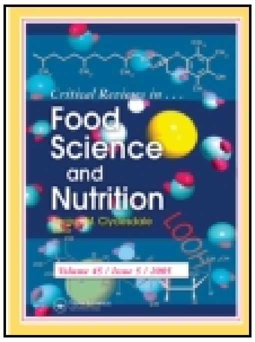

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The Health Potential of Fruits and Vegetables Phytochemicals: Notable Examples

Arantxa Rodriguez-Casado

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The Health Potential of Fruits and Vegetables Phytochemicals: Notable Examples

ARANTXA RODRIGUEZ-CASADO
IMDEA Food Institute, Madrid, Spain

Fruit and vegetables are essential components of a healthy diet. The World Health Organization (WHO) recommends an intake of five to eight portions (400–600 g) daily of fruits and vegetables to reduce risk of cardiovascular disease, cancer, poor cognitive performance, and other diet-related diseases, as well as for the prevention of micronutrient deficiencies. Much of their potential for disease prevention is thought to be provided by phytochemicals, among which the preventive activity of antioxidants is most well documented. Since numerous meta-studies published indicate variable and often contradictory results about the impact of isolated phytochemicals on health, their consumption as supplements must be carried out with care, because doses may exceed the recommended nutritional intake. Nonetheless, there is a general consensus that whole fruit and vegetable intake is more important in providing health benefits than that of only one of their constituent, because of additive and synergistic effects. This review describes the most recent literature regarding the health benefits of some selected fruits and vegetables. Importantly, since some phytochemicals regulate the same genes and pathways targeted by drugs, diets rich in fruits and vegetables in combination with medical therapies are being considered as novel approaches to treatment. Therefore, phytochemicals in fruits and vegetable might be a promising tool for the prevention and/or amelioration of a wide range of diseases.

Keywords Broccoli, dandelion, garlic, cocoa, olives, grapes

INTRODUCTION

The onset and progression of certain diseases are clearly influenced by lifestyle factors. Nutrition is one of the most important determinants of health and increasing evidence suggests that diets rich in fruits and vegetables may prevent a wide range of diseases (Traka and Mithen, 2011; Aune et al., 2012a,b; Boeing et al., 2012). Although mechanisms underlying these effects have not been fully elucidated, the presence of secondary metabolites, commonly referred as phytochemicals, in fruits and vegetables might play major roles (Traka and Mithen, 2011; Aune et al., 2012a; Boeing et al., 2012). Many of such phytochemicals possess the ability to interfere with cellular functions, altering activation of transcription factors that regulate expression of genes, and change cellular metabolism in different ways (Tsao, 2010; Traka and Mithen, 2011). Accordingly, the past two decades witnessed increased scientific interest in fruits and vegetables and their putative health-promoting properties (Badimon et al., 2010; Ferrari et al., 2011; Speciale et al., 2011). Many lines of evidence demonstrate that the majority of phytochemicals exhibit antioxidant (Lipinski, 2011; Speciale et al., 2011; Chiva-Blanch and Visioli, 2012; Giampieri et al., 2012) and anti-inflammatory (Zhao et al., 2011a,b; Singh et al., 2012) activities that confer them pharmacological properties likely important to prevent and maybe even treat (to a limited degree) different diseases (Baldrick et al., 2011). Among the thousands of phytochemicals found in our diets, phenolic compounds stand out as the most important group of natural antioxidants (De Kok et al., 2010; Chiva-Blanch and Visioli, 2012; Giampieri et al., 2012; Visioli, 2012).

Of the major areas of human health, cancer and cardiovascular disease are the best characterized ones. Free radicals, which induce oxidative stress, can cause DNA damage, which in turn can lead to base mutation, DNA cross-linking, and chromosomal breakage and rearrangement (De Kok et al., 2010). This damage may be limited by dietary antioxidants in fruits and vegetables through modulation of detoxification enzymes, scavenging of oxidative agents, stimulation of the immune system, hormone metabolism, and regulation of gene expression in cell proliferation and apoptosis (De Kok et al., 2010; Lipinski, 2011; Niki, 2011; Speciale et al., 2011). Indeed, epidemiologic studies

Address correspondence to Arantxa Rodriguez-Casado, IMDEA Food Institute, Carretera de Cantoblanco 8, 28049 Madrid, Spain. E-mail: arantxa.rodriguez@imdea.org

support an inverse relationship between a regular consumption of fruits and vegetables and the risk of cancers of the colon (Magalhaes et al., 2012), oesophagus (Berretta et al., 2012), oral cavity (Lu et al., 2011), stomach (Steevens et al., 2011), pancreas (Cappellani et al., 2012), prostatic (Sebastiano et al., 2012), breast (Aune et al., 2012a; Aune et al., 2012b), and ovary (Paxton et al., 2012). Cancer is a disease that features a strong genetic component and numerous genes that code for oncogenes or tumors suppressor genes have been identified. Extended treatment with physiologic concentrations of dietary phytochemicals results in altered gene expression, reduced growth, and apoptosis of cancer cells (McCullough and Giovannucci, 2004; Lu et al., 2011; Steevens et al., 2011; Aune et al., 2012a; Aune et al., 2012b; Berretta et al., 2012; Cappellani et al., 2012; Paxton et al., 2012; Sebastiano et al., 2012; Singh et al., 2012). On the other hand, many studies also indicate a strong link between fruit and vegetable intake and a reduced risk for cardiovascular disease (Badimon et al., 2010; Perez-Vizcaino and Duarte, 2010; Finks et al., 2012; Vasanthi et al., 2012). Likewise, the intake of this type of food has been inversely correlated with mortality from coronary disorders as well as incidence of risk factors such as diabetes, hypertension, and hyperlipidemia (Choudhary and Tran, 2011; El Haouari and Rosado, 2011). Oxidized low density lipoprotein (LDL) is considered an atherogenic factor in heart disease, promoting cholesterol ester accumulation and foam cell formation. Dietary antioxidants from fruits and vegetables get incorporated into LDL, and become oxidized themselves, thus preventing oxidation of polyunsaturated fatty acids, and modulate the synthesis and absorption of cholesterol (Choudhary and Tran, 2011; El Haouari and Rosado, 2011). Phytochemicals from fruit and vegetable also reduce platelet aggregation (Vita, 2005; El Haouari and Rosado, 2011), blood pressure (Galleano et al., 2010; Zhao et al., 2011a,b), insulin resistance index, and serum insulin concentration (Omar et al., 2010), and obesity (Calder et al., 2011), all of them important risk factor for cardiopathologies.

Moreover, fruits and vegetables also ameliorate systemic inflammation that may be a critical factor in cardiovascular disease (Calder et al., 2011; Zhao et al., 2011,b; Singh et al., 2012). Cytokines (IL-1, IL-6, TNF-α), peptide hormones secreted by both inflammatory and adipose stromal cells that mediate the inflammatory response, are signals that stimulate tumor growth and are associated to obesity (Calder et al., 2011).

Finally, diets rich in fruits and vegetable in combination with medical therapies have been considered as novel treatment approaches since some phytochemicals regulate the same genes and pathways targeted by drugs (Shukla and George, 2011).

This review describes the most recent literature regarding the health benefits of some fruits and vegetable and their phytochemicals. Broccoli, for example, contains glucosinolates, which have been associated with a decreased risk of cancer; dandelion possesses important anti-inflammatory properties; garlic contains allyl sulphides that inhibit cancer cell growth; cocoa intake is being linked with decreased risk of cardiovascular disease; olives might play cardio-protective roles due to their antioxidant and anti-inflammatory properties; and, finally, grapes might be a source of beneficial phytochemicals in Alzheimer's disease and age-related cognitive decline.

Research continues proving the effectiveness of a plant-based diet with regard to weight loss, body fat distribution, cholesterol and glucose levels, blood pressure, and protective against numerous chronic diseases including cancer, cardiovascular, and Alzheimer's diseases (Bach-Faig et al., 2011). The Mediterranean diet is characterized by a dietary pattern that has remained constant over time and space rich in plant foods (cereals, fruits, vegetables, legumes, tree nuts, seeds, and olives), with olive oil as the principal source of added fat, along with high to moderate intakes of fish and seafood, moderate consumption of eggs, poultry and dairy products, low consumption of red meat and a moderate intake of alcohol (Bach-Faig et al., 2011). However, the Mediterranean diet is something else food. It constitutes a set of skills, knowledge, practices, and traditions ranging that makes the Mediterranean diet is acknowledged as an Intangible Cultural Heritage of Humanity by UNESCO (2010) (Bach-Faig et al., 2011).

HEALTH POTENTIAL OF SELECTED FRUITS AND VEGETABLES

Although multiple factors could contribute to incidence and prevalence of chronic diseases, the contribution of some fruit and vegetables is worthy being considered.

Broccoli (Brassica oleracea)

Broccoli is a cruciferous vegetable that belongs the *Brassicaceae* (formerly called Cruciferae) family, together with cauliflower, Brussel's sprouts, kohlrabi, cabbage and mustard (Buck, 1956). The flower heads (commonly called broccoli, broccoli florets, or broccoli heads) are eaten before the flower buds open (Buck, 1956).

Principal components of broccoli are glucosinolates, which are present in all members of the *Brassicaceae* family (Buck, 1956). Glucosinolates may be hydrolyzed to yield a variety of biologically-active products, including isothiocyanates, thiocyanates, nitriles, and oxazolidine-2-thiones (Buck, 1956; No authors listed, 2010).

These products influence a number of cellular processes through the regulation of transcription factor levels, signaling pathways, the cell cycle, and apoptosis (Buck, 1956; No authors listed, 2010). Broccoli contains high levels of the isothiocyanate sulforaphane and of other glucosinolate derivatives thought to have beneficial health properties (Zhang et al., 1992; No authors listed, 2010).

Several other secondary plant metabolites have been identified in broccoli, and include a series of flavonoids, 2-caffeoylquinic acid derivatives, and cinnamic acid derivatives (Aires et al., 2011). These compounds are accompanied by ascorbic acid, xanthophylls (lutein, zeaxanthin), carotenoids, tocopherols, proteins, sugars, and chlorophyll (Aires et al., 2011). Broccoli is also rich in minerals such as selenium and calcium, fiber and vitamins as well as various amino acids (Aires et al., 2011). Broccoli has been highly valued due to its flavor, but also because of its beneficial effects on human health (Latté et al., 2011). Sulforaphane, an isothiocyanate biologically active metabolite of glucoraphanin, has been identified in broccoli as the compound responsible for many of their health benefits (Zhang et al., 1992). Glucoraphanin, also referred to as sulforaphane glucosinolate, is the most potent naturally occurring inducer of phase 2 detoxification enzymes (Zhang et al., 1992) and is a long-acting antioxidant (No authors listed, 2010).

Sulforaphane also exhibits broad-spectrum antimicrobial activity against numerous gram-positive and gram-negative bacteria (No authors listed, 2010). In addition, preclinical and clinical studies have concluded that sulforaphane possesses anti-inflammatory activity by inhibition of cytokine production (Juge et al., 2007). Sulforaphane's multiple molecular targets and clinical trials currently underway to assess its effects on various cancers (Kensler et al., 2012) and cardiovascular diseases (Park et al., 2012).

A wide range of studies in humans, animals, and in vitro has confirmed an inverse association between broccoli intake and risk of different cancers (Vasanthi et al., 2009; Kensler et al., 2012). Numerous in vitro studies on human colon (Gamet-Payrastre et al., 2000), leukemia (Fimognari et al., 2002), pancreatic (Pham et al., 2004), lung (Liang et al., 2008), and prostate (Singh et al., 2004) cancers have demonstrated the inhibitory effects of sulforaphane. Intake of broccoli sprouts has been associated with decreased incidence and tumor growth prostate and breast cancer in animal models (No authors listed, 2010). Epidemiological studies suggest that intake of more than one portion of cruciferous vegetables per week lowers both the incidence and the development of aggressive prostate cancer (Traka et al., 2008). Specifically, results suggest that by consuming—during 12 months—a broccoli-rich diet complex changes are produced in signaling pathways associated with inflammation and carcinogenesis (Traka et al., 2008). These changes may be mediated through the chemical interaction of isothiocyanates with signaling peptides in the plasma (Traka et al., 2008; Traka and Mithen, 2011; Dinkova-Kostova and Kostov, 2012). Apart from isothiocyanates and indoles (Riso et al., 2009), minerals (selenium) in broccoli play a critical key role in cancer prevention (Holst and Williamson, 2004).

Numerous clinical studies indicate that broccoli sprouts could have favorable effects on risk factors for cardiovascular disease. A phase I trial involving 12 subjects consuming 100 g broccoli sprouts daily for one week, demonstrated decreased serum total and LDL cholesterol levels, and reductions in all oxidative stress markers in all subjects (No authors listed, 2010). Another study, a randomized clinical trial including 81 type II diabetic patients, has shown that broccoli sprout as supplementary treatment (10 g/day for four weeks) significantly decreased serum triglycerides, oxidized LDL, and the atherogenic index of plasma (Bahadoran et al., 2012a). In the same clinical trial, a significant decreased of insulin resistance index and serum insulin concentration was observed (Bahadoran et al., 2012b). Broccoli sprouts decrease renal and vascular oxidative stress and inflammation as well as blood pressure in spontaneously hypertensive stroke-prone rats (Senanayake et al., 2012).

Furthermore, research has suggested that the compounds in broccoli can protect the eyes against macular degeneration (Tanito et al., 2005), and alleviates inflammation, synovial hyperplasia, and bone destruction in mice suffering arthritis rheumatoid (Kong et al., 2010).

Dandelion (Taraxacum officinale)

Dandelion (lion's tooth, blow ball, telltime) is a perennial plant that belongs to the *Composite* family as well as Artichokes (Williams et al., 1996; Schütz et al., 2005; Gonzalez-Castejon et al., 2012). The young leaves of dandelion are consumed fresh as a salad, and the roots are roasted and are utilized as a coffee substitute (Williams et al., 1996; Schütz et al., 2005; Gonzalez-Castejon et al., 2012). In addition, flowers extracts are used as flavor components in various food products, including soft drinks, frozen dairy desserts, baked goods, puddings and cheese (Gonzalez-Castejon et al., 2012). Apart from being consumed as food, dandelion is traditionally used as herbal medicine for the treatment of digestive complaints, hepatobiliary disturbances, hyperlipidemia, dyspepsia, rheumatism, and renal disorders (Williams et al., 1996; Schütz et al., 2005; Gonzalez-Castejon et al., 2012).

The health-promoting potential of dandelion is attributed to its high phenolic content, mainly hydroxycinnamic acid derivatives and flavonoids like chlorogenic and chicoric acids, luteolin, and quercetin glycosides (Williams et al., 1996; Schütz et al., 2005; Gonzalez-Castejon et al., 2012). Furthermore, several sesquiterpene lactones have been identified as the bitter principles typical of *Compositae* in dandelion (Williams et al., 1996; Schütz et al., 2005; Gonzalez-Castejon et al., 2012). Besides these secondary metabolites, dandelion contains inulin, a characteristic carbohydrate of *Compositae*, minerals, and some amino-acids (Williams et al., 1996; Schütz et al., 2005; Gonzalez-Castejon et al., 2012).

Many studies have demonstrated the antioxidant activity of dandelion, both in vitro (Menghini et al., 2010; You et al., 2010) and in vivo (Choi et al., 2010; Menghini et al., 2010; You et al., 2010). In terms of constituents, dandelion flowers are a potentially exploitable source of antioxidants, because of their elevated phenolic content attributed to caffeic and chlorogenic acids, and to the flavones luteolin and luteolin 7-*O*-glucoside (Hu and Kitts, 2005).

Mechanistically, dandelion downregulates the expression of certain pro-inflammatory mediators. Its antiinflammatory properties, in part attributed to sesquiterpene glucosides, have been proven showing a potent inhibitory activity of 86% against leukotriene B4 (Kashiwada et al., 2001). The high content in polyphenols also mediates the downregulation of NO, prostaglandin E_2, and proinflammatory cytokines production. Some researchers observed that luteolin and luteolin 7-*O*-glucoside (<20 μM) from dandelion downregulate both inducible iNOS and COX-2 expression (Hu and Kitts, 2004; Koh et al., 2010). Very recent animal studies have reported protective antiinflammatory effects of dandelion on acute lung injury (Liu et al., 2010a,b) *via* blocking mitogen-activated protein kinase, extracellular signal-regulated kinases, and Akt-related signaling cascades and attenuation of neutrophil chemotaxis and respiratory burst (Lee et al., 2010).

A wide range of studies in animals and in vitro reported the positive effects of different dandelion extracts on various risk factors of cardiovascular disease (Choi et al., 2010; Gonzalez-Castejon et al., 2012). The hypoglycemic properties of dandelion have been studied in vitro and in vivo. It appears that certain dandelion extracts (40 μg/mL) stimulate the release of insulin by pancreatic β-cell and hypoglycemic activities (Hussain et al., 2004). In vivo, a significant decreasing in serum glucose concentrations was observed in diabetic rats after administration of dandelion leaf extracts (Cho et al., 2002). Dandelion root extracts exert inhibitory effects on human platelet aggregation, at least in vitro (Neef et al., 1996). Such extracts exert a maximal inhibition of 85% at a concentration corresponding to 40 mg dried root/mL of human platelet-rich plasma. Low-molecular polysaccharides produce a 91% inhibition, while a fraction enriched in triterpenes and steroids showed an 80% inhibition of platelet aggregation, at equivalent concentrations (Neef et al., 1996).

Dandelion has also been considered as a potential anti-obesity agent with limited side effects. Its potent inhibitory activity on pancreatic lipase was evaluated in vitro and in vivo proving a pancreatic lipase inhibitory activity—at a concentration of 250 μg/mL—about 90.2% of that of Orlistat, a pancreatic lipase inhibitor used as anti-obesity medication endowed with several untoward side effects (Zhang et al., 2008).

On the other hand, dandelion has been used in traditional medicine for the treatment of various types of cancer. In in vitro studies have been observed that extracts at concentrations of 0.2 mg/mL induce apoptosis in human hepatoma cells and exhibit cytotoxic activities in human intestinal carcinoma cells (Koo et al., 2004). Recent results indicate that dandelion extracts decrease the growth of breast cancer cells by 40%, after 96 hours of incubation, and block invasion of prostate cancer cells (Sigstedt et al., 2008). A recent study indicates that components of dandelion root act either alone or synergistically to induce selectively cancer cell death in human leukemia with no toxicity to noncancerous cells (Ovadje et al., 2010).

Dandelion roots decrease lipid peroxidation, in turn protecting against alcoholic liver damage (You et al., 2010). Recent animal studies have revealed the hepatoprotective effect of two polysaccharides isolated from dandelion (Park et al., 2010; You et al., 2010). These polysaccharides (305 mg/kg body weight, for 7 days) attenuate hepatic damage in Sprague-Dawley rats through the regulation of NF-κB and its mediators such as iNOS, COX-2, TNF-α, and IL-1 (Domitrovic et al., 2010). Such polysaccharides promote the immune-modulator activities of dandelion (Yoon, 2008). The health benefits of dandelion roots have also been explored in relation to their proportion of inulin, which works as demulcent and prebiotic agent that strongly enhances immune function. An infusion of dandelion root stimulates—in vitro—the growth of 14 strains of bífidobacterias (Trojanová et al., 2004). Furthermore, an animal study showed that dandelion extract for six weeks upregulates the expression of estrogen and progesterone receptors, and follicle-stimulating hormone receptor in the adipose tissue and reproductive organs of mice, suggesting its potential application to treat reproductive hormone-related disturbances (Zhi et al., 2007).

Garlic (Allium sativum)

Allium sativum, commonly known as garlic, belongs to the *Liliaceae* family (Block, 2010). Its close relatives include onions, shallots, leek, and chive (Block, 2010). Garlic has been used for both culinary and medicinal purposes for hundreds of years in many cultures (Simonetti, 1990; Newall et al., 1996). It contains a higher concentration of sulfur compounds such as diallyl sulphate, alliin, ajoene, allicin than any other *Allium* species, in addition to several enzymes, amino acids, and minerals such as selenium (Simonetti, 1990; Newall et al., 1996; Block, 2010). The sulfur compounds are responsible for both garlic's pungent odor and many of its medicinal effects (Simonetti, 1990; Newall et al., 1996; Block, 2010).

In in vitro studies, garlic has been found to have anti-bacterial, anti-viral, and anti-fungal properties (Sohn et al., 2009). Clinical trials have reported that fresh garlic has significant anti-microbial activities (Groppo et al., 2007; Sohn et al., 2009). In addition, scientific studies have shown that garlic has anti-inflammatory actions (Keiss et al., 2003; Sohn et al., 2009; Block, 2010), anti-cancer properties (Kaschula et al., 2010; Antony and Singh, 2011), and beneficial effects on several risk factors for cardiovascular disease (Block, 2010; Ginter and Simko, 2010; Sobenin et al., 2010).

Notably, human studies have evaluated garlic's lipid lowering effects (Durak et al., 2004). Case series and controlled trials in healthy adults given garlic supplements along with cholesterol-rich diets indicate that garlic reduces serum cholesterol levels and increases fibrinolytic activity (Durak et al., 2004). Furthermore, garlic helps reducing blood pressure

(Ried et al., 2010) and total lipid concentrations (Durak et al., 2004; Kojuri et al., 2007). Also, garlic improves the elasticity of blood vessels and increases blood circulation, relieving cramps and circulatory disorders (Chan et al., 2007; Kojuri et al., 2007). Several studies found that garlic supplementation reduces accumulation of cholesterol in the vascular walls of animals (Chan et al., 2007), inhibits vascular calcification in human patients with high blood cholesterol, and reduces platelet aggregation (Steiner and Lin, 1998; Durak et al., 2004; Rahman, 2007). Different studies also found that moderate amounts of garlic could help regulating blood glucose levels and potentially lessen diabetes complications, as well as fight infections (Kook et al., 2009).

Several epidemiological studies show an association between increased intakes of garlic and reduced risk of certain types of cancer (Fleischauer and Arab, 2001). An analysis of data from seven population studies showed that the higher the amount of garlic consumed, the lower the risk of stomach, esophagus, pancreatic, and colorectal cancer (Tanaka et al., 2004; Chan et al., 2005; Gonzalez et al., 2006). Evidence also indicates that increased ($>$10 g/day vs. $<$2.2 g/day) allium intake is associated with an approximately 50% reduction in the prostate cancer risk (Hsing et al., 2002). Mechanistic studies showed that garlic reduces the development of mammary cancer in animals and suppresses the growth of human breast cancer cells (Tsubura et al., 2011).

Cocoa (Theobroma cacao)

Cocoa beans and their derived products such as chocolate are rich in antioxidants, mostly catechins, epicatechin, and especially the polymers procyanidins (Hooper et al., 2012). In addition to these phytochemicals, cocoa also contain flavonoids and xanthines, with theobromine as the main representative of the latter, which have vasodilatory properties (Hooper et al., 2012). Due to its high concentration of this series of phytochemicals with a variety of biological functions, cocoa as a plant and chocolate as food may have beneficial health effects against oxidative stress and chronic inflammation, in addition to ameliorate cardiovascular disorders, cancer, and other pathological conditions (Hooper et al., 2012; Ramos-Romero et al., 2012).

Many clinical and epidemiological studies indicate that appropriate intakes of cacao reduce the incidence of cardiovascular disease and of several of its risk factors (Corti et al., 2009). Chocolate consumption has a positive influence on hypertensive, inflammatory, atherogenic, and thrombotic health conditions as well as impact on insulin sensitivity and vascular endothelial function (Buijsse et al., 2010; Mostofsky et al., 2010; Oba et al., 2010; Djousse et al., 2011). As an example, the Stockholm Heart Epidemiology Program (Janszky et al., 2009) is a study including a cohort of 1169 patients who had suffered myocardial infarction, who are being followed for eight years. Its results show that chocolate consumption is associated with lower cardiac mortality in a dose-dependent manner. Recent meta-analysis reported that higher levels of chocolate consumption are associated with a reduction of about a third in the risk of cardio-metabolic disorders (Desch et al., 2010; Buitrago-Lopez et al., 2011). This beneficial association was significant for any cardiovascular disease (37% reduction), diabetes (31% reduction), and stroke (29% reduction) (Buitrago-Lopez et al., 2011).

There are few epidemiological studies and scant data that correlate the incidence of cancer with consumption of cocoa. While several studies of intervention—despite their short duration—have reported favorable changes in biomarkers assessing antioxidant status, there is very little evidence related to cancer markers (Maskarinec, 2009). However, these metabolic studies indicate that regular intake of cocoa and its derivatives increase plasma level of antioxidants, which might be a desirable effect because it would protect against reactive oxygen species (ROS) (Weisburger, 2001).

Olives (Olea europaea)

The olive tree, *Olea europaea*, is native to the Mediterranean countries and parts of Asia Minor. In folk medicine, the fruit and its oil have a wide range of therapeutic and culinary applications (López-Miranda et al., 2010; Belarbi et al., 2011; Visioli, 2012). Traditionally, olives have been used as emollients, laxatives, nutritive, sedatives, and tonics (Belarbi et al., 2011). Specific conditions traditionally treated include colic, alopecia, paralysis, rheumatic pain, sciatica, and hypertension (López-Miranda et al., 2010; Belarbi et al., 2011). Raw olives are very bitter and inedible and, therefore, must be treated before consumption (Waterman and Lockwood, 2007). They can be harvested when still unripe (green olives) or when fully ripe (black olives) (Waterman and Lockwood, 2007). Ripe olives are pressed to obtain olive oil (Waterman and Lockwood, 2007).

In vitro and animal studies show that olives have potent antioxidant activities and could partially account for the observed health benefits of the Mediterranean diet (Raederstorff, 2009; Kawaguchi et al., 2011).

Although the composition of olives is complex, the major groups of compounds thought to contribute to the observed health benefits include oleic acid, phenols, and squalene (Owen et al., 2000), all of which have been found to inhibit oxidative stress (Visioli and Bernardini, 2011). Major phenols include hydroxytyrosol, tyrosol, oleuropein (Perona et al., 2006). Hydroxytyrosol and oleuropein are more potent at scavenging free radicals than the endogenous antioxidant vitamin E and the exogenous antioxidants dimethyl sulfoxide and butylated hydroxytoluene (Owen et al., 2000; Visioli et al., 2002). Human intervention studies indicate that these two phenols inhibit LDL oxidation in plasma and regulate several biomarkers of oxidative damage in the micro-molar range (Baroni et al., 1999; Owen et al., 2000; Visioli et al., 2002).

The olive has been widely studied for its effects on cardiovascular disease, specifically for its ability to reduce blood pressure and LDL-cholesterol (Baroni et al., 1999; Waterman and Lockwood, 2007). In vitro studies have demonstrated hydroxytyrosol and oleuropein are capable of inhibiting production of isoprostanes, a marker of LDL oxidation (Salami et al., 1995). Several studies have also demonstrated the antihypertensive properties of olives and olive oil (Alonso et al., 2006; Belarbi et al., 2011), and since hydroxytyrosol has biological activity beyond its antioxidant capacity, it affect a wide range of enzymes, including cyclooxygenase and NAD (P)H oxidase, and reduce platelet aggregation (Fabiani et al., 2002; Visioli et al., 2002).

Strong epidemiological evidence suggests that regular intake of olive and derivative products low the incidence of certain cancers, including breast, skin, and colon (Owen et al., 2000; Harwood and Yaqoob, 2002). One mechanism associated with the anti-cancer effects of hydroxytyrosol and oleuropein is through the prevention of DNA damage that in turn prevents mutagenesis and carcinogenesis (Visioli et al., 2002). In addition, oleuropein has been shown to exert hepatoprotective activities (Domitrovic et al., 2012). In vitro studies have demonstrated the anti-microbial activity of hydroxytyrosol, tyrosol, and oleuropein against several strains of bacteria implicated in intestinal and respiratory infections (Romero et al., 2007). Furthermore, the administration of olive in lipid emulsions may exert beneficial effects on the immune system (Puertollano et al., 2010).

Grapes (Vitis vinifera l.)

The health effects of grapes on cardiovascular disease risk, mainly on endothelial function, LDL oxidation, progression of atherosclerosis, and reduction in oxidative stress, have been thoroughly investigated (Folts, 2002; Dohadwala and Vita, 2009; Feringa et al., 2011; Weseler et al., 2011). There is evidence suggesting that moderate consumption of grapes can decrease mortality (Vislocky and Fernandez, 2010). Numerous studies in vitro as well as in animals and humans demonstrate beneficial effects of grape polyphenols on cardiovascular risk factors including hypertension (Schini-Kerth et al., 2011) and diabetes (Zunino, 2009; Chuang and McIntosh, 2011), among others.

Many studies have also suggested chemopreventive benefits (Athar et al., 2007; Neves et al., 2012). Data are particularly compelling in the area of skin cancer prevention (Athar et al., 2007; Neves et al., 2012). Further favorable effects of grapes on oral health (Wu, 2009), immune function (Percival, 2009), anti-inflammatory (Chuang and McIntosh, 2011; Zhou et al., 2011; Lee et al., 2012), and anti-allergic (Lee et al., 2012) systems have also been reported. Others studies show that grape phenolic compounds possess antibacterial (Baydar et al., 2004) and antiviral (Liu et al., 2010a,b) activities. Novel and exciting results from independent research demonstrate that grapes have beneficial effects on other devastating illnesses, such as Alzheimer's disease, and age-related cognitive decline (Nakata et al., 2012; Wang et al., 2012).

These effects are often attributed to a valuable source of phytochemicals found in grapes with strong antioxidant activity that helps to prevent oxidative damage as well as other actions such as increasing nitric oxide production (Folts, 2002; Iriti and Faoro, 2009; Xia et al., 2010; Kawaguchi et al., 2011). Grapes contain high concentrations of polyphenols, especially flavonoids (Folts, 2002; Iriti and Faoro, 2009). The main grape polyphenols are anthocyanins in red grapes and flavan-3-ols in the white grapes; red grapes contain more total polyphenols than white grapes (Folts, 2002; Iriti and Faoro, 2009; Lee et al., 2012). Grape seeds contain significant amounts of proanthocyanidins or condensed tannins with therapeutic potential in the prevention and treatment of vascular complications in diabetic patients (Folts, 2002; Iriti and Faoro, 2009; Lee et al., 2012). Studies in human and experimental models demonstrate antioxidant properties closely associated with the maintenance of endothelial function, protection against LDL oxidation, and neuroprotective effects (Feringa et al., 2011). The flavonoids ellagic acid and the phytpalexin resveratrol have been suggested to reduce the risk of coronary heart disease (Folts, 2002; Iriti and Faoro, 2009; Xia et al., 2010; Ramprasath and Jones, 2010). Even though human evidence is lacking, resveratrol has been proposed to have heart-protective potential (Folts, 2002; Ramprasath and Jones, 2010), and cancer chemopreventive activities in different stages of carcinogenesis (Athar et al., 2007; Iriti and Faoro, 2009; Xia et al., 2010; Nakata et al., 2012; Neves et al., 2012). It must be underlined that these proposed activities await in vivo proof and that the concentrations of resveratrol in grapes are extremely low (Rotches-Ribalta et al., 2012).

CONCLUSIONS

The influence of diet on the overall health status has been recognized since ancient times, when pathologic conditions were treated with plants and natural foods believed to have medicinal properties. Currently, epidemiological studies have confirmed the association between diets rich in fruits and vegetables and lower risk for chronic diseases such as cancer and cardiovascular disease. A reduced risk of obesity and better control of diabetes are some additional benefits from increased consumption of plant foods. In addition, evidence also suggests that diets rich in fruit and vegetables decrease the risk of premature mortality. Fruits and vegetables, apart from being rich sources of vitamins, minerals, and fiber, also contain a wide variety of phytochemicals with potent bioactivity, among which polyphenols are mostly well known. Recently, the consumer perception is that phytochemicals with antioxidant properties present in these foodstuffs might prevent some of the processes involved in the development of cancer (i.e. by protecting DNA from oxidative damage) and in the development of cardiovascular disease (i.e. by inhibiting oxidative damage to LDL-cholesterol). However, epidemiologic studies on the impact of phytochemicals in human health have been inconclusive. Even when good evidence exists, results need to be interpreted and divulged carefully in relation to human health benefits, as phytochemicals may have limited bioavailability and may also be extensively metabolized. In addition, some phytochemicals can be toxic and mutagenic in some cell culture systems. Also, it should be borne in mind that fruits and vegetables contain a complex mixture of metabolites that cannot be simulated by single purified phytochemicals. In this context—and until more is known about the activity, bioavailability, and the distribution of phytochemicals in the organism—it appears correct to recommend fruits and vegetables in their entirety (minimum of 400 g/day) rather than isolated components as dietary supplements.

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STATEMENT OF INTEREST

The author declares no competing interests.

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