Chapter

Vitamin E: Natural Antioxidant in the Mediterranean Diet

Samia Ben Mansour-Gueddes and Dhouha Saidana-Naija

Abstract

Oxidation has been related to several diseases in humans. Indeed, to protect the body from high free radical damages, organism requires natural resources of antioxidant compounds, such as phenols, tocopherols (α, β, γ, and σ) which have important roles in the cell antioxidant defense system. In Mediterranean areas, olive oils and pepper fruits are considered among the best foods in a diet, which keeps on attracting the interest of scientists due to the health benefits linked with its consumption. The Olive oil and pepper fruits are among the most consumed nutrients in the Mediterranean diet; their richness in naturally powerful antioxidants, such as alpha-tocopherols, polyphenols, carotenoïds, and capsaicinoïds (specific of capsicum species), and monounsaturated fatty acids in olive and seed pepper oils, constitutes good health protection against oxidative damages and inflammation. Also, these phytochemicals shield and prevent the human body from many diseases such as cardiovascular, coronary, Alzheimer's diseases, and cancers.

Keywords: tocopherols, antioxidants, *Olea europaea*, *Capsicum* sp., fruits, oils, Mediterranean areas

1. Introduction

In recent years, oxidation constitutes a major problem in human health. Oxygen is considered a vital element, but its instability has deleterious effects on the human body. At high concentration, free radicals cannot gradually be destroyed, their accumulation in the organism generate oxidative stress. This process can damage all cell structures as lipids, proteins, and DNA and trigger many human diseases, such as cancer, arteriosclerosis, and rheumatoid arthritis. Moreover, it may play a role in neurodegenerative diseases and aging processes [1]. Hence, to protect human organisms against reactive oxygen species (ROS) a request for external nutritional intake rich in antioxidants can assist in coping with this oxidative stress. Many studies accorded that dietary vitamin antioxidants and polyphenols have been explored extensively as an exogenous mechanism of defense against oxidative stress [1, 2].

The antioxidants exert their activity by scavenging the 'free-oxygen radicals' thereby giving rise to a fairly 'stable radical'. The human body produces an insufficient level of antioxidants which are essential for preventing oxidative stress. To protect against oxidant radicals, organism requires natural resources of antioxidant compounds from nutrients of different origins. These bioactive molecules play an important role in helping endogenous antioxidants for the neutralization of free radicals. Nutrient antioxidant deficiency is one of the causes of numerous chronic and degenerative pathologies [3].

It has been demonstrated that many vegetables, fruits, medicinal plants, and other foods contain compounds with bioactivity against oxidative stress. This activity has been attributed to vitamin C, vitamin E, α-tocopherol, β-carotene, and polyphenolic compounds [4, 5]. Therefore, research regarding natural antioxidants from foods and plants, particularly from folk medicinal plants, is receiving increasing attention around the world.

In Mediterranean areas, nutrition is specific to each country. The Mediterranean diet takes into account the various religious and cultural traditions, as well as the various national identities, the current needs of Mediterranean populations, respecting regional dietary variations. The Mediterranean model, qualified as a healthy lifestyle [6]. It is considered as a model of sustainable nutrition [7] due to its richness in vegetables, fruits, in a quantity moderate fish, dairy, and meat products, condiments, and spices [8]. In fact, in Mediterranean countries, especially in North Africa, as Tunisia, the diet is based on olive oils, olive derivatives, cereals, Solanaceae species (pepper, tomatoes, potatoes), green vegetables, legumes, fresh and dried fruits. These sources of aliment are rich in macro and micro-nutrient such as fibers, antioxidants (vitamins, polyphenols, carotenoids), oligo-elements. In general, the Mediterranean diet is low in animal fat and fast sugar, but it is rich in fiber, omega 3, and antioxidants. The abundance of fresh fruits and vegetables and the use of olive oil instead of hard fats are key factors for which the Mediterranean diets are renowned. So many researches showed that Mediterranean eating habits appeared to meet all the criteria for a healthy and prudent diet [6, 9, 10].

In addition to macronutrients, humans need vitamins and minerals which are micronutrients required by the body to carry out a range of normal functions. However, these micronutrients are not produced in our bodies and must be derived from the food we eat. Vitamins, such as Vitamin A, B, C, E... are crucial for normal development. These micronutrients protect the organism against many diseases by their antioxidant property. In this context, this work aims to evaluate the richness in antioxidants, especially vitamin E, of the main Mediterranean nutriment olive oils, and pepper and their role in preventing many diseases.

2. Properties of vitamin E

2.1 Chemical properties

Vitamin E is composed of eight naturally isoforms, four tocopherols with the same molecular formula C28H48O2 (α-, β-, γ-, and σ-tocopherols), and four tocotrienols with a molecular formula C26H38O2 (α-, β-, γ-, and σ-tocotrienols) (**Figure 1**). These molecules are synthesized by photosynthetic organisms including plants, algae, and cyanobacteria, from homogentisic acid and phytyl-diphosphate or farnesyl-diphosphate reaction in plastid membranes [11]. All homologs are derivatives of 6-chromanol and differ in the number and position of methyl groups on the ring structure. The four tocopherol homologs have a saturated 16-carbon phytyl side chain. Whereas, the tocotrienols homologs have three double bonds on the side chain. The tocopherols and tocotrienols have the same basic chemical structure; the main difference is in the saturation of the aliphatic side chain attached to the chromanol ring [12, 13] (**Figure 1**). The various isoforms are not interchangeable and only α-tocopherol meets the human vitamin E requirements [14].

The reaction of aromatic chromanol ring with phytyl-diphosphate or farnesyl-diphosphate, in plastid membranes, synthesize different isomers of tocopherol or tocotrienol.

Vitamin E is a fat-soluble vitamin that exists in different chemical forms. The most active compound is alpha-tocopherol which existed in natural and synthetic forms.

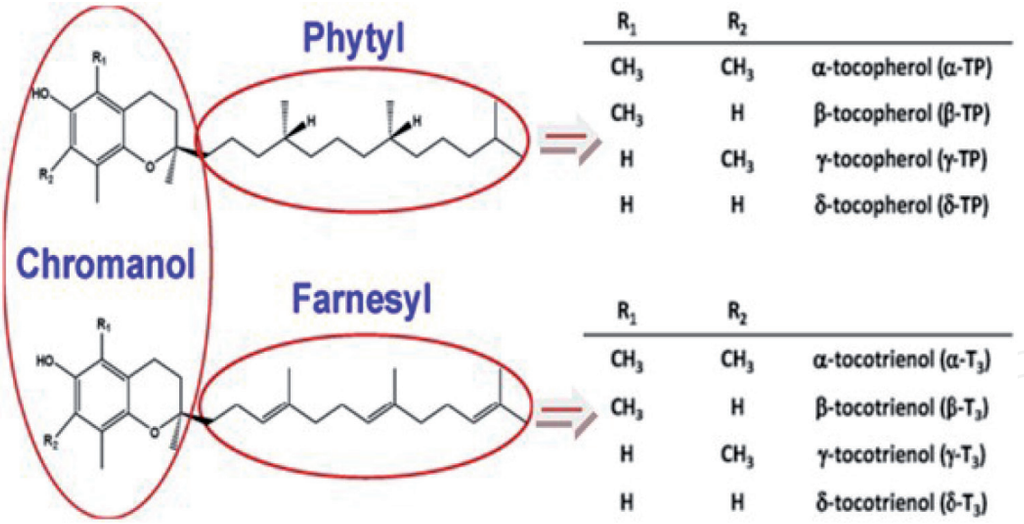

Figure 1.
Chemical structure of different isoforms of vitamin E [13].

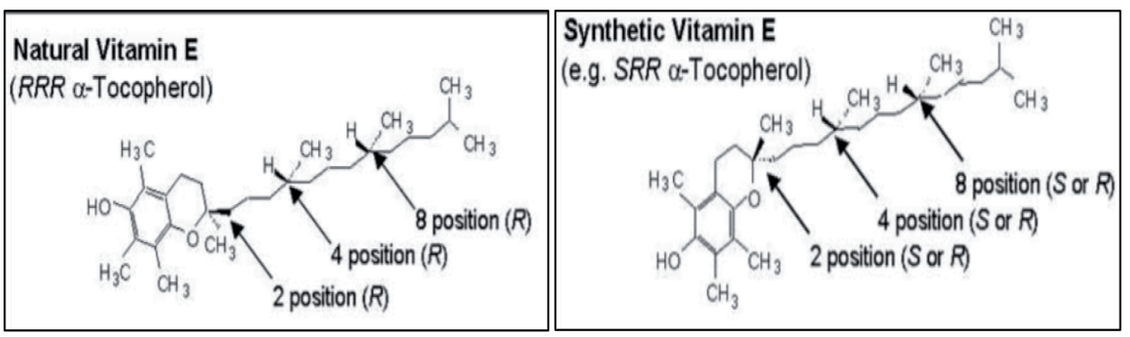

Figure 2.
Natural and synthetic Sterio-isoforms of vitamin E [14].

The natural vitamin E (RRR-α-tocopherol or D-α-tocopherol) consists of a single stereoisomer. While, synthetic vitamin E is a mixture of eight stereoisomers (RRR, RSR, RSS, RRS, SRR, SRS, SSR, SSS) distributed equally (**Figure 2**). Only one of them (1/8th) has a molecular structure identical to that of the natural vitamin. According to many studies, the natural vitamin E is twice as powerful and fixed twice as good as the synthetic version. This means that natural vitamin E reaches the blood and organs at least twice as good as synthetic ones [13, 14].

The stereoisomer S and R are the spatial arrangements of the alpha-tocopherol; The RRR refers to R at the 2,4 and 8 positions, hence RRR-α-tocopherol which correspond to Natural vitamin E. The synthetic Vitamin E agree to eight stereoisomers S and/or R at positions 2, 4 and 8.

2.2 Biological properties of vitamin E in the human body

Vitamin E is considered a natural phytochemical that is frequently associated with human health [15]. This vitamin is an example of a phenolic antioxidant; it serves as an antioxidant and protects membrane lipids from oxidative degeneration [16]. Therefore, both lipophilicity and membrane localization of vitamin E explain its antioxidant property. In this context, the incorporation of vitamin E into the cell membrane explained their major biologic role to protect polyunsaturated fatty acids (PUFAs) and other components of cell membranes and low-density lipoprotein (LDL) from oxidation by free radicals. Via their localization, within the phospholipid bilayer of cell membranes; It is particularly effective in preventing lipid peroxidation, a series of chemical reactions involving the oxidative deterioration of PUFAs [14].

Vitamin E under the term α-tocopherol is a powerful biological antioxidant. It is the major lipid-soluble component in the cell antioxidant defense system and is exclusively obtained from the diet. Among the eight isomers, The RRR-α-tocopherol is the most isoform of vitamin E that is essential for humans and is preferentially retained within the organism [14, 17, 18]. This is explained in part by the specific selection of RRR-α-tocopherol by the α-tocopherol transfer protein and in part by its low rate of degradation and elimination compared with the other vitamers, especially tocotrienols, which are rapidly metabolized and excreted similarly as other xenobiotics [14]. Also, [19] mentioned that γ-Tocopherol is slightly less efficient than α-tocopherol as a scavenger of oxygen radicals, but it is an efficient scavenger of reactive nitrogen species due to the unsubstituted 5-position on the chromanol ring. This isomer of Tocopherol is present in significant amounts in the human diet especially in several widely consumed vegetable oils [14].

This form is considered the most important fat-soluble antioxidant in humans metabolizing peroxyl radicals [19]. Such molecules readily donate the hydrogen from the hydroxyl (-OH) group on the ring structure to free radicals, which then become unreactive. On donating the hydrogen, the phenolic compound itself becomes a relatively unreactive free radical because the unpaired electron on the oxygen atom is usually delocalized into the aromatic ring structure thereby increasing its stability [14].

The potent lipid-soluble antioxidant property of α-tocopherol is to maintain the integrity of long-chain polyunsaturated fatty acids in the membranes of cells and thus maintain their bioactivity [20]. The α-tocopherol protects the peroxidation of unsaturated fatty acids of the cell membrane. When peroxyl radicals ($ROO^{\bullet}$) are formed, these react 1000-times faster with vitamin E (Vit E-OH) than with polyunsaturated fatty acids (PUFA: ROOH) [21]. The hydroxyl (OH) group in the chromanol head of α-tocopherol can donate hydrogen to scavenge lipid peroxyl radicals ($ROO^{\bullet}$) generated from the peroxidation of the lipids to form the corresponding lipid hydroperoxide and the tocopheryl radical (Vit E-$O^{\bullet}$). The tocopheryl radical (Vit E-$O^{\bullet}$) reacts with vitamin C, thereby oxidizing the latter and returning

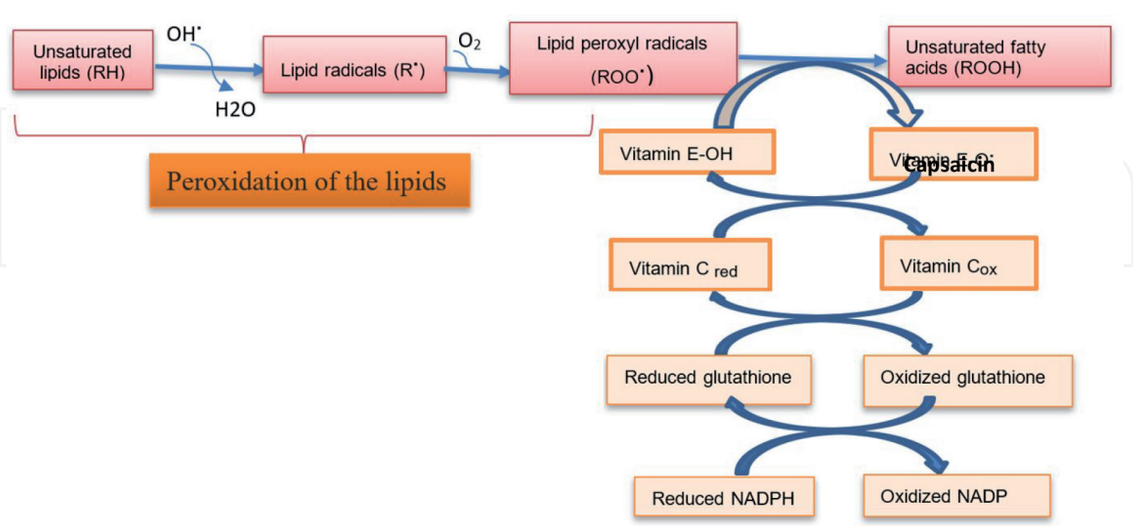

Figure 3.
The antioxidant property of Vitamin E and its regeneration by other antioxidants "Vitamin E recycling". Vitamin E-OH: alpha-tocopherol; Vitamin E-O.: tocopheryl radical; NADP: nicotinamide adenine diphosphate; NADPH: reduced NADP. The peroxidation of unsaturated lipids leads to forming lipid peroxyl radicals (ROO·). α-tocopherol easily diffuses into cell membranes, due to its lipophilic nature, and scavenges rapidly, with a hydroxyl group, the lipid peroxyl radicals and protects polyunsaturated fatty acids from lipid peroxidation. The redox reaction between tocopherol and harmful lipid peroxide radicals leads to forming neutral lipid hydroperoxide and an unreactive vitamin E radical (Vitamin E-O.). The presence of other antioxidants, such as vitamin C, is required to regenerate the antioxidant capacity of α-tocopherol.

vitamin E to its reduced state. The presence of other antioxidants such as vitamin C is required to regenerate the antioxidant capacity of α-tocopherol (**Figure 3**).

The interaction of vitamins E and C has led to the idea of "vitamin E recycling", where the antioxidant function of oxidized vitamin E is continuously restored by other antioxidants (**Figure 3**).

3. Role of vitamin E against diseases

The Mediterranean diet (MedDi) is characterized by a high content of bioactive phytochemicals especially the antioxidants such as polyphenols, carotenoids, vitamins C and E which are key components of many plant foods. These bioactive compounds in (MedDi) have a particular interest in the prevention of many diseases such as cancer, cardiovascular diseases, etc. [22]. Also, the major dietary sources of vitamin E are fruits, vegetables, nuts, and oils. Vitamin E is known to inhibit lipid peroxidation eventually protecting DNA from damage involved in the pathogenesis of cancer [23].

Antioxidants from our diet play an important role in helping endogenous antioxidants for neutralizing free radical species. Thus, free radicals are involved in some diseases including tumor inflammation, hemorrhagic shock, atherosclerosis, diabetes, infertility, gastrointestinal ulcerogenesis, asthma, rheumatoid arthritis, cardiovascular disorders, neurodegenerative diseases, etc. [24, 25].

By its natural antioxidant property, vitamin E plays a key role in maintaining health and preventing many chronic and degenerative diseases [26]. In fact, vitamin E could help avoid or delay coronary heart disease, it could also prevent atherosclerosis by inhibits or reduces the oxidation of low-density lipoprotein (LDL) cholesterol which is associated with the development of atherosclerosis [27]. Also, the supplement of this nutrient plays a cardioprotective role and decreases cardiovascular events [28, 29], and avoids the formation of blood clots that could lead to a heart attack or venous thromboembolism [30]. Nutrient antioxidant deficiency is one of the causes of numerous chronic and degenerative pathologies [1].

Among the different forms of vitamin E, alpha-tocopherol constitutes the most biologically active form and is preferentially absorbed and retained in the body. It has anti-inflammatory, antiplatelet, and vasodilator properties with which vitamin E enhances the immune system presents the capacity to promote health, prevents and treats many diseases [29, 31]. Also, due to its natural properties to be fat-soluble and to incorporate into biological membranes, alpha-tocopherol prevents protein oxidation and inhibits lipid peroxidation, thereby maintaining cell membrane integrity and protecting the cell against damage [32]. Alpha-tocopherol also modulates the expression of various genes, plays a key role in neurological function, inhibits platelet aggregation, and enhances vasodilatation. Many researches showed that the supplementation of vitamin E (200–400 mg/day) may be suitable to moderate some aspects of degenerative diseases such as Parkinson's disease, reduce tissue injury arising from ischaemia and reperfusion during surgery, delay cataract development, and improve mobility in arthritis sufferers [33].

4. Vitamin E in olive trees

4.1 Importance of vitamin E in olive oil

Olive fruits and olive oils are considered excellent Mediterranean nutriments. Their consumption in the Mediterranean diet (MedDi) constitutes the cause of

many health-promoting effects. The olive oils are characterized by their richness in oleic acid, vitamin E, polyphenols, and some other minor components some of which are known to be anti-inflammatory, make it the model functional food [34]. Olive oils, virgin, and extra virgin are a symbol of the Mediterranean Diet. Alpha-tocopherol was the most abundant tool and detected in all the studied olive oil samples [35]. Many research proved that the levels of tocopherols in olive oils are high variety and geographic areas-dependent.

The alpha-tocopherol is more active than others $\beta > \gamma > \delta$ against free radicals. It protects free fatty acids from peroxidation. The tocopherol radicals are resonance stabilized within the chromanol ring and do not propagate the chain reactions or are rapidly recycled back to the corresponding tocopherol, allowing each tocopherol to participate in many peroxidation chain-breaking events. One tocopherol molecule can protect about 103–108 polyunsaturated fatty acids at low peroxide values [36]. According to [37], α-tocopherol represented almost 95% of total tocopherols and their contribution is greater than the rest of tocopherols; their content in virgin olive oils varies from 97 to 785 mg/kg. In fact, α-tocopherol concentration ranges from 170 to 485 mg/kg in Spanish varieties [37]; 160 to 428 mg/kg in the

Countries	**Varieties**	**Total Tocopherol (mg/kg)**	**α- tocopherol (mg/kg)**	**References**
Spain	Arbequina	371 ± 16	373 ± 16	[37]
	Morisca	501 ± 26	485 ± 27	
	Picual	355 ± 19	346 ± 20	
	Manzanilla-cacerena	336 ± 31	333 ± 31	
	Corniche	366 ± 31	366 ± 31	
	Verdial de Badajoz	292 ± 23	311 ± 22	
	Carrasquena	310 ± 58	280 ± 56	
Greece	Koroneiki	121 ± 22	117 ± 21	[42]
	Kolovi	123 ± 28	110 ± 15	
Turkey	Ayvalik	183.27 ± 15.5	180.43 ± 15.17	[35]
	Domat	160.78 ± 18.7	106.8 ± 18.27	
	Gemlik	114.87 ± 9.73	112.59 ± 9.49	
Italy	Leccino	455.25 ± 4.4	405.6 ± 4.6	[43]
	Frantoio	270.7 ± 1.7	230.0 ± 1.6	
Tunisia	Chetoui	405.65 ± 4.17	385.35 ± 2.48	[44]
	Chemlali	199	184	[44]
	Chemlali Sfax	467	425	[45]
	Chemlali Zarzis	400	374	[45]
	Oueslati	204	185	[45]
	Sayali	282	264	[45]
	Zalmati	351	336	[45]
	Zarrazi	208	193	[46]
	Meski	-	74.6 ± 4.6	[47]
	Neb Jmal	-	232.29 ± 2.00	[47]
	El Hor	-	335.27 ± 1.16	[47]
	Jdallou	-	364.23 ± 3.30	[47]
Maroc	Picholine marocaine	311 ± 11.4	272.0 ± 8.0	[48]
Algeria	Chemlal Bordj	202.35	193.55	[49]
	Arima	188.55	179.72	
	Chemlal Zenata	240.1	228.11	
	Chemlal (SBA)	215.6	202.9	
	Sigoise Sebra			

Table 1.
Total tocopherols and α-tocopherol composition in olive oils of different varieties from Mediterranean countries.

Argentinean oils [38]; 98–370 mg/kg in the Greek oils [37], 97–403 mg/kg in oils from Turkey [39], 120–478 mg/kg in oils from Tunisia [40], and 138–298 mg/kg in the Portuguese oils [41] (**Table 1**).

4.2 Effect of olive oils in many diseases

Olive oil is the main source of fats in Mediterranean diets. This type of diet has often been associated with improving the resistance to certain diseases, including cardiovascular disease and illness degenerative. Many scientific studies have focused on the nutritional aspect of olive oil to understand the mechanisms of this phenomenon. The first explanation is its specific fatty acid composition. The proportion of saturated fatty acids is very low (14%); while the majority of monounsaturated fatty acids (MUFA) is oleic acid. Essential polyunsaturated fatty acids (PUFA) are also present in interesting proportions in the oil. MUFA supplement allows to increase the resistance of LDL to oxidation [50], thus reducing one of the factors that can cause coronary heart disease [9].

The Extra Virgin Olive Oil (EVOO) is one of the most important health-protective foods in the Mediterranean diet [51]. The high-quality EVOO is considered as a true pharm-food. This oil contains a relevant concentration of efficient chemopreventive molecules, including Tyrosol, hydroxytyrosol, tocopherols (vitamin E), β-carotene, and phenolic compounds [51, 52]. [53] showed the ability of VOO phenolic compounds to shield lipoproteins from oxidation and to reduce systolic blood pressure in hypertensive individuals. These antioxidants compounds are thought to be beneficial to protect against neurodegenerative diseases and cardiovascular diseases [54]. Also, [27] suggested that the antioxidants compounds in EVOO can prevent and treat cancers, diabetes, neurodegenerative diseases, inflammation, and aging. They have an antimicrobial property and also play an important role in strengthening the immune system and protecting certain tissues and organs from damage. The presence of phenolic compounds and tocopherols in Extra Virgin Olive Oil (EVOO) protects the unsaturated fatty acids from peroxidation, thus contributes to the stability of cellular brain structures [51, 55] and it has beneficial effects on learning and memory [55]. The phenolic compound and tocopherols have often been linked to reducing the risk of cognitive decline and are essential for proper brain function.

5. Impact of pepper composition in human health

5.1 Importance of pepper in Mediterranean diet

Pepper is a very important vegetable worldwide and has economic and agro-food importance in many countries. In the Mediterranean, pepper is cultivated in the warm regions particularly in Tunisia where its cultivation has spread due to its strong uses in Tunisian cuisine. Pepper fruits were appreciated and consumed mostly as fresh food or dried as a spice. The nutritional contribution due to the presence of beneficial healthy-related compounds, Pepper is among the most fascinating and consumed spice foods, largely appreciated for its flavor, high nutritional and health contribution to human diets [56].

Pepper is a usual part of a traditional Mediterranean diet. Hot peppers are intensively used as food additives for their pungency, aroma, and color [57]. Their consumption is nutritionally valuable and also contains ingredients that promote health. The presence of phytochemicals and antioxidants in fruits increases its importance in controlling diseases to protect the human body from the harmful

effects of free radicals [58]. Therefore, integrating a pepper-rich diet in our daily meals can prevent cardiovascular diseases, could help in fighting blood cholesterol levels, and can have, by capsaicin, an antidiabetic activity [58, 59].

5.2 Antioxidants in pepper fruits

Pepper fruits are recognized for their richness in phytochemicals and antioxidants with high nutritional value. The fruits are considered an excellent source of macro and micro-nutrients such as provitamin A, vitamins C and E, carotenoïds, capsaicinoïds, minerals, polyphenols, phytosterol, metabolites with famous antioxidant properties that positively affect human health [60–62]. These phytochemicals are influenced by a variety of peppers and environmental factors. The analysis of 23 accessions of peppers, collected from multiple Peruvian locations, showed that the tocopherols varied strongly from 0.23 to 29.1 mg/100 g, the total polyphenols between 0.97 and 2.77 g gallic acid equivalents (GAE)/100 g and the concentrations of capsaicinoïds range from 1.0 mg/100 g to 1515.5 mg/100 g (GAE)/100 g [63]. So, the consumption of pepper fruits and integrating a pepper-rich diet into our daily meals can be helpful in the continuing quest to combating micronutrient deficiency [64].

Peppers are considered one of the best sources of natural vitamin E and C. Many studies showed that the level of α-tocopherol in dry red pepper powder is similar to those in spinach and asparagus and four-fold higher than that in dry tomatoes [64]. The recommended daily intake of vitamin E was 15 mg/day of α-tocopherol for both women and men. Pepper fruits can supply above 100% α-tocopherol per 100 g serving depending on the cultivar [61]. Also, the red pepper seed oils showed a high antioxidant capacity due to their richness in bioactive phytochemical compounds such as polyphenols, carotenoids, tocopherols,

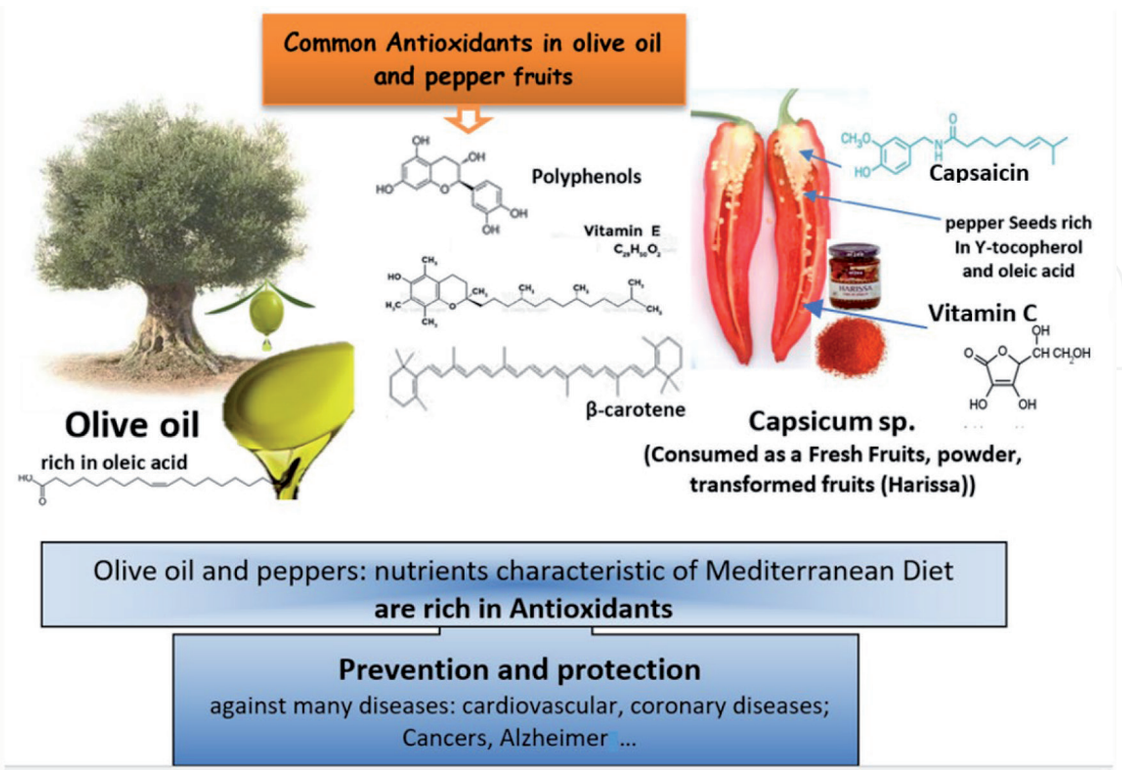

Figure 4.
Graphical abstract of the main antioxidants commonly present in olive oils and pepper fruits, characteristic of the Mediterranean diet, such as phenolic compounds, carotenoids, tocopherols and oleic acid. The capsaicin is specific to capsicum species, which have anti-inflammatory properties.

phytosterols, and unsaturated fatty acids especially the linoleic acids which are higher than those of oleaginous seed oils [62]. It has been reported that polyphenols and tocopherol were the predominant antioxidant compounds in red pepper seed oils; Which γ-tocopherol was the main tocopherol at 278.65 mg/100 g seed oil, followed by alpha-tocopherol and delta-tocopherol [62]. The ratio between α- and γ-tocopherol depends on the number of seeds in the chili powder. As a matter of fact, the amount of α-tocopherol in the pericarp is higher, however, γ-tocopherol is more dominating in the seeds [63].

Hot pepper fruits are rich in capsaicinoïds, unique compounds of Capsicum species, which are responsible for the pungency. Capsaicin is widely influenced by the variety and maturity stages and by environmental factors [65]. These alcaloïds have antioxidant, anti-inflammatory, analgesic properties and are characterized by great medical and pharmacological values [58, 66]. These molecules also have a therapeutic effect as a neuropharmacological tool. Their effect in the treatment of painful conditions has been evaluated, such as rheumatic diseases [66]. Many recent studies have shown the effective treatment of capsaicinoïds for several sensory nerve fiber disorders, including arthritis and human immunodeficiency virus [67]. In this context, the proposed diet rich in pepper fruits can be considered an excellent strategy to improve the nutritional value of the population due to its high antioxidants and phenolic compound content.

The pepper fruits and olive oil constitute an excellent nutrient, for their richness in antioxidants (**Figure 4**). Since these Mediterranean foods have an important effect on human health, it is encouraged, around the world, to consume them.

6. Conclusion

The Mediterranean diet is rich in nutrients that have antioxidant properties. Particularly olive oil and pepper fruits constitute the most abundant and consumed vegetable nutriments in MedDi areas. Their richness in polyphenols, tocopherols, carotenoids, chlorophylls, unsaturated fatty acids, olive oils constitute a health treasure. These minor components are known to prevent and protect the human organism against many diseases such as cardiovascular, coronary diseases; also, some of these antioxidants have anti-inflammatory action, make it the model functional food. Pepper fruits are mostly consumed by the Mediterranean population as traditional spices and food products. Fruits are characterized by a means of antioxidants such as vitamin A alpha and gamma tocopherols, vitamin C, capsaicinoïds, polyphenols. The consumption of both nutriments rich in natural powerful antioxidants, such as tocopherols and polyphenols, constitutes a good strategy for reducing oxidative damage and to improve the health state of the human body, and preventing it from diseases.

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Conflict of interest

The authors declare no conflict of interest for this chapter.

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