with greater breast cancer risk (84).Using volunteers from the European Prospective Investigation into Cancer and Nutrition (EPIC) study, Masala et al (84) examined the effect of diet and lifestyle on MBD and concluded consumption of olive oil is inversely related to the risk of H-MBD. Women who reported olive oil intake of ≥30.5 g/day were 30% less likely to be classified into the H-MBD group. Using data from the European Community Multicenter Study on Antioxidants, Myocardial Infarction and Breast Cancer (EURAMIC), Simonsen et al (79) looked at the relationship between monounsaturated fat intake, the storage of monounsaturated fatty acids in breast tissue, and postmenopausal breast cancer. They found a strong inverse relationship between oleic acid consumption and breast cancer only in the Spanish group (82), possibly due to the reported high consumption of olive oil in Spain. Animal studies using dimethylbenz(α)anthracene-induced cancer have shown a diet rich in olive oil has a non-promoting effect on carcinogenesis. This effect is backed up by histopathological and morphological features (85, 86).

Anti-viral effect

Early evidences reported the antiviral activity of olive leaf extract through the constituent calcium elenolate, a derivative of elenolic acid (87, 88). The isolated calcium salt of elenolic acid was tested as a broad-spectrum antiviral agent active against all viruses tested (89). Some viruses inhibited by calcium elenolate in vitro include rhinovirus, myxoviruses, Herpes simplex type I, Herpes simplex type II, Herpes zoster, Encephalomyocarditis, Polio 1, 2, and 3, two strains of leukemia virus, many strains of influenza and para-influenza viruses (89-91). The mechanism of action of the antiviral activity is reported to include an ability to interfere with critical amino acid production, inactivating viruses or by preventing virus shedding, budding, or assembly at the cell membrane, directly penetrate infected cells and stop viral replication, neutralize the production of reverse transcriptase and protease (in Retroviruses) and stimulation of phagocytosis (87).

Antimicrobial effects

Olive leaves are known to resist insect and microbial attack, and in-vitro studies have been conducted to establish the range of activity of olive leaf extracts (47, 92). Olive leaf extract has been reported to be an effective antimicrobial agent against a variety of pathogens, including Salmonella typhi, Vibrio parahaemolyticus, and Staphylococcus aureus (including penicillin-resistant strains); and Klebsiella pneumonia, and Escherichia coli, causal agents of intestinal or respiratory tract infections in humans (92). Olive leaf could be considered a potentially effective antimicrobial agent for the treatment of intestinal or respiratory tract infections. The component usually associated with olive leaf's antimicrobial properties is oleuropein (93, 94). Oleuropein has also been reported to directly stimulate macrophage activation in laboratory studies (68). Hydroxytyrosol demonstrated broader antimicrobial activity than oleuropein and is comparable to ampicillin and erythromycin in spectrum and potency (92). In vitro studies have demonstrated the antimicrobial activity of hydroxytyrosol, tyrosol, and oleuropein against several strains of bacteria implicated in intestinal and respiratory infections. Hydroxytyrosol and oleuropein have antimicrobial action against both American Type Culture Collection (ATCC) and patient-derived clinical bacterial strains, with slightly greater activity against ATCC strains. It has been proposed that this action is due to the two ortho-positioned phenolic groups in their structure (Figure 2) (17). A recent study found virgin olive oil has bactericidal action against *Helicobacter pylori* (21), the primary cause of gastric ulcers and linked to gastric cancers. In recent years some strains have shown resistance to the typical antibiotics used to eradicate the infection and aid ulcer healing, spurring research on other compounds to treat the infection. Because phenolic compounds have been identified as having antibacterial properties, olive oil, with its high phenolic content, has been studied for *H. pylori*. Romero et al (21) concluded phenols inhibited bacterial growth at low concentration and were stable for several hours in the highly acidic environment of the stomach. They found the secoiridoid aglycones, particularly the dialdehydic form of decarboxymethyl ligstroside, have the greatest anti-*H. pylori* activity and are not hydrolyzed in the stomach (21); hydrolysis, if it occurs, produces the less active hydroxytyrosol and tyrosol. As the concentration of phenolics needed to kill *H. pylori*cells is higher than that for antibiotics, the researchers suggest virgin olive oil should be considered as preventive rather than a treatment agent. Because the research was conducted *in vitro*, the researchers also suggest *in vivo* testing is needed to confirm or reject the conclusions, an especially important note since other foods that demonstrate good activity against *H. pylori in vitro* do not appear to have any action *in vivo*. The exact mechanism by which phenolic compounds affect *H. pylori* is unknown at present (21) but different theories have been proposed, for example, inhibition of the urease activity (95), adhesion to human gastric mucus (96), disintegration of the outer membrane (97), and inhibition of VacA citotoxin activity which causes the development of inflammation and ulceration in patients (98, 99).

Passive smoking and olive

Epidemiological studies have shown that the intake of antioxidants results in a reduced risk for several degenerative disorders such as cancer and atherosclerosis. Olive mill waste water is a byproduct of olive oil production and is phenols,

such as hydroxytyrosol. Visioli et al (100) showed the effect of a low dose of olive mill waste extract on rats, which were exposed to smoke-induced oxidative stress. The oxidative damage was quantified by measuring the level of 8-iso-prostaglandin-$F_{2\alpha}$ (indicator of lipid peroxidation) in the urine. Passive smoking considerably increased oxidative damage. Treatment with the olive mill waste water resulted in considerably less oxidative damage and a low dose of hydroxytyrosol, administered through olive mill waste water, reduces the oxidative stress of rat exposed to passive smoking (Visioli et al. 100).

Anti-HIV effect

AIDS patients have begun to use olive leaf extract for a variety of indications, among them to strengthen the immune system, to relieve chronic fatigue, to boost the effects of anti-HIV medications, and to treat HIV-associated Kaposi's sarcoma and HSV infections. There has been one anecdotal report that OLE augments the activity of the HIV-RT inhibitor 3TC (101). Lee-Huang et al (102) reported the anti-HIV effects of olive leaf extract are dose dependent, with EC_{50S} of around 0.2µg/ml. Treatment with OLE reverses many of these HIV-1 infection-associated changes. Treatment of HIV-1-infected cells with OLE also up-regulates the expression of the apoptosis inhibitor proteins IAP1 and 2, as well as the calcium and protein kinase C pathway signaling molecules IL-2, IL-2Ra, and ornithine decarboxylase ODC1.

STABILITY

Okogeri and Tasioula-Margari (103) studied the changes in the concentrations of tocopherols, total polyphenols, and complex polyphenols due to environmental conditions. Rastrelli et al (104) found changes in extra virgin olive oil quality with the presence of oxygen in the bottles (alpha tocopherols was reduced 20% after 2 months and 92% after 12 months). Under diffused light, 45% of the polyphenols were lost in 4 months, whereas tocopherols were decomposed by 79% during the same period (103). Hrncirik and Fritsche (105) tested 3 different extra virgin olive oil for 88 days at 60° (140 F°) and found decreased of 88% the total polyphenols. Gutiérrez et al (106) reported that changes occurred in the major and minor components of virgin olive oil during oxidation. During the induction period or slow phase of oxidation, polyphenols, tocopherols, and pigments undergo the most important alterations. Other compounds, such as FA or volatiles, suffer significant modifications only during the rapid or exponential phase of oxidation when the natural antioxidant systems fall to minimal values. The evolution of the different compounds and parameters analyzed suggests that the tocopherol and orthodiphenol contents are the best indices to determine the average life of the oils. The beneficial high content of minor compounds in the extra virgin olive oil can be maintained by keeping it in a cool, dark place, away from oxygen (107).

CONCLUSION

The olive (Oil, Leaf & fruit) showed various physiological effects which were proven by a large number of preclinical and clinical studies. There is still need of further research on its some physiological effects on human.

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