

## Review Article

# Mediterranean Diet Ingredients: Their Antioxidant and Anti-Inflammatory Potential

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## Abstract

Attractive for its palatability and unique flavourful food choices, the Mediterranean Diet (MD) is one of the most studied dietary patterns due to its numerous health and well-being benefits. MD is, also, an example of a sustainable food system and lifestyle that can be easily implemented outside the Mediterranean basin. It is mainly a plant-based diet, which emphasizes abundant consumption of unprocessed or minimally processed fruits, vegetables, whole grains, nuts, legumes, seeds, herbs and spices, followed by moderate consumption of fish, poultry, eggs and low-fat dairy and fermented dairy products. Extra Virgin Olive Oil (EVOO), the cornerstone of the MD, is the main source of healthy fats, while the consumption of red meat products and products with refined sugars is low. Plenty of fluids like water, juices, herb teas, coffees, and soups are frequently consumed to maintain a good hydration, as well as red wine consumed in moderation with the meals is practiced in some of the Mediterranean countries depending on the culture, traditions and religious beliefs. An updated MD food pyramid describing the main ingredients of this dietary pattern is proposed. The phytonutrients, consumed daily within the MD and acting in synergy, are responsible for the highly antioxidant and anti-inflammatory nature of this diet and are briefly described.

**Keywords:** Mediterranean Diet; Phytonutrients; Polyphenols; Antioxidants; Anti-inflammatory potential

## Introduction

The Mediterranean Diet (MD) does not refer only to the dietary patterns of the people living in the Mediterranean basin, but also to their lifestyles, cooking habits, rituals, traditions, and beliefs. Due to its uniqueness and benefits, MD became a part of the UNESCO's intangible cultural heritage in 2010, where it is defined as "a set of skills, knowledge, rituals, symbols and traditions concerning crops, harvesting, fishing, animal husbandry, conservation, processing, cooking, and particularly the sharing and consumption of food."

Although MD differs from country to country in terms of food choices and cooking practices, religious beliefs and other traditions, it still has a common set of features capturing the dietary and lifestyle habits of the people around the Mediterranean Sea. From a dietary aspect, MD is mostly a plant-based diet, which emphasizes consumption of fruits, vegetables, whole grains, nuts, legumes, seeds, herbs and spices, followed by moderate consumption of fish, poultry, low-fat dairy and fermented dairy products. Extra Virgin Olive Oil (EVOO), as a main source of healthy fats, is used in abundance, while the consumption of processed red meat products and products with refined sugars is limited. Plenty of water, fruit juices, herbal teas, broths and soups are also frequently consumed, while a moderate amount of red wine is usually taken with the meals. The food preparation and consuming the meals together with family and friends are common habits in the Mediterranean area. Adequate sleep, taking rests during the day, daily physical activities and being a part of the community are, also, features of the Mediterranean lifestyle. The socializing aspect and the dietary characteristics of MD have been associated with the

longevity and reduced risk of many diseases of the people living in the Mediterranean basin. Furthermore, MD has been widely studied and presented as a great example of a sustainable food system with numerous health benefits. The diet's compliance with all seventeen UN's Sustainable Development Goals (SDGs) has been also proposed for the first time by the authors [1-3].

## Nutritional Profile of Mediterranean Diet Ingredients

The ingredients of MD are usually presented in a form of a MD food pyramid, originally developed by Oldways Preservation Trust, Harvard School of Public Health, and the World Health Organization [2,4-7]. The pyramid has been updated and revised over the years mainly in the direction to capture the lifestyle habits of the people in the Mediterranean basin beside the dietary choices. In general, the pyramid contains the foods consumed daily and in abundance are usually located in the base of the pyramid, followed by those that are moderately consumed, while the foods consumed in limited amounts, or occasionally consumed, are at the top of the pyramid. Herein, we present a modified food pyramid, the MD Inspired® pyramid, which contains the foods often consumed within this dietary pattern (Figure 1).

The MD is based on the daily consumption of plenty of raw or minimally processed fruits and vegetables, whole grains, legumes (beans, peas), nuts, seeds and variety of spices and herbs. Extra virgin olive oil is, also, consumed in abundance for preparing salads and variety of traditional Mediterranean dishes. In fact, EVOO, along with the nuts and the seeds, are the main source of healthy unsaturated fats



**Figure 1:** MD Inspired® diet pyramid of foods frequently consumed within the Mediterranean dietary pattern.

in this diet. Low-fat milk and fermented milk products, such as sour milk, yogurt, cheese, curds, then fish and seafood, and poultry and eggs are moderately consumed during the day or several times per week. Desserts containing refined sugars are consumed very rarely or occasionally for special occasions, such as holidays and family celebrations. The main difference in the traditional Mediterranean cuisine is that the traditional Mediterranean desserts are usually prepared with natural ingredients, such as dried fruits, nuts, spices and honey. Red meat and processed red meat products are also minimally consumed within the traditional Mediterranean dietary pattern [2,7-15].

Seasonal and locally harvested foods, such as fruits and vegetables, whole grains, legumes, nuts and seeds are in the base of the pyramid, meaning their frequent consumption and in abundance during the day. The nutrient-dense character of the plant-derived foods along with the complex blends of various nutrients (phytochemicals) found in these foods are the reason for their multiple bioactive functionalities, such as anti-inflammatory and antioxidant activities, resulting in numerous health benefits for those who adhere to the Mediterranean dietary pattern. Besides the favorable nutritional profiles, the unique combinations of different parts of these edible plants, *viz.* fruits, seeds, leaves and roots result in palatable dishes with unique smell, taste and flavor [14-17].

Raw vegetables and fruits, e.g. various leafy greens, spinach,

chard, cabbage, broccoli, peppers, tomatoes, eggplants, carrots, olives, onion, garlic, citrus fruits, berries, apples, pomegranate, figs, grapes, pumpkins, squash, watermelon, cantaloupe, and others, are great daily sources of diverse phytonutrients. They are usually consumed in the seasons when they are harvested and ripe, and locally, meaning not being transported long distances and not being frozen. In addition, vegetables and fruits are mostly consumed raw or minimally processed, thus, having unaffected nutritional profiles during consumption. The variety of “colors and textures” of the fruits and vegetables consumed within the diet usually means a broad spectrum of consumed protective phytochemicals. For instance, vegetables are important sources of polyphenolic compounds, such as flavonols, flavones, stilbenes, and others, dietary fibers, vitamins A, C, K, E, B6, folate, and choline, minerals such as Copper (Cu), Potassium (K), Magnesium (Mg), Iron (Fe), and Manganese (Mn) among many others, some of them presented in Figure 2. Moreover, the richness of the plants with dietary fibers promotes the feeling of satiety - the feeling of being and staying full for a longer time, which is beneficial for the gut health and digestion, as well as maintaining a healthy weight. Fruits are rich in dietary fibers, potassium, vitamin C, flavonoids and terpenes. Seasonal fruits are used daily, often as desserts replacing the sweets and cakes, which contain refined carbohydrates [2,9,10,18-23].

The allium family of vegetables (garlic, onions, leeks, shallots, scallions, and chives), often considered as key savory ingredients

of the MD, add the characteristic culinary flavor to the traditional Mediterranean dishes. They are rich in organosulfur compounds, e.g. allicin, diallyl disulfide and others, and many powerful antioxidants (quercetin, kaempferol), which reduce the oxidative stress known to cause cellular damage, thus, having the anti-cancerogenic and anti-inflammatory activities, among others [24-33].

Spices and herbs, such as basil, rosemary, oregano, black cumin, thyme, ginger, cinnamon, clove, dill, parsley, licorice, mint, as well as garlic and onions are often added in the Mediterranean cuisine to introduce variety of flavors and tastes to traditional recipes replacing

partially a portion of the salt. This is very beneficial, as the salt intake is becoming an alarming issue in modern diets and has been linked to hypertension and other heart-related diseases. Moreover, herbs and spices are rich sources of micronutrients, antioxidant and anti-inflammatory compounds. They have been also used for preservation of foods and beverages due to the high phytochemicals' content [34-39].

In the traditional MD, seasonal vegetables and fruits are mostly consumed in the seasons when available, while for the remaining seasons, usually for the winter, they are usually preserved mainly

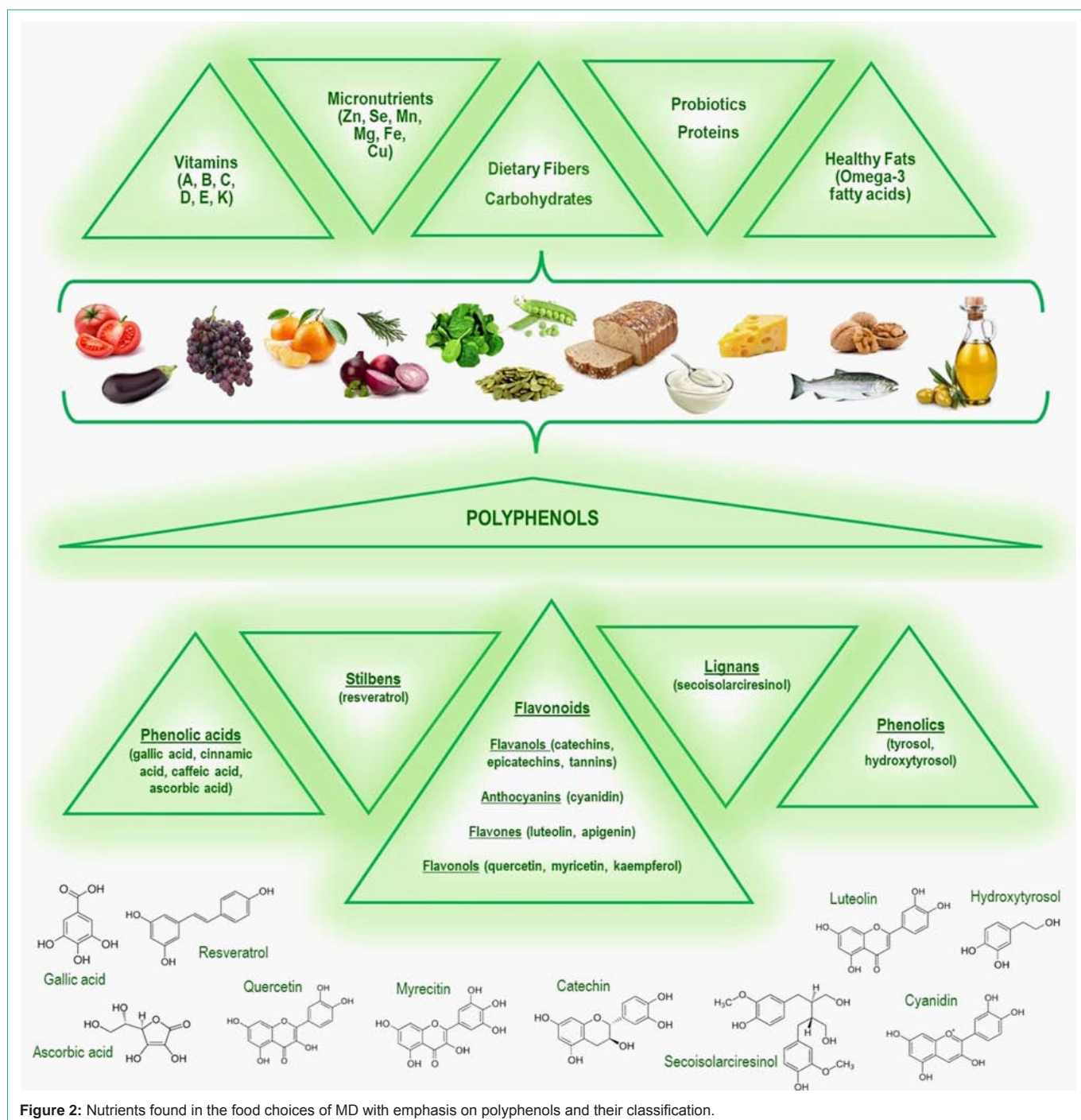


Figure 2: Nutrients found in the food choices of MD with emphasis on polyphenols and their classification.



via fermentation and sun-drying processes. Fermentation as one of the oldest techniques for food preservation is often used in the Mediterranean basin for fermenting foods and drinks, e.g. wine. During the fermentation process, natural bacteria are using the sugar and starch in the food and are creating environment that preserves the food and promotes beneficial enzymes, B vitamins, and omega-3 fatty acids, as well as various species of good bacteria. Fermented vegetables, such as cabbage, cauliflower, peppers, green tomatoes, cucumbers, carrots, olives and others are rich with probiotics and are often used during off-seasons. Diets involving high content of fermented foods, i.e. foods rich in probiotics have been found to result in gut microbiome diversity, which is beneficial for the overall health, improved immunity and reduced inflammation [40,41].

Sun-dried fruits, such as dried figs, dates, apricots, prunes, raisins and others, rich with selenium, copper, potassium, magnesium, B-complex vitamin, vitamin C, carotenoids, and dietary fibers are used as snacks and for preparation of traditional desserts replacing a large portion of sugar [42,43].

Fruits, vegetables, and legumes are also known as sources of prebiotics. Prebiotics are actually plant fibers that contain complex carbohydrates. These carbohydrates aren't digestible by the body, so they pass through the digestive system and serve as food for the gut bacteria and other microbes. The prebiotics stimulate the growth of healthy bacteria, while the probiotics increase the number of microbes in the gut. Probiotics are different from the prebiotics, because they do contain live organisms, usually specific strains of bacteria that directly add to the population of healthy microbes in the gut [44-53].

Seeds, namely, black cumin, hemp, flax, pumpkin, sunflower quinoa, and sesame seeds are usually used in the form of intact raw or dry seeds, oils, or as powder to enrich variety of foods as flavorings, ingredients, or for health purposes. Majority of seeds are low-calorie rich sources of proteins, fibers, vitamins E and B, minerals (calcium, magnesium, manganese, phosphorus, iron, zinc) and unsaturated fatty acids which account for more than 85% of their fatty acid composition. Many seeds also contain polyphenols, which provide health benefits and have strong antioxidant activities [54,55].

Whole grains, such as rice, oatmeal and products made of whole grains, viz. variety of breads, pastries, cereals, pasta, crackers and variety of traditional pies filled with cheese, vegetables or fruits, are consumed often. Whole grains are a good source of nutrients, such as dietary fibers, iron, zinc, manganese, folate, magnesium, copper, thiamine, niacin, vitamin B6, phosphorus, selenium, and riboflavin [56].

Protein- and fiber-rich legumes, such as different types of beans, peas, lentils, chickpeas and others, are often used in many Mediterranean dishes combined together with various herbs, spices and vegetables. Phytonutrients often found in the legumes are vitamin B6, folate, flavones, phytosterols and various minerals (Figure 2) [54,55].

Nuts, such as walnuts, almonds, hazelnuts, pistachios, peanuts, pine nuts, cashews, and so on, are frequent snacks, or are often used as ingredients in the Mediterranean dishes and especially in Mediterranean desserts. They are good sources of healthy fats (omega-3 fatty acids), proteins, vitamins (tocopherols-vitamin

E, vitamin B2, folate), minerals (potassium, copper, phosphorus, selenium, magnesium), phytosterols, fibers and significant loads of antioxidants. In particular, nuts are also excellent sources of antioxidant phenolics, with some nuts having particularly high levels of proanthocyanidins and hydrolysable tannins (gallotannins and ellagitannins), as shown in Figure 2. Besides their satiating effect, the nuts' intake usually does not promote obesity and has beneficial effects on many diseases and disorders, such as metabolic syndrome, diabetes, cardiovascular (CVD) and other diseases. Nuts are cholesterol-free and have been shown that their phytosterols actually interfere with the cholesterol absorption, and thus, help to lower the blood cholesterol level. Among the nuts, the walnuts have the highest polyphenol content and are one of the most used nut in the traditional Mediterranean desserts [9,57-62].

The whole grains, legumes, nuts, seeds, vegetables and fruits provide a plethora of dietary fibers, which are essential nutrients for the gut microbiota and the gut lining, and thus, promote good overall health and protection from external "invaders" [44-49].

Extra virgin olive oil is a cornerstone of the MD. Numerous epidemiological studies have linked the consumption of EVOO and better overall health and well-being. Namely, *in vitro* and *in vivo* studies have indicated that the regular intake of EVOO is associated with enhanced neuroprotective, antioxidant, anti-inflammatory, anti-atherosclerotic and anti-cancer activity. EVOO is a main source of healthy fats in the traditional MD, beside the fats provided by the consumed nuts and seeds. Its unique composition, the fatty acid composition and the richness with bioavailable polyphenols, is responsible for the health protective benefits of EVOO and its resistance to elevated temperatures, which makes it good for both, cooking and salad dressings. EVOO as one of the most studied oils to-date has been associated with extended life expectancy and reduction of the risks of many age-related degenerative diseases in people who consume it regularly. Moreover, EVOO has been reported to be inversely associated with the risks for several cancers and CVDs, as well as positively affects the blood lipids, i.e. cholesterol and triglyceride levels. All these benefits are due to the richness of the EVOO with valuable bioavailable phytochemicals, such as the optimal fatty acid profile, especially Monounsaturated Fatty Acids (MUFA) viz. oleic, palmitic, linoleic, and  $\alpha$ -linoleic acid, tocopherols (vitamin E), beta-carotene and a variety of polyphenols. Furthermore, EVOO has been implicated in modulation of the aging processes due to its effectiveness in reducing the inflammatory and oxidative processes. Diversity of the polyphenols, such as phenolic acids (caffeic, p-cumaric, ferulic acid), phenolic alcohols (hydroxytyrosol, tyrosol), secoiridoids (oleuropein), flavonoids (quercetin, luteolin, apigenin), lignans and others (Figure 2), result in a strong antioxidative activity of EVOO, capable to scavenge oxidative species, increase cellular endogenous antioxidant defenses, and thus, reduce the oxidative stress in the body. Hydroxytyrosol and tyrosol, which comprise over 90% of the total phenolic content of EVOO, have been proven for their very high rates of absorption in humans upon ingestion (40-95% depending on the EVOO quality), while oleuropein in EVOO has been shown to have superior anti-oxidation effects on blood lipids when compared with other cooking oils with similar fatty acid content. Moreover, the EVOO's phytochemicals decrease the inflammation via modulation of pro-inflammatory cytokines and enhance the immune function

in the body, as well as act toward enhanced fat metabolism and enhanced energy expenditure [12,62-73].

A moderate consumption of dairy products, fish (salmon, tuna and sardines), seafood, and other animal-based foods, such as poultry and eggs, is another characteristic of the traditional MD. Low-fat dairy products and especially fermented milk products, such as feta cheese and other types of cheeses, yogurt, kefir, curds, and sour milk products, are consumed moderately during the day or week. These products are rich in vitamin D and calcium, and the fermented dairy products are rich in probiotics and other nutrients important for the optimal gut, bone and heart health [14,19,74,75]. Fish and seafood, are rich in omega-3 long-chain Polyunsaturated Fatty Acids (PUFAs), *viz.* Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA), and are consumed moderate-to-often i.e. several times per week. EPA and DHA promote the production of anti-inflammatory compounds important for suppression of chronic inflammation which has been implicated in the etiology of numerous diseases, such as type 2 diabetes, CVD, cancer, obesity, rheumatoid arthritis, neuro-degenerative diseases, etc. Poultry (e.g. chicken, turkey) and eggs are consumed in moderation and represent good sources of proteins, vitamins (vitamin D), minerals (zinc, selenium) and healthy fats [2,14].

Lean red meat (lamb, pork, goat, veal, beef) is consumed rarely in the traditional MD depending on preference, availability and religious beliefs, usually few times per week or even few times per month, or in some countries, only for special occasions, festivities and holidays [19,76]. The meat is usually cooked in small quantities with plenty of vegetables, thus is used more for giving the flavor, and rather as a main ingredient in the Mediterranean dishes.

Hydration is an important factor for an optimal health. Daily intake of plenty of water, non-sugary drinks (juices, herbal teas), fermented drinks (yogurt), coffee, broths and different soups, are frequently consumed in the traditional MD during the day. Often consumption of wine with the meals, but in moderation, is a common practice used in parts of the Mediterranean area and proven to have positive effects on health and longevity due to its polyphenol (resveratrol) content [2,19,77-80].

Processed food products, e.g. sweets, cakes, processed meat products, fast food, frozen food, pizzas, carbonated sugary beverages, and others, are consumed very rarely within the traditional Mediterranean dietary pattern, or during special occasions and holidays. The processed foods usually contain high amounts of refined sugars, salt, emulsifiers and other food additives, unhealthy saturated and trans fats (e.g. butter, margarine) – all of them proven to promote inflammatory processes in the body. Moreover, as these foods are usually energy-dense foods, they do give “immediate” energy boost, but not lasting satiety, and in long term, do contribute to weight gain and development of obesity [17].

MD is characterized with food choices using raw or minimum-cooked ingredients (vegetables, grains, and seeds). These ingredients can act as carriers enabling phytochemicals to reach the colon where they may be released by the actions of gut bacteria. For example, grain fibers from raw vegetables and fruits carry the polyphenols to the colon and release the polyphenols there, rather than earlier release in the gastrointestinal tract. The cooking methods can have beneficial

effects not only on the palatability of the prepared food, but also on improving the digestibility and bioavailability of phytonutrients. It can enhance the attractiveness of the food by way of appealing texture, flavor and taste, while preventing the loss of nutrients and the formation of toxic compounds. However, the influence of the food processing techniques, e.g. the food preparation and cooking, on the nutrient composition and nutritional value of the foods is not usually taken into consideration when different diets are compared. The food processing methods greatly affect the phytochemicals and the final nutritional profiles of the prepared dishes, and thus, influence the protective effects of the particular diets against chronic diseases. It is known that loss of antioxidant phytochemicals can occur during cooking due to thermal degradation and/or from release of toxic polar compounds from the cooking oil. MD cooking methods usually involve EVOO, which has been found to be one of the best cooking oils due to its higher stability at higher temperatures resulting in less release of polar compounds, while still preserving the majority of its polyphenolic antioxidants. Moreover, EVOO has been found to act as an efficient extracting medium for many phytochemicals from the vegetables cooked in EVOO and making them more bioavailable. An example is the sofrito dip, when tomatoes and other vegetables are cooked along in EVOO, which has been proven for its anti-inflammatory and anti-oxidants efficacies [2,19,81-87].

Besides the food choices of the MD, the socializing aspect of the MD, i.e. the conviviality is a very important component of this diet. It adds meaningful social and cultural values to the traditional meals, beyond their nutritional values. The social support and interactions, enjoying life events together with family and friends, preparing and cooking the food together, sharing the food, having lengthy meals with others and mealtime conversations are common practices in the traditional Mediterranean lifestyle. In the past, the mealtimes have been even considered as opportunities for social interactions and have been used to keep families and communities together. The pleasure associated with the conviviality of meals seems to positively affect the well-being and the health status of the people involved, who have been associated with lower risk of CVDs, lower cancer incidence, improved overall mortality and increased longevity [2,19,22,88-93].

## Antioxidant and Anti-Inflammatory Potential of Mediterranean Diet Ingredients

The oxidative stress is a result of the generation of oxidative species (free radicals, reactive oxygen and reactive nitrogen species) in the body, which is usually triggered by unhealthy diet and external factors, such as smoke, pollution, chemicals, drugs, UV rays, unhealthy lifestyle, etc. The oxidative stress further causes structural and functional damages of the main biomolecules in the body, such as DNA, lipids, and proteins and has been implicated in the pathogenesis of many chronic degenerative diseases, inflammation, neuro-degenerative disorders and aging processes. In particular, the imbalance between the production of oxidative species in the body and the antioxidant defense could lead to many pathological situations (i.e. diseases). To counteract this oxidative stress caused by the reactive species, the body needs various types of antioxidants. The body tries to fight with its own antioxidative defense mechanism, but *de novo* antioxidants' production in the human cells is limited. Therefore, the body needs a continuous supply of external antioxidants, which to ensure better health is preferred to come from

the diet in form of dietary antioxidants [10,11,20,94,95].

The inflammation processes usually occur as the immune system's response to the external invaders, like viruses, bacteria, and subsequent cells' injuries, but sometimes the immune system can trigger the inflammation even when no external invaders are present, like in the case of autoimmune diseases. In both cases, inflammatory processes have been implicated as undelaying cause of many serious diseases; actually many chronic metabolic diseases, *viz.* obesity, metabolic syndrome, type 2 diabetes, CVDs, depression, Alzheimer's disease, certain types of cancers and so on, start in the gut, where 70% of the body immunity is located, and further progress as a result of a long-term inflammation. MD is considered as a highly antioxidant and anti-inflammatory diet due to the richness of phytochemicals originated from different MD ingredients, all acting in synergy and having antioxidant and anti-inflammatory effects. The frequently-found nutrients in MD are given in Figure 2. Emphasis on polyphenolic compounds and their classification along with the chemical structures of some of the representatives of each class are also given in Figure 2 [14-17,94-106].

The phytochemicals, *viz.* polyphenols, carotenoids, tocopherols, vitamins and minerals are found in MD food ingredients, such as EVOO, vegetables, fruits, nuts, seeds, grains, spices, herbs, tea, wine and others. The polyphenols as products of the secondary metabolism in the plants usually accumulate in the plant organs, like leaves, fruits, roots, and stems. They are essential for the plant life; they provide defense against harmful microorganisms and make the plants unpalatable to predators. On the other hand, the wide spectrum of dietary phenolic compounds provides the health benefits and reduced risks for many Non-Communicable Diseases (NCDs) associated with this diet. More specifically, the polyphenols coming from dietary sources in conjunction with the traditional Mediterranean cooking methods making them more bioavailable are characterized with high antioxidant, anti-cancer, anti-inflammatory, and anti-aging activities [18,96,101,107-111]. These phenolic compounds are also responsible for the organoleptic properties of the foods; the intensity of these properties mostly depends on the phenolic concentration and their structure. For instance, the phenolics are responsible for the bitterness, astringency, color, flavor, odor and oxidative stability of the food products where they are present [82,107,112-117].

The antioxidant properties of the phenolic compounds are expressed via different mechanisms, which can be summarized as follows: a) ability to remove free radicals and inhibit the formation of reactive species, b) ability to prevent the damage of lipids, proteins, nucleic acids, and c) ability to prevent consequent cell damage and death as a result of the previous two mechanisms. All of them are commonly associated with preventing the development of many human diseases, such as cardiovascular diseases, neurodegenerative diseases, autoimmune diseases, diabetes, cancer, but also very important is that they could modulate human gut microbiota [107].

Polyphenols cover wide range of compounds and are classified in different ways; mainly they are divided into flavonoids and non-flavonoids (phenolic acids, stilbenes, lignans, and other phenolics), but there are also other classifications in literature. In general, polyphenols contain at least one aromatic ring with one or more hydroxyl groups (Figure 2). Briefly, some of the polyphenolic

compounds are described below along with their beneficial properties.

Phenolic acids, such as gallic, vanillic, cinnamic, ascorbic caffeic, ferulic, and p-coumaric acids are non-flavonoids can be found in fruits, legumes, herbs and vegetables mainly as free phenolic acids, whereas grains contain bound phenolic acids. They have high efficacy in food preservation, as well as antimicrobial, anticancer, anti-inflammatory, anti-mutagenic protective effects [118-120].

Resveratrol is a stilbene (non-flavonoid polyphenol), which is found in red grapes and its products (red wine), and berries. The moderate wine consumption with meals in the Mediterranean dietary pattern has been linked to lower incidence of coronary heart diseases exactly due to the presence of resveratrol and other polyphenols found in the red wine. Moreover, resveratrol has chemoprotective, anti-inflammatory and neuroprotective activities, because it can effectively scavenge free radicals and chelate metals [121-127].

Quercetin is a flavonol found in many vegetables (onions, broccoli, peppers, cauliflower and cabbage) and fruits (berries, apples), nuts, seeds and grains. It has been used for used for the treatment of allergic, metabolic, and inflammatory disorders, eye and cardiovascular diseases, and arthritis due to its pronounced antioxidant, antiviral, antibacterial, anti-cancer and anti-inflammatory properties [128,129].

Catechins are simple flavonols, such as Epicatechin (EC), Epigallocatechin (EGC), Epicatechin Gallate (ECG), and Epigallocatechin Gallate (EGCG). They are usually present in apples, teas, grapes, berries, cacao, red wine, beer, etc. and have been found to reduce the incidence of CVDs, inhibit angiogenesis and, therefore, the cancer progression [130-132].

Anthocyanins are flavonoids known for their effects as pigments, which determine the color of the fruits and vegetables (blue, red, and purple). They are found naturally in a number of foods, such as berries, currants, grapes, leafy vegetables, roots, and grains and offer antioxidant, antiviral, anti-inflammatory, anti-obesity, antidiabetic and anti-cancer benefits. The beneficial properties attributed to the consumption of anthocyanin-rich foods have been linked to improved eye health, reduced cardiovascular diseases, and beneficial neuroprotective effects [112-114,133].

Luteolin is a flavone that is found in broccoli, leaves, parsley, thyme, rosemary, green pepper, carrots, olive oil and chamomile tea and has anti-oxidant, anti-inflammatory, anti-bacterial, anti-diabetic and anti-proliferative activities [134-137].

Lignans are present in a wide variety of plant foods, including seeds (flax, pumpkin, sunflower, poppy and sesame), whole grains, beans, fruits and vegetables and they reduce the risk of certain cancers and cardiovascular diseases [138-140].

## Final Remarks

Worldwide, NCDs, such as obesity, diabetes, metabolic syndrome, and cardiovascular events account for 70 % of deaths. The modifiable risk factors that contribute to this high percentage NCDs include unhealthy dietary and lifestyle habits, such as consumption of nutrient-poor food rich in refined sugars, ultra-processed fast-food choices, smoking, sleep deprivation, polluted environments, etc. Mediterranean diet, as a healthy dietary pattern and a lifestyle with a proven track that can be easily implemented outside the



Mediterranean basin, could significantly reduce the incidence of NCDs worldwide [110,141].

MD is a plant-based dietary pattern, which emphasizes abundant consumption of fruits, vegetables, whole grains, nuts, legumes and seeds, herbs, spices and EVOO as a main source of healthy fats, followed by a moderate consumption of fish, poultry, low-fat dairy and fermented dairy products [2,142]. The plant origin of the food choices in the MD, and especially the high polyphenolic content, variety of vitamins and minerals, healthy fats, probiotics and dietary fibers, have been linked to be responsible for the reduction of inflammatory and the oxidative processes in the body. Beside the MD ingredients, the cooking methods characteristic for the Mediterranean cuisine are believed to help in preserving the phytochemicals and make them more bioavailable. Overall, all consumed phytochemicals in synergy contribute to the good health and the overall well-being of the people adhering to MD; in particular, reduced risks for many chronic diseases, CVDs and several types of cancers have been documented for those adhering to MD.

## References

- Trajkovska Petkoska A, Trajkovska-Broach A. Mediterranean Diet: A Nutrient-Packed Diet and a Healthy Lifestyle for a Sustainable World, *Journal of the Science of Food and Agriculture*. 2020; 101: 2627-2633.
- Serra-Majem L, Tomaino L, Dernini S, Berry EM, Lairon D, de la Cruz JN, et al. Updating the Mediterranean Diet Pyramid towards Sustainability: Focus on Environmental Concerns. *Int. J. Environ. Res. Public Health*. 2020; 17: 8758.
- Krzmaric Ž, Karas I, Ljubas Kelecic D, Vranešić Bender D. The Mediterranean and Nordic Diet: A Review of Differences and Similarities of Two Sustainable, Health-Promoting Dietary Patterns. *Front. Nutr*. 2021; 8: 683678.
- Mediterranean Diet. <https://oldwayspt.org/traditional-diets/mediterranean-diet>
- Bach-Faig A. Mediterranean diet pyramid today. *Science and cultural Updates, Public Health Nutrition*. 2011; 14: 2274-2284.
- Vitiello V, Germani A, Dolcetta EC, Donini LM, Del Balzo V. The New Modern Mediterranean Diet Italian Pyramid. *Ann Ig*. 2016; 28: 179-186.
- D'Alessandro A, Lampignano L, De Pergola G. Mediterranean Diet Pyramid: A Proposal for Italian People. A Systematic Review of Prospective Studies to Derive Serving Sizes. *Nutrients*. 2019; 11: 1296.
- Dreher ML. Whole Fruits and Fruit Fiber Emerging Health Effects. *Nutrients*. 2018; 10: 1833.
- Rajaram S, Jones J, Lee GJ. Plant-Based Dietary Patterns, Plant Foods, and Age-Related Cognitive Decline. *Adv Nutr*. 2019; 10: S422-S436.
- Leri M, Scuto M, Ontario ML, Calabrese V, Calabrese EJ, Bucciantini M, et al. Healthy Effects of Plant Polyphenols: Molecular Mechanisms. *Int. J. Mol. Sci*. 2020; 21: 1250.
- Muralidharan J, Galie S, Hernandez-Alonso P, Bullo M, Salas-Salvado J. Plant-Based Fat, Dietary Patterns Rich in Vegetable Fat and Gut Microbiota Modulation. *Front. Nutr*. 2019; 6: 157.
- Trajkovska-Petkoska A, Trajkovska-Broach A. Health benefits of extra virgin olive oil. M. Akrami, editor. In: *Olive oil-New perspectives and applications*. IntechOpen. 2021.
- Trajkovska Petkoska A, Trajkovska-Broach A. Mediterranean Diet-A Healthy Dietary Pattern and Lifestyle for Strong Immunity. Agarwal P, Nieto JJ, Ruzhansky M, Torres DFM, editors. In: *Analysis of Infectious Disease Problems (Covid-19) and Their Global Impact*. Infosys Science Foundation Series. Springer, Singapore. 2021.
- Roman GC, Jackson RE, Gadhia R, Roman AN, Reis J. Mediterranean diet: The role of long-chain n-3 fatty acids in fish; polyphenols in fruits, vegetables, cereals, coffee, tea, cacao and wine; probiotics and vitamins in prevention of stroke, age-related cognitive decline, and Alzheimer disease. *Revue Neurologique*. 2019; 175: 724-741.
- Davis C, Bryan J, Hodgson J, Murphy K. Definition of the Mediterranean Diet: A Literature Review. *Nutrients*. 2015; 7: 9139-9153.
- Gantenbein KV, Kanaka-Gantenbein C. Mediterranean Diet as an Antioxidant: The Impact on Metabolic Health and Overall Wellbeing. *Nutrients*. 2021; 13: 1951.
- Merra G, Noce A, Marrone G, Cintoni M, Tarsitano MG, Capacci A, et al. Influence of Mediterranean Diet on Human Gut Microbiota. *Nutrients*. 2021; 13: 7.
- Issaoui M, Delgado AM, Caruso G, Micali M, Barbera M, Atrous H, et al. Phenols, Flavors, and the Mediterranean Diet. *Journal of Aoac International*. 2020; 103: 915-924.
- Radd-Vagenas S, Kouris-Blazos A, Singh AF, Flood VM. Evolution of Mediterranean diets and cuisine: concepts and definitions. *Asia Pac J Clin Nutr*. 2017; 26: 749-763.
- Visioli F, Galli C. The role of antioxidants in the Mediterranean diet. *Lipids*. 2001; 36: S49-S52.
- Fong BYF, ChiuW-K, ChanWFM, Lam TY. A Review Study of a Green Diet and Healthy Ageing. *Int. J. Environ. Res. Public Health*. 2021; 18: 8024.
- A Trajkovska Petkoska and AT Broach. Mediterranean Way of Living as an Optimal Lifestyle and a Dietary Pattern for Healthy Gut and Strong Immunity, *EC Nutrition*. 2021; 16: 141-171.
- Dolkar D, Bakshi P, Wali VK, Sharma V, Shah RA. Fruits as nutraceuticals. *Eco. Env. And Cons*. 2017; 23: S113-S118.
- Liaqat A, Chughtai MFJ, Saeed K, Khaliq A, Mehmood T, Ahsan S, et al. A natural shield against detrimental effect of microorganisms. *J Food Technol Pres*. 2021; 5: 1-7.
- Salehi B, Zucca P, Orhan IE, Azzini E, Adetunji OC, et al. Allicin and health: A comprehensive review. *Trends in Food Science & Technology*. 2019; 86: 502-516.
- Bianchini F, Vainio H. Allium Vegetables and Organosulfur Compounds: Do They Help Prevent Cancer? *Environmental Health Perspectives*. 2001; 109: 893-902.
- Slimestad R, Fossen T, Vågen IM. Onions: A Source of Unique Dietary Flavonoids. *J. Agric. Food Chem*. 2007; 55: 10067-10080.
- Wan Q, Li N, Du L, Zhao R, Yi M, Xu Q, et al. Allium vegetable consumption and health: An umbrella review of meta-analyses of multiple health outcomes. *Food Sci Nutr*. 2019; 7: 2451-2470.
- Asemani Y, Zamani N, Bayat M, Amirghofran Z. Allium vegetables for possible future of cancer treatment. *Phytotherapy Research*. 2019; 33: 3019-3039.
- Nicastro HL, Ross SA, Milner JA. Garlic and onions: Their cancer prevention properties. *Cancer Prev Res (Phila)*. 2015; 8: 181-189.
- Mikaili P, Maadirad S, Moloudizargari M, Aghajanshakeri S, Sarahroodi S. Therapeutic Uses and Pharmacological Properties of Garlic, Shallot, and Their Biologically Active Compounds. *Iran J Basic Med Sci*. 2013; 16: 1031-1048.
- Shang A, Cao S-Y, Xu X-Y, Gan R-Y, Tang G-Y, Corke H, et al. Bioactive Compounds and Biological Functions of Garlic (*Allium sativum* L.). *Foods*. 2019; 8: 246.
- Sami R, Elhakem A, Alharbi M, Almatrafi M, Benajiba N, Ahmed Mohamed T, et al. *in-Vitro* Evaluation of the Antioxidant and Anti-Inflammatory Activity of Volatile Compounds and Minerals in Five Different Onion Varieties. *Separations*. 2021; 8: 57.
- Bower A, Marquez S, de Mejia EG. The Health Benefits of Selected Culinary Herbs and Spices Found in the Traditional Mediterranean Diet. *Critical Reviews in Food Science and Nutrition*. 2016; 56: 2728-2746.
- Vallverdú-Queralt A, Regueiro J, Martínez-Huélamo M, Alvarenga JF,

- Leal LN, Lamuela-Raventos RM. A comprehensive study on the phenolic profile of widely used culinary herbs and spices: rosemary, thyme, oregano, cinnamon, cumin and bay. *Food Chemistry*. 2014; 154: 299-307.
36. Fernández-Ochoa A, Borrás-Linares I, Pérez-Sánchez A, Barrajón-Catalán E, González-Álvarez I, Arráez-Román D, et al. Phenolic compounds in rosemary as potential source of bioactive compounds against colorectal cancer: In situ absorption and metabolism study. *Journal of Functional Foods*. 2017; 33: 202-210.
37. Ivanišova E, Kačaniova M, Savitskaya TA, Grinshpan DD. Medicinal Herbs: Important Source of Bioactive Compounds for Food Industry. In: *Herbs and Spices - New Processing Technologies*. 2021.
38. Jiang TA. Health Benefits of Culinary Herbs and Spices. *Journal of AOAC International*. 2019; 102: 395-411.
39. Opara EI. Culinary herbs and spices: what can human studies tell us about their role in the prevention of chronic non-communicable diseases? *J Sci Food Agric*. 2019; 99: 4511-4517.
40. Garcia-Gonzalez N, Battista N, Prete R, Corsetti A. Health-Promoting Role of Lactiplantibacillus plantarum Isolated from Fermented Foods. *Microorganisms*. 2021; 9: 349.
41. Gille D, Schmid A, Walther B, Vergères G. Fermented Food and Non-Communicable Chronic Diseases: A Review. *Nutrients*. 2018; 10: 448.
42. Kundu JK, Surh Y-J. Cancer chemopreventive effects of selected dried fruits. Alasalvar C, Shahidi F, editors. In: *Dried Fruits: Phytochemicals and Health Effects, First Edition*. John Wiley & Sons, Inc. 2013.
43. Alasalvar C, Shahidi F. Composition, phytochemicals, and beneficial health effects of dried fruits: an overview. Alasalvar C, Shahidi F, editors. In: *Dried Fruits: Phytochemicals and Health Effects, 1st Ed.* John Wiley & Sons, Inc. 2013.
44. Hannah D. Dietary fiber and prebiotics and the gastrointestinal microbiota. *Gut Microbes*. 2017; 8: 172-184.
45. Tap J, Furet JP, Bensaada M, Philippe C, Roth H, Rabot S, et al. Gut microbiota richness promotes its stability upon increased dietary fibre intake in healthy adults. *Environmental Microbiology*. 2015; 17: 4954-4964.
46. Makki K, Deehan EC, Walter J, Bäckhed F. The Impact of Dietary Fiber on Gut Microbiota in Host Health and Disease. *Cell Host and Microbe*. 2018; 23: 705-715.
47. Slavin J. Fiber and prebiotics: mechanisms and health benefits. *Nutrients*. 2013; 5: 1417-1435.
48. Edwards CA, et al. Polyphenols and health: Interactions between fibre, plant polyphenols and the gut microbiota. *Nutrition Bulletin*. 2017; 42: 356-360.
49. Toribio-Mateas M. Harnessing the Power of Microbiome Assessment Tools as Part of Neuroprotective Nutrition and Lifestyle Medicine Interventions. *Microorganisms*. 2018; 6: 35.
50. Saulnier DM, Ringel Y, Heyman MB, Foster JA, Bercik P, Shulman RJ, et al. The intestinal microbiome, probiotics and prebiotics in neurogastroenterology. *Gut Microbes*. 2013; 4: 17-27.
51. Umbrello G, Esposito S. Microbiota and neurologic diseases: Potential effects of probiotics. *Journal of Translational Medicine*. 2016; 14: 298.
52. Westfall S, Lomis N, Kahouli I, Dia SY, Singh SP, Prakash S. Microbiome, probiotics and neurodegenerative diseases: Deciphering the gut brain axis. *Cellular and Molecular Life Sciences*. 2017; 74: 3769-3787.
53. Sánchez B, Delgado S, Blanco-Míguez A, Lourenço A, Gueimonde M, Margolles A. Probiotics, gut microbiota, and their influence on host health and disease. *Molecular Nutrition and Food Research*. 2017; 61: 240.
54. Sikalidis AK, Kelleher AH, Kristo AS. Mediterranean Diet. *Encyclopedia* 2021; 1: 371-387.
55. Caradonna F, Consiglio O, Luparello C, Gentile C. Science and Healthy Meals in the World: Nutritional Epigenomics and Nutrigenetics of the Mediterranean Diet. *Nutrients*. 2020; 12: 1748.
56. Foscolou A, D' Cunha NM, Naumovski N, Tyrovolas S, Chrysohoou C, Rallidis L, et al. The Association between Whole Grain Products, Consumption and Successful Aging: A Combined Analysis of MEDIS and ATTICA Epidemiological Studies. *Nutrients*. 2019; 11: 1221.
57. Del Mar Bibiloni M, Julibert A, Bouzas C, Martínez-González MA, Corella D, Salas-Salvadó J, et al. Nut Consumptions as a Marker of Higher Diet Quality in a Mediterranean Population at High Cardiovascular Risk. *Nutrients*. 2019; 11: 754.
58. Blomhoff R, Carlsen MH, Andersen LF, Jacobs DR Jr. Health benefits of nuts: potential role of antioxidants. *British Journal of Nutrition*. 2006; 96: S52-S60.
59. Bulló M, Lamuela-Raventós R, Salas-Salvadó J. Mediterranean diet and oxidation: nuts and olive oil as important sources of fat and antioxidants. *Current Topics in Medicinal Chemistry*. 2011; 11: 1797-1810.
60. Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, et al. Primary prevention of cardiovascular disease with a mediterranean diet supplemented with extra-virgin olive oil or nuts. *The New England Journal of Medicine*. 2018; 378: e34.
61. Fukuda T, Ito H, Yoshida T. Antioxidative polyphenols from walnuts (*Juglans regia* L.). *Phytochemistry*. 2003; 63: 795-801.
62. Urpi-Sardaa M, Casasa R, Chiva-Blanca G, Romero-Mamania ES, Valderas-Martínez P, Arranza S, et al. Virgin olive oil and nuts as key foods of the Mediterranean diet effects on inflammatory biomarkers related to atherosclerosis. *Pharmacological Research*. 2012; 65: 577-583.
63. Jimenez-Lopez C, Carpena M, Lourenço-Lopes C, Gallardo-Gómez M, Lorenzo JM, Barba FJ, et al. Bioactive Compounds and Quality of Extra Virgin Olive Oil. *Foods*. 2020; 9: 1014.
64. Mazzocchi A, Leone L, Agostoni C, Pali-Schöll I. The Secrets of the Mediterranean Diet. Does [Only] Olive Oil Matter? *Nutrients*. 2019; 11: 2941.
65. Rossi M, Caruso F, Kwok L, Lee G, Caruso A, Gionfra F, et al. Protection by extra virgin olive oil against oxidative stress *in vitro* and *in vivo*. Chemical and biological studies on the health benefits due to a major component of the Mediterranean diet. *Plos One*. 2017; 12: e0189341.
66. Francisco V, Ruiz-Fernández C, Lahera V, Lago F, Pino J, Skaltsounis L, et al. Natural Molecules for Healthy Lifestyles: Oleocanthal from Extra Virgin Olive Oil. *Journal of Agricultural and Food Chemistry*. 2019; 67: 3845-3853.
67. Luisi MLE, Lucarini L, Biffi B, Rafanelli E, Pietramellara G, Durante M, et al. Effect of Mediterranean Diet Enriched in High Quality Extra Virgin Olive Oil on Oxidative Stress, Inflammation and Gut Microbiota in Obese and Normal Weight Adult Subjects. *Frontiers in Pharmacology*. 2019; 10: 1366.
68. Sánchez-Villegas A, Cabrera-Suárez B, Molero P, González-Pinto A, Chiclana-Actis C, Cabrera C, et al. preventing the recurrence of depression with a Mediterranean diet supplemented with extra-virgin olive oil. The PREDI-DEP trial: study protocol. *BMC Psychiatry*. 2019; 19: 63.
69. Fernandes J, Fialho M, Santos R, Peixoto-Plácido C, Madeira T, Sousa-Santos N, et al. Is olive oil good for you? A systematic review and meta-analysis on anti-inflammatory benefits from regular dietary intake. *Nutrition*. 2020; 69: 110559.
70. Cicerale S, Lucas LJ, Keast RS. Antimicrobial, antioxidant and anti-inflammatory phenolic activities in extra virgin olive oil. *Current Opinion in Biotechnology*. 2012; 23: 129-135.
71. Serreli G, Deiana M. Extra Virgin Olive Oil Polyphenols: Modulation of Cellular Pathways Related to Oxidant Species and Inflammation in Aging. *Cells*. 2020; 9: 478.
72. Alkhatib A, Tsang C, Tuomilehto J. Olive Oil Nutraceuticals in the Prevention and Management of Diabetes: From Molecules to Lifestyle. *International Journal of Molecular Sciences*. 2018; 19: 2024.
73. Lanza B, Ninfali P. Antioxidants in Extra Virgin Olive Oil and Table Olives: Connections between Agriculture and Processing for Health Choices. *Antioxidants*. 2020; 9: 41.
74. Wade AT, Davis CR, Dyer KA, Hodgson JM, Woodman RJ, Murphy KJ. A Mediterranean diet supplemented with dairy foods improves markers of



- cardiovascular risk: results from the MedDairy randomized controlled trial. *The American Journal of Clinical Nutrition*. 2018; 108: 1166-1182.
75. Fernandez MA, Marette A. Potential Health Benefits of Combining Yogurt and Fruits Based on Their Probiotic and Prebiotic Properties. *Advances in Nutrition*. 2017; 8: 155S-164S.
76. O'Connor LE, Paddon-Jones D, Wright AJ, Campbell WW. A Mediterranean-style eating pattern with lean, unprocessed red meat has cardiometabolic benefits for adults who are overweight or obese in a randomized, crossover, controlled feeding trial. *Am J Clin Nutr*. 2018; 108: 33-40.
77. Giacosa A, Barale R, Bavaresco L, Faliva MA, Gerbi V, La Vecchia C, et al. Mediterranean Way of Drinking and Longevity. *Critical Reviews in Food Science and Nutrition*. 2016; 56: 635-640.
78. Ditano-Vázquez P, Torres-Peña JD, Galeano-Valle F, Pérez-Caballero AI, Demelo-Rodríguez P, Lopez-Miranda J, et al. The Fluid Aspect of the Mediterranean Diet in the Prevention and Management of Cardiovascular Disease and Diabetes: The Role of Polyphenol Content in Moderate Consumption of Wine and Olive Oil. *Nutrients*. 2019; 11: 2833.
79. Naumovski N, Foscolou A, D'Cunha NM, Tyrovolas S, Chrysohoou C, Sidossis LS, et al. The Association between Green and Black Tea Consumption on Successful Aging: A Combined Analysis of the ATTICA and MEDiterranean ISlands (MEDIS) Epidemiological Studies. *Molecules*. 2019; 24: 1862.
80. Guerrero RF, García-Parrilla MC, Puertas B, Cantos-Villar E. Wine, resveratrol and health: a review. *Natural Product Communications*. 2009; 4: 635-658.
81. Hoffman R, Gerber M, Food Processing and the Mediterranean Diet. *Nutrients*. 2015; 7: 7925-7964.
82. Arfaoui L. Dietary Plant Polyphenols: Effects of Food Processing on Their Content and Bioavailability. *Molecules*. 2021; 26: 2959.
83. Rinaldi de Alvarenga JF, Quifer-Rada P, Westrin V, Hurtado-Barroso S, Torrado-Prat X, Lamuela-Raventós RM. Mediterranean Sofrito Home-Cooking Technique Enhances Polyphenol Content in Tomato Sauce. *Journal of the Science of Food and Agriculture*. 2019; 99: 6535-6545.
84. Rinaldi de Alvarenga JF, Tran C, Hurtado-Barroso S, Martínez-Huélamo M, Illan M, Lamuela-Raventós RM. Home cooking and ingredient synergism improve lycopene isomer production in Sofrito. *Food Research International*. 2017; 99: 851-861.
85. Ramírez-Anaya JP, Castañeda-Saucedo MC, Olalla-Herrera M, Villalón-Mir M, Serrana HL, Samaniego-Sánchez C. Changes in the Antioxidant Properties of Extra Virgin Olive Oil after Cooking Typical Mediterranean Vegetables. *Antioxidants*. 2019; 8: 246.
86. Ramírez-Anaya JD, Samaniego-Sánchez C, Castañeda-Saucedo MC, Villalón-Mir M, de la Serrana HL. Phenols and the antioxidant capacity of Mediterranean vegetables prepared with extra virgin olive oil using different domestic cooking Techniques. *Food Chemistry*. 2015; 188: 430-438.
87. Rinaldi de Alvarenga JF, Quifer-Rada P, Francetto Juliano F, Hurtado-Barroso S, Illan M, Torrado-Prat X, et al. Using Extra Virgin Olive Oil to Cook Vegetables Enhances Polyphenol and Carotenoid Extractability: A Study Applying the sofrito Technique. *Molecules*. 2019; 24: 1555.
88. Cavaliere A, De Marchi E, Banterle A. Exploring the Adherence to the Mediterranean Diet and Its Relationship with Individual Life-style: The Role of Healthy Behaviors, Pro-Environmental Behaviors, Income, and Education. *Nutrients*. 2018; 10: 141.
89. Mamalaki E, Anastasiou CA, Kosmidis MH, Dardiotis E, Hadjigeorgiou GM, Sakka P, et al. Social life characteristics in relation to adherence to the Mediterranean diet in older adults: findings from the Hellenic Longitudinal Investigation of Aging and Diet (HELIAD) study. *Public Health Nutrition*. 2020; 23: 439-445.
90. Mamalaki E, Anastasiou CA, Ntanasi E, Tsapanou A, Kosmidis MH, Dardiotis E, et al. Associations between the mediterranean diet and sleep in older adults: Results from the hellenic longitudinal investigation of aging and diet study. *Geriatrics and Gerontology International*. 2018; 18: 1543-1548.
91. Theorell-Haglöw J, Lemming EW, Michaëlsson K, Elmståhl S, Lind L, Lindberg E. Sleep duration is associated with healthy diet scores and meal patterns: results from the population-based EpiHealth study. *Journal of Clinical Sleep Medicine*. 2020; 16: 9-18.
92. Godos J, Ferri R, Caraci F, Cosentino FII, Castellano S, Galvano F, et al. Adherence to the Mediterranean Diet is Associated with Better Sleep Quality in Italian Adults. *Nutrients*. 2019; 11: 976.
93. Foscolou A, D'Cunha NM, Naumovski N, Tyrovolas S, Rallidis L, Matalas AL, et al. Midday Napping and Successful Aging in Older People Living in the Mediterranean Region: The Epidemiological Mediterranean Islands Study (MEDIS). *Brain Sciences*. 2020; 10: 14.
94. Kumar P, Kumar M, Bedi O, Gupta M, Kumar S, Jaiswa G, et al. Role of vitamins and minerals as immunity boosters in COVID-19. *Inflammopharmacology*. 2021; 29: 1001-1016.
95. Verediano TA, Martino HSD, Dias Paes MC, Tako E. Effects of Anthocyanin on Intestinal Health: A Systematic Review. *Nutrients*. 2021; 13: 1331.
96. Maruca A, Catalano R, Bagetta D, Mesiti F, Ambrosio FA, Romeo I, et al. The Mediterranean Diet as source of bioactive compounds with multi-targeting anti-cancer profile. *European Journal of Medicinal Chemistry*. 2019; 181: 111579.
97. Gkouskou K, Lazou E, Skoufas E, Eliopoulos AG. Genetically Guided Mediterranean Diet for the Personalized Nutritional Management of Type 2 Diabetes Mellitus. *Nutrients*. 2021; 13: 355.
98. Tzekaki E, Prodromou S, Tsolaki M, Pantazaki AA. The multifunctional therapeutic potentiality of extra virgin olive oil administration through the intervention in pathophysiological mechanisms: Focus on Alzheimer's disease. *GSC Advanced Research and Reviews*. 2021; 07: 101-113.
99. Ventriglio A, Sancassiani F, Contu MP, Latorre M, Di Slavatore M, et al. Mediterranean Diet and its Benefits on Health and Mental Health: A Literature Review. *Clinical Practice & Epidemiology in Mental Health*. 2020; 16: 156-164.
100. Caprar G. Mediterranean-Type Dietary Pattern and Physical Activity: The Winning Combination to Counteract the Rising Burden of Non-Communicable Diseases (NCDs). *Nutrients*. 2021; 13: 429.
101. Briguglio G, Costa C, Pollicino M, Giambò F, Catania S, Fenga C. Polyphenols in cancer prevention: New insights (Review). *International Journal of Functional Nutrition*. 2020; 1: 9.
102. Alaswad HA, Mahbub AA, Le Maitre CL, Jordan-Mahy N. Molecular Action of Polyphenols in Leukaemia and Their Therapeutic Potential. 2021; 22: 3085.
103. Kubina R, Iriti M, Kabała-Dzik A. Anticancer Potential of Selected Flavonols: Fisetin, Kaempferol, and Quercetin on Head and Neck Cancers. *Nutrients*. 2021; 13: 845.
104. Guasch-Ferre M, Willett WC. The Mediterranean diet and health: a comprehensive overview. *J Intern Med*. 2021; 290: 549-566.
105. Nagpal R, Shively CA, Register TC, Craft S, Yadav H. Gut microbiome-Mediterranean diet interactions in improving host health. *F1000Research*. 2019; 8: 699.
106. Davinelli S, Trichopoulou A, Corbi G, De Vivo I, Scapagnini G. The potential nutrigenoprotective role of Mediterranean diet and its functional components on telomere length dynamics. *Ageing Research Reviews*. 2018; 49: 1-10.
107. Pinto T, Vilela A. Healthy Drinks with Lovely Colors: Phenolic Compounds as Constituents of Functional Beverages. *Beverages*. 2021; 7: 12.
108. Shakoor H, Feehan J, Apostolopoulos V, Platat C, Al Dhaheri AS, et al. Immunomodulatory Effects of Dietary Polyphenols. *Nutrients*. 2021; 13: 728.
109. Rasouli H, Farzaei MH, Khodarahmi R. Polyphenols and their benefits: A review. *International Journal of Food Properties*. 2017; 20: 1700-1741.
110. Shannon OM, Ashor AW, Scialo F, Saretzki G, Martin-Ruiz C, Lara J, et al. Mediterranean diet and the hallmarks of ageing. *European Journal of Clinical Nutrition*. 2021; 75: 1176-1192.
111. Yammine A, Namsi A, Vervandier-Fasseur D, Mackrill JJ, Lizard G, Latruffe, N. Polyphenols of the Mediterranean Diet and Their Metabolites in the Prevention of Colorectal Cancer. *Molecules*. 2021; 26: 3483.

112. Khoo HE, Azlan A, Tang ST, Lim SM. Anthocyanidins and anthocyanins: colored pigments as food, pharmaceutical ingredients, and the potential health benefits. *Food & Nutrition Research*, 2017; 61: 1361779.
113. Alappat B, Alappat J. Anthocyanin Pigments: Beyond Aesthetics. *Molecules*. 2020; 25: 5500.
114. Fang J. Classification of fruits based on anthocyanin types and relevance to their health effects. *Nutrition*. 2015; 31: 1301-1306.
115. El-Missiry MA, Fekri A, Kesar LA, Othman AI. Polyphenols are potential nutritional adjuvants for targeting COVID-19. *Phytotherapy Research*. 2021; 35: 2879-2889.
116. Montenegro-Landívar MF, Tapia-Quirós P, Vecino X, Reig M, Valderrama C, Granados M, et al. Polyphenols and their potential role to fight viral diseases: An overview. *Science of the Total Environment*. 2021; 801: 149719.
117. Bhattacharya T, Dutta S, Akter R, Rahman MH, Karthika C, Nagaswarupa HP, et al. Role of Phytonutrients in Nutrigenetics and Nutrigenomics Perspective in Curing Breast Cancer. *Biomolecules*. 2021; 11: 1176.
118. Kumara N, Goel N. Phenolic acids: Natural versatile molecules with promising therapeutic applications. *Biotechnology Reports*. 2019; 24: e00370.
119. Kiokias S, Proestos C, Oreopoulou V. Phenolic Acids of Plant Origin—A Review on Their Antioxidant Activity *in Vitro* (O/W Emulsion Systems) Along with Their *in Vivo* Health Biochemical Properties. *Foods*. 2020; 9: 534.
120. Goleniowski M, Bonfill M, Cusido R, Palazon J. Phenolic Acids. K.G. Ramawat, J.M. Merillon, editors. In: *Natural Products*. 2013; 1951-1973.
121. Salehi B, Mishra AP, Nigam M, Sener B, Kilic M, Sharifi-Rad M, et al. Resveratrol: A Double-Edged Sword in Health Benefits. *Biomedicines*. 2018; 6: 91.
122. Gomes MJC, Kolba N, Agarwal N, Kim D, Eshel A, Koren O, et al. Modifications in the Intestinal Functionality, Morphology and Microbiome Following Intra-Amniotic Administration (*Gallus gallus*) of Grape (*Vitis vinifera*) Stilbenes (Resveratrol and Pterostilbene). *Nutrients*. 2021; 13: 3247.
123. Berman AY, Motechin RA, Wiesenfeld MY, Holz MK. The therapeutic potential of resveratrol: A review of clinical trials. *NPJ Precis. Oncol*. 2017; 1: 35.
124. Cho S, Namkoong K, Shin M, Park J, Yang E, Ihm J, et al. Cardiovascular Protective Effects and Clinical Applications of Resveratrol. *J. Med. Food* 2017; 20: 323-334.
125. Man AWC, Li H, Xia N. Resveratrol and the Interaction between Gut Microbiota and Arterial Remodelling. *Nutrients*. 2020; 12: 119.
126. Weiskirchen S, Weiskirchen R. Resveratrol: How Much Wine Do You Have to Drink to Stay Healthy? *Adv Nutr*. 2016; 7: 706-718.
127. Gresele P, Cerletti C, Guglielmini G, Pignatelli P, de Gaetanob G, Violi G. Effects of resveratrol and other wine polyphenols on vascular function: an update. *Journal of Nutritional Biochemistry*. 2011; 22: 201-211.
128. Cione E, La Torre C, Cannataro R, Caroleo MC, Plastina P, Gallelli L. Quercetin, Epigallocatechin Gallate, Curcumin, and Resveratrol: From Dietary Sources to Human MicroRNA Modulation. *Molecules*. 2020; 25: 63.
129. El-Saber Batiha G, Beshbishy AM, Ikram M, Mulla ZS, Abd El-Hack ME, Taha AE, et al. The Pharmacological Activity, Biochemical Properties, and Pharmacokinetics of the Major Natural Polyphenolic Flavonoid: Quercetin. *Foods*. 2020; 9: 374.
130. Musial C, Kuban-Jankowska A, Gorska-Ponikowska M, Beneficial Properties of Green Tea Catechins. *Int. J. Mol. Sci*. 2020; 21: 1744.
131. Isemura M. Catechin in Human Health and Disease. *Molecules*. 2019; 24: 528.
132. Fathima A, Rao JR. Selective toxicity of Catechin—a natural flavonoid towards bacteria. *Appl Microbiol Biotechnol*. 2016; 100: 6395-6402.
133. Tena N, Martín J, Asuero AG. State of the Art of Anthocyanins: Antioxidant Activity, Sources, Bioavailability, and Therapeutic Effect in Human Health. *Antioxidants*. 2020; 9: 451.
134. Pandurangan AK, Esa NM. Luteolin, A Bioflavonoid Inhibits Colorectal Cancer through Modulation of Multiple Signaling Pathways: A Review. *Asian Pacific Journal of Cancer Prevention*. 2014; 15: 5501-5508.
135. Yong Lin, Ranxin Shi, Xia Wang and Han-Ming Shen. Luteolin, a flavonoid with potentials for cancer prevention and therapy. *Curr Cancer Drug Targets*. 2008; 8: 634-646.
136. Imran M, Rauf A, Abu-Izneid T, Nadeem M, Ali Shariati M, Ali Khan I, et al. Luteolin, a flavonoid, as an anticancer agent: A review. *Biomedicine & Pharmacotherapy*. 2019; 112: 108612.
137. Kwon Y. Luteolin as a potential preventive and therapeutic candidate for Alzheimer's disease. *Experimental Gerontology*. 2017; 95: 39-43.
138. Rodríguez-García C, Sánchez-Quesada C, Toledo E, Delgado-Rodríguez M, Gaforio JJ. Naturally Lignan-Rich Foods: A Dietary Tool for Health Promotion? *Molecules*. 2019; 24: 917.
139. Adlercreutz H. Lignans and Human Health. *Critical Reviews in Clinical Laboratory Sciences*. 2007; 44: 483-525.
140. Hu Y, Li Y, Sampson L, Wang M, Manson JE, Rimm E, et al. Lignan Intake and Risk of Coronary Heart Disease. *Journal of the American College of Cardiology*. 2021; 78: 666-678.
141. Dominguez LJ, Di Bella G, Veronese N, Barbagallo M. Impact of Mediterranean Diet on Chronic Non-Communicable Diseases and Longevity. *Nutrients*. 2021; 13: 2028.
142. Santos-Buelga C, González-Manzano S, González-Paramás AM. Wine, Polyphenols, and Mediterranean Diets. What Else Is There to Say? *Molecules*. 2021; 26: 5537.