Research Article – Biology

The effects of the Mediterranean diet on chronic diseases: cardiovascular diseases, oxidative stress, dyslipidemia, diabetes mellitus, blood pressure, cancer, neurodegenerative disease and obesity

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Abstract

Poor dietary habits lead to the emergence of chronic diseases such as coronary heart disease, stroke, hypertension, diabetes mellitus, dyslipidemia, cancer, dementia, obesity and oxidative stress involved through the aggression of cells by free radicals. Knowing that these diseases cause a global burden both individually and economically. Several studies focus on the relationship between diet and chronic disease. Studies suggest that the Mediterranean diet, (MD) traditional eating habits and lifestyle specific to the Mediterranean region, reduce the incidence of chronic diseases and improve longevity. The MD is known to be one of the healthiest diets, this diet is based on herbs, spices, vegetables, fruits, olive oils, cereals (preferably whole grains), legumes and nuts, fish and shellfish, white meat, so the main source of dietary fat from MD is olive oil. Moderate consumption of eggs and dairy products, and reduced consumption of red meats, processed meats and foods rich in sugars and fats. MD has a beneficial fatty acid profile with a higher content of monounsaturated fatty acids (MSFA) and a higher MSFA / saturated fatty acid (SFA) ratio than non-Mediterranean diets. High consumption of dietary fiber, a low glycemic index, anti-inflammatory effects, and antioxidant compounds, can work together to produce favorable effects on health status. MD is rich in vitamins and minerals, such as: vitamin B (B1, B2, niacin, B6, folate and B12) and antioxidant vitamins (vitamins E and C), and polyphenol, flavonoids, phytosterols, n-fatty acids 3 (alpha linoleic acid), resveratrol, quercetin, oleic acid, carotenoids and lutein. The purpose of this review is to provide an update on the current state of science regarding the relationship between the traditional Mediterranean diet and lifestyle related chronic diseases, and discuss the mechanisms involved and opportunities. In this area of research, to clarify and increase the confidence of the role of nutrition in the etiology of chronic diseases.

Key words: Mediterranean diet, Chronic diseases, Cardiovascular diseases, Oxidative stress, Dyslipidemia, Diabetes mellitus, Blood pressure, Cancer, Neurodegenerative disease, Dementia and Obesity

I. Introduction

Currently, more than one in three adults (about 92.1 million) with at least one type of cardiovascular disease in the USA. [1], and cardiovascular disease (CVD) kills an estimated 17.7 million people each year, or 31% of all deaths worldwide [2]. WHO predicts that diabetes will be the seventh leading cause of death in 2030 [3] [4]. The type 2 diabetes pandemic is a huge public health problem, with 380 million cases worldwide by 2025 [5] [6] The number of people with diabetes rose from 108 million in 1980 to 422 million in 2014 [7]. The global prevalence of diabetes among adults over 18 has increased from 4.7% in 1980 to 8.5% in 2014 [7]. In 2015, 1.6 million deaths from diabetes [7], drug therapy often fails over time [8], and some drugs have cardiovascular risks [9] [10] a major cause of blindness, insufficiency kidney, heart attack, stroke and lower limb amputation [11].

About 47 million people have dementia and there are nearly 10 million new cases each year.
Evidence suggesting that more than 115 million people will be affected by 2050 [13].

Dementia is a syndrome characterized by progressive global deterioration of cognitive abilities in multiple domains: memory, learning, orientation, behavior, language, comprehension and judgment, and ability to perform daily activities. Although there are several types of dementia, the most common is Alzheimer's disease (AD) [14] [15] [16]. Dementia is one of the leading causes of disability and dependence worldwide. Dementia has a physical, psychological, economic and social impact on caregivers, families and society [17]. The burden of dementia, both from the disease itself and financially, is great on individuals, families, and public health services, and the efficacy of current pharmacological treatments is inconsistent [27] [28]. High cholesterol increases the risk of heart disease and stroke. Overall, one third of ischemic heart disease is attributable to high cholesterol levels. The rise in total cholesterol is a major cause of the burden of disease in developed and developing countries, as a risk factor for ischemic heart disease and stroke. In Ireland, a 30% reduction in the death rate from heart disease was attributed to a 4.6% reduction in the average population for total cholesterol. In Finland, 50% of the decline in mortality from ischemic heart disease has been explained by the reduction of blood cholesterol levels in the population [18].

Obesity, a chronic disorder whose prevalence is increasing in adults, adolescents and children, is now considered a global epidemic and a real problem for health facilities [19] [20]. In many populations, the prevalence of overweight and obesity has increased rapidly over the last 20 years. In the United States, more than 35% of adults and nearly 17% of young people were classified obese in 2009-2010 [21] and the risk of being overweight or obese was estimated at 50% and 25% respectively [22]. High health costs worldwide [23] Global obesity has almost tripled since 1975. In 2016, over 1.9 billion adults aged 18 and over were overweight. Of these, more than 650 million were obese. 39% of adults 18 years and older were overweight in 2016 and 13% were obese. The majority of the world's population lives in countries where overweight and obesity kill more people than underweight. [24]. The global burden of cancer will double over the next two decades. [25] raising the prospect of a huge public health problem and, consequently, medical care. [25] [26]. The mortality attributed to chronic diseases is increasing especially among the elderly population. In parallel with bad eating habits, in addition that the population adopts more sedentary lifestyles. All of these factors contributed to the increase in chronic noncommunicable diseases [57]. Over the past three decades, various dietary strategies have been developed to promote dietary fitness and reduce the burden of chronic disease. Compared to Western eating habits, MD favors local and seasonal food production to a greater extent. The studies have helped to find the link between MD and the risk reduction of chronic diseases such as cancer, cardiovascular disease, diabetes, dyslipidemia and neurodegenerative diseases [57].

1. Objectives of the review

This review highlights some of the opportunities and challenges for adopting a traditional Mediterranean diet, and serves to provide an update on the current state of science regarding the relationship between the traditional Mediterranean diet and lifestyle in relation to chronic diseases, and discuss the mechanisms involved and opportunities in this area of research, to clarify and increase confidence in the role of nutrition in the etiology of chronic diseases, and thus promote aging in good health.

II. Materials and methods

II-1. Strategy of research

This review is based on bibliographic research that has been done on various databases and search engines: PubMed, Sciencedirect, Google Scholar, Cochrane Library, ClinicalTrials.gov and Psychinfo. The research was reduced to studies published in English, additional publications were identified from the references of the articles searched, and those published studies from January 1, 2008 to October 23, 2017, and which focused on Mediterranean diet and its relationship to the prevention and treatment of chronic diseases, such as: cardiovascular diseases, dyslipidemia, diabetes mellitus, hypertension,
obesity and oxidative stress and neurodegenerative diseases. Epidemiological and clinical studies were included. The main search terms with various combinations were used: "Mediterranean Diet", "Micronutrients", "Macronutrients", "Lifestyle", "Chronic Diseases", "Diabetes Mellitus", "Glucose Intolerance", "Prevention", "Treatment", "Blood pressure", "Dyslipidemia", "Cardiovascular diseases", "Oxidative stress", "Neurodegenerative diseases", "Dementia", "Hypertension", "Metabolic syndrome", "Obesity", "Clinical trials", "Cohort", "Cases / Witnesses". There were 53 studies after the exclusion of duplicate studies (7 studies) and the exclusion of studies after reading the title and summary (12 studies). 34 studies were selected dealing with the Mediterranean diet and its relation to chronic diseases.

### III. Results

#### III-1. The Mediterranean diet

MR seems to provide a balanced diet, suitable for all age groups and significantly reduces the risk of chronic disease [63]. Several studies [64] [65] have proven the cardio protective and neuroprotective roles of MD and its protective roles against metabolic disorders, certain cancers, and other age-related degenerative diseases. Several publications have highlighted the correlation between MD and longevity [66] [67]. Sofi et al. [68] [69] [70] [71] [72] have shown that greater adherence to MD is associated with a significant

<table>
<thead>
<tr>
<th>The compound</th>
<th>Nutrient</th>
<th>Mechanism involved</th>
<th>Effect on health</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyphenol [225] [226]</td>
<td>Vegetables and fruits, Olive oil</td>
<td>Antioxidant effect, and reduction of inflammation</td>
<td>Protector against type 2 diabetes, Protector against cardiovascular disease, Reduced risk of lung cancer,</td>
</tr>
<tr>
<td>Flavonoids [226] [227]</td>
<td>The fat of the seeds</td>
<td>Antiproliferative</td>
<td>Breast cancer prevention</td>
</tr>
<tr>
<td>Phytosterols [225] [228]</td>
<td>Soy, Vegetables</td>
<td>Reduces serum cholesterol, Reduces oxidative stress and inflammation</td>
<td>Risk reduction of cardiovascular diseases, Prevention of obesity</td>
</tr>
<tr>
<td>N-3 fatty acids (alpha-linoleic acid) [225] [226]</td>
<td>Pisces, Flax seed, Soya oil, Walnut, Green leafy vegetables</td>
<td>Anti-angiogenesis, Reduces oxidative stress, Reduces aggregation of thrombocytes, Anti-lipidemiant, Antiplatelet, Anti-inflammatory, Antiarrhythmic</td>
<td>Stroke prevention, Protector of the cardiovascular system, Prevention of sudden deaths, Reduced risk of colon and rectal cancer,</td>
</tr>
<tr>
<td>Resveratrol [228] [226]</td>
<td>The fat of the seeds</td>
<td>Reduces aggregation of thrombocytes, Reduces serum cholesterol</td>
<td>Protector of the cardiovascular system</td>
</tr>
<tr>
<td>Quercetin [226]</td>
<td>Grape seed</td>
<td>Vasodilatation, Anti-aggregating effect</td>
<td>Anti-coagulation, Reduced risk of hypertension</td>
</tr>
<tr>
<td>Oleic acid [228] [226]</td>
<td>Olive oil</td>
<td>Inhibits HER2 which plays a role in the etiology of metastasis, Protects against atherosclerosis</td>
<td>Antihypertensive effect, Reduced risk of cardiovascular disease, Reduced risk of breast cancer</td>
</tr>
<tr>
<td>Carotenoids [226]</td>
<td>Red, yellow and orange fruits, Vegetables, Tomato</td>
<td>Antioxidant</td>
<td>Reduced risk of lung cancer</td>
</tr>
<tr>
<td>Lutein [225] [253]</td>
<td>Green vegetables, Grains</td>
<td>Antioxidant</td>
<td>Reduced risk of diabetes, Reduced risk of cancer</td>
</tr>
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improvement in health status, as evidenced by a significant reduction in overall mortality (9%), mortality due to cardiovascular diseases (9%), and the incidence of Parkinson's disease and Alzheimer's disease (13%) [69] [70] [71] [72] [73]: Several studies have shown that adherence to traditional MD is associated with a significant reduction in cancer incidence, based on an examination of the different components of MD [73]. [74] thus benefits of MD related to the protective role of phenolic components, reducing daily oxidative stress, and the effects of MD in the modulation of inflammation [75].

### III-1. Polyunsaturated fatty acids: Omega-3:

The Mediterranean diet containing several nutrients such as fish, which are rich in polyunsaturated fatty acids, omega-3, which are recommended by American Heart Association (AHA) as a cardio-protective [77] especially for patients with cardiovascular disease [76]. Thus the beneficial effects of fish include the improvement of lipid profiles [78] and the reduction of blood pressure [79] [80] through the reduction of inflammation, oxidation, and coagulation [81] [82].

### III-1-2. Unsaturated fatty acids (such as olive oil):

One of the most important aspects of the Mediterranean diet is the high concentration of unsaturated fatty acids in its fiber and protein sources, coupled with a lack of saturated fat [83] [84] as well, AHA and the European Society of Cardiology (ESC) strongly support the substitution of mono- and polyunsaturated fats in place of saturated fats and trans-fatty acids [85] [77].

Extra virgin olive oil containing potent antioxidant properties, including simple and complex phenols, which are present in its phenolic compounds, mainly include: hydroxytyrosol and oleuropein which are potent antioxidants [86].

### III-1-3. Fruits and vegetables

The dietary use of fruits and vegetables is considered as cornerstone of the Mediterranean diet. In fact, the European Society of Cardiology encourages the daily consumption of several servings of fruits and vegetables [77], the AHA strongly recommends the addition of a variety of phytochemicals, including fruits and vegetables in large quantities [87].

### III-1-4. Fiber-rich whole grain foods

Many data suggest beneficial effects of whole grains on cardiovascular disease, morbidity and mortality, as well as AHA guidelines indicate that diets high in fiber, such as whole grains, oats and barley, reduce morbidity and mortality related to cardiovascular disease lipid-lowering, and recommends a total dietary fiber intake of 25 to 30 g per day [88]. Consumption of whole grains increases the consumption of foods high in dietary fiber to promote health [77].

Randomized control trials show significant improvements in CRP levels, cholesterol profile, and beneficial effects on body mass index and waist circumference in the randomized group consuming low calorie whole grains versus those consuming grain [89] Thus, observational studies show that the benefits go up to the improvement of glucose metabolism [90] [91] weight reduction [92], and reinforcement of antioxidant capacities [93].

### III-1-5. Nuts and legumes

Replacing the consumption of carbohydrates and saturated fats with nuts, peanuts, almonds, reduces the level of blood fats and the risk of cardiovascular disease by 30% to 45% [94] [95] In addition, the increased consumption of nuts leads to a significant reduction in LDL cholesterol, inflammatory proteins and oxidative mediators [96] thus soy consumption has beneficial effects on endothelial functions [97].

### III-2. Chronic diseases

The Mediterranean diet is considered a protective factor against many chronic diseases. By reducing the important risk factors and comorbidities of cardiovascular diseases, such as high blood pressure, dyslipidemia and diabetes, the cardio-protective effect provided by the Mediterranean diet could be an important route for the protective effect of the diet. the Mediterranean on cognition and dementia [98][99][101][102] RM has also been associated with a low risk of cardio-metabolic syndrome [100].

### III-2-1. Cardiovascular diseases

Adherence to the traditional Mediterranean diet has always been beneficial for cardiovascular risk. [103] [104] and is considered the most likely
dietary model for providing protection against coronary heart disease. [105]. A key feature of this diet is its low trans fat content. [85] [77]. Extra virgin olive oil, the main source of fat in the RM, along with plant foods and nuts, makes this dietary diet beneficial to health as these fresh foods undergo minimal treatment. They are therefore rich in fiber, antioxidant polyphenols and essential trace elements and macronutrients. Recently, primary prevention trials have shown dietary intervention to promote adherence to traditional DM significantly reducing the risk of cardiovascular disease [106].

III-2-2. Cognitive Function and Dementia

The neuroprotective effect can be used to improve preventative measures and to critically change the way people at high risk of dementia are managed. The interactions between nutrition and the aging brain are numerous and complex, but there are 3 main features that may play a pivotal role [107]: Reduced blood flow [108], thought to be related to atherosclerosis and arterial plaque formation [108]; Mitochondrial dysfunction, resulting from the accumulation of reactive oxygen species in the brain; and inflammation, which is generally considered a natural process of aging [109]. A distinct feature of Alzheimer Disease is the accumulation of β-amyloid and the formation of neurofibrillary tangles composed of highly phosphorylated forms of microtubule-associated tau protein [107], so that β-amyloids increase the production of reactive oxygen species, which exacerbates the formation of tau entanglements as a compensatory mechanism for oxidative stress [107].

Among other benefits, adherence to MD has been associated with a lower risk of various chronic diseases [110] [111], and its protective properties are seen as a combination of high monounsaturated fatty acid consumption and polyphenols of olive oil and polyunsaturated fatty acids of fish; and antioxidants from fruits, vegetables [112].

Long-term observational studies show that MD as a diet reduces biomarkers of oxidative stress and positively affects cognition. Taking unsaturated fatty acids (both monounsaturated fatty acids and polyunsaturated fatty acids) has been associated with improved cognitive performance and decreased risk of age-related cognitive decline [113]. consumption of micronutrients such as vitamins C, E, B12 and folate [60] [61] flavonoids [62] and carotenes [61] have been associated with a decreased risk of cognitive decline and Alzheimer Disease in human observational studies. RM could reduce oxidative stress [114] and inflammation [115] associated with an increased risk of cognitive decline [116]. In addition, a growing body of evidence, mainly from prospective studies, suggests that MD slows down the decline age-related cognitive and progression of dementia. A meta-analysis, also published in 2013, assessed the effects of Parkinson's disease on stroke, cognitive impairment and depression and included a total of 22 studies, including 8 on cognitive impairment [119]. High and moderate adhesion to the mediterranean diet has been shown to be associated with a reduced risk of cognitive impairment [119].

Despite the fact that the causes of dementia are multifactorial, there is growing evidence that modifiable risk factors such as cardio-metabolic diseases and lifestyle play an important role; Thus, nutrition is a key role [120] [121] [117] [118]. The typical mechanisms of aging of brain cells show signs of atrophy, most of which are related to 3 main mechanisms, as explained (above) in setting up, namely, the decline in supply flow blood and, mitochondrial dysfunction (caused by oxidative stress), increasing inflammation of the patient's brain [107]. There are several mechanisms that could explain the positive effects of MD on cognitive function. The first is the reduction of vascular risk factors and thus improving the blood circulation to the brain, so MD adherence favorably increases HDL cholesterol and reduces LDL cholesterol vascular risk which is strongly correlated with cognitive dysfunction [122].

Second, MD can protect cognition through its effect on oxidative stress. MD is known to be a rich source of antioxidants such as vitamin E, vitamin C, folate, and polyphenols [123]. Epidemiological studies suggest that vitamin E is used for protection against cognitive disorders [124] and nutrients, such as folate [125]. Third, the effect MD on cognitive function can be mediated by the lowering of inflammation in the brain. MD
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with the ability to reduce inflammatory biomarkers such as C-reactive protein (CRP) in neuritic plaques and nfts in the brain and serum [126] [127]. Thus, diet, such as fruits, vegetables, cereals, and unsaturated fatty acids in the Mediterranean diet, is associated with a lower risk of cognitive decline [128] [129].

III-2-3. Type 2 diabetes

Diabetes prevention studies focusing on lifestyle [136] have shown strong reductions in the risk of type 2 diabetes [137] [138] in favor of this beneficial effect, the American Diabetes Association recommends that patients with newly diagnosed type 2 diabetes are being treated with lifestyle-related pharmacotherapy [139] and also recommends low-carbohydrate or low-fat diets for weight loss in overweight or obesity associated with type 2 diabetes [140] because drug therapy alone often fails over time [141], and some drugs are at risk for cardiovascular disease and other serious complications [142] [143]. For these reasons, the combination of pharmacotherapy and lifestyle changes is proving to be the most effective.

Regarding lifestyle, taking the example of the Mediterranean diet characterized by its low carbohydrate content and high proportion of monounsaturated fatty acids provide cardiovascular benefits and increase insulin sensitivity [144] [145] in addition to changes in fashion of life promote weight loss and increase activity levels, which facilitates the management of diabetes [139]. A study published by United Kingdom Prospective Diabetes Study (UKPDS) evaluating the effect of the Mediterranean diet on body weight in 190 overweight women who were followed for 2 years in a Mediterranean diet, lost weight in a significant way [146] also prospective studies have shown that Mediterranean dietary habits are associated with reduced risk of type 2 diabetes, in healthy participants [147]. Trials have shown that Mediterranean diets protect against insulin resistance and metabolic syndrome, thus, a mechanism through which Mediterranean diets can improve glycemic control may be through improved insulin sensitivity mediated increased levels of circulating adiponectin [144] [148] [174].

III-2-4. The arterial pressure

According to the medical diagnosis based on the guidelines of the National Mixed Committee [152] hypertension is defined as an increase in blood pressure: systolic beyond 140 mmHg or diastolic blood pressure greater than 90 mmHg [152]. High blood pressure is a major risk factor for cardiovascular disease and is independent of other factors [31]. Therefore, from the point of view of public health, it is urgent to find ways to fight this disease.

The Mediterranean diet is of the utmost importance in the prevention and treatment of hypertension [149] and the reduction of its complications such as cardiovascular disease and stroke. In fact, several publications reporting results of clinical studies that confirm the protective role of the Mediterranean diet vis-à-vis systolic blood pressure both systolic and diastolic [150]. Thus a study by Beitz R, et al. showed a systolic blood pressure drop of 3.0 mmHg in women who consumed a high amount of fruit, vegetables or vitamin C [153]. also, a prospective cohort study has shown that consumption of fruits and vegetables is inversely associated with blood pressure in the population of the Mediterranean basin with a high intake of vegetable fats [154].

III-2-5. Obesity

Obesity predisposes to a number of conditions, including cardiovascular diseases [155] [156], type 2 diabetes [157] [158], metabolic syndrome [159], non-alcoholic fatty liver disease [160], certain types of cancer [161] [162], obstructive sleep apnea [163], osteoarthritis [164] and asthma [165] and increases the risk of premature death [166], resulting in health costs raised all over the world [23]. Factors predisposing to obesity include excessive food intake, lack of physical activity, and genetic susceptibility [167]. However, obesity is a heterogeneous condition and thus intra-abdominal adipose tissue accumulation has a greater impact on the development of cardio-metabolic risk factors and significant lipid profile effects [168]. The increased availability of free fatty acids, the release of pro-inflammatory cytokines and adipokines from adipose tissue, hepatic insulin resistance, inflammation, and the resulting dyslipidemia are among the many metabolic disorders associated with this affection,
also hormonal status and drug treatments may also play an important role [169]. Low-calorie diet is still the main and essential step in the treatment of obesity, associated with increased physical activity and lifestyle changes [170].

RM is the most common tool for weight reduction in obese individuals [171]. Even moderate weight loss of about 10% or less has been shown to contribute to several health benefits including improved metabolic parameters, reduced blood pressure, and increased longevity [172] [173]. Evidence that calorie restriction improves insulin sensitivity and reduces systemic inflammation [174] [175]. Several studies have shown the benefits of the Mediterranean diet for weight loss in obese patients, by evaluating physical and biochemical markers after at least 6 months after adherence to the Mediterranean diet [176] [177] [178]. Mediterranean diet has been shown to be associated with greater improvement in insulin sensitivity parameters [176].

Adipose tissue is an endocrine organ with a large and biologically active secretome [180] [181] and fat tissue in obese individuals is characterized by increased expression and/or secretion of several pro-inflammatory cytokines, as well as adipokine to promote inflammation, atherogenesis and insulin resistance, while the biosynthesis of anti-inflammatory, anti-atherogenic and insulin-sensitizing adipokines such as adiponectin decreases [182] [183]. Several studies have shown an increase in circulating levels of leptin and an increase in adiposity associated with leptin resistance and that this condition may contribute to the onset and/or maintenance of obesity [184]. [185]. One study shows decreased circulating levels of Epidermal Growth Factor (EGF) after introduction of the Mediterranean diet in obese subjects in parallel with an improvement in insulin sensitivity [190]. During fasting, salivary and plasma EGF increases physiologically [191] to inhibit gastric acid secretion and preserve the esophageal and gastrointestinal system (as a sign of intestinal adaptation to food). Increased EGF may result in insulin-like biological activities in tissues expressing high numbers of EGFR receptors (EGFR), such as fat and skeletal muscle [192]. By binding to EGFR, a receptor belonging to the family of tyrosine kinase receptors, such as the insulin receptor [201], EGF can amplify downstream signaling of insulin by PI3-kinase recruitment, additional, leading to EGF-induced translocation of GLUT4 on plasma membranes and stimulation of glucose uptake into target tissues [192]. These molecular mechanisms are important in insulin resistance states, including obesity, in which the increase in EGF due to dietary restriction can trigger insulin-like compensatory mechanisms, so insulin regulates expression of EGF [193]. This explains the parallel decrease in insulin and EGF in patients with more constant weight loss, in which insulin sensitivity has been improved or restored [193].

Lactate Dehydrogenase (LDH) is an intracellular enzyme that is released into the bloodstream when tissues are destroyed or injured. Therefore, LDH is an important clinical marker of tissue or cell integrity. In obese patients, adipose tissue is dysfunctional [194] [195] has a reduced ability to store and retain non-esterified fatty acids (NEFA), resulting in increased circulating levels of AGNE, thereby promoting the development of lipotoxicity in peripheral tissues [196].

III-2-6. Cancer

Tobacco control, reduction of excessive alcohol consumption, vaccination against human papillomavirus and reduced exposure to ultraviolet light are obvious strategies for reducing cancer incidence rates [197] [198]. As citing the World Cancer Research Fund (WCRF) such examples; Aflatoxins with liver cancer, red meat and/or processed meat with colorectal cancer, alcohol with cancers of the gastrointestinal tract, and, for smokers, β-carotene increases the risk of lung cancer [199] [200].

Guidelines proposed by WCRF and recommendations on nutrition and physical activity for cancer prevention [202] [203], have been consistent with those aimed at preventing other chronic diseases, such as diabetes and heart disease [203] [204] [205], which raises the prospect of a huge public health problem and, therefore, medical care, [204] [205]. Both the aging of the population and changes in the distribution of risk factors contribute to the increased burden of cancer [25] [26] nutrition and...
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Physical activity are also among the most important determinants cancer risk in humans, through their contributions to obesity, which is a risk factor for many malignancies [199] [206].

III-2-7. Oxidative stress

MR reduces oxidative stress [114] and C-reactive protein and interleukins involved in the mechanisms of oxidative stress leading to chronic pathophysiology [132] [133]. The neuroprotective effects of the Mediterranean diet are related to its ability to reduce inflammation and oxidative stress, which are also related to the pathophysiology of degenerative diseases [134] [135] adherence to RM, with higher consumption of fruit and vegetable rich in phytochemicals, demonstrates an increase in endogenous and exogenous antioxidant levels, enhancing immunity and protecting the selected sample against oxidative stress and maintaining a healthy state. Thus vegetable consumption has been closely associated with a low risk of degenerative diseases [241] [242]. Eating habits can play a key role in regulating the redox state of human plasma improving defense against oxidation. [245] [246, 247, 249]. The Mediterranean diet is associated with a significant reduction in several risk factors, including cardiovascular risk [250, 251, 252].

III-2-8. Cholesterol and oxidative stress

The bioavailable quantity of bioactive molecules in subjects with high consumption of fruits and vegetables promotes their protective and preventive action against lipid oxidation and therefore against oxidative stress [233]. Also, the influence of the rate Plasma cholesterol on the atherosclerotic process and the effects of diet-induced cholesterol influence the progression and development of cardiovascular disease [235]. Several researchers have also suggested that diets have a significant effect on the mechanisms of progression of atherosclerosis and thrombosis [236, 237].

Numerous studies have demonstrated the inhibitory activity of several compounds present in fruits and vegetables on the oxidation of LDL in vitro [238, 239]. Thus, interesting results seem to highlight the circulating levels of carotenoids (lutein, zeaxanthin, cryptoxanthin, lycopene, a and b-carotene), vitamin A and vitamin E have reached the highest values in subjects with a higher great adherence to the Mediterranean diet [238, 239]. Several studies show that vitamin A reduces the production of pro-inflammatory cytokines such as TNF-a and IL-12 and promotes the activation of lymphocyte subpopulations through the secretion of specific cytokines (eg IL-10). [240], thus the phytochemical components of fruits and vegetables consist of different phytochemicals beneficial to the systemic circulation, thus absorbed antioxidants reach the large intestine and contribute to the protection against gastrointestinal diseases induced by oxidation [243, 244].

III-2-9. Dietary recommendations

The guidelines and recommendations published in several reports to maintain body weight within the normal range [199, 218]. The equivalent of 60 minutes of exercise per day to be physically active; consume a plant-based diet comprising a variety of fruits and vegetables; choose unprocessed cereals and grains over processed products; limit the intake of red meat and salt; avoid or limit alcohol consumption, to meet nutritional needs without the use of food supplements [218] avoid energy-rich foods, sugary drinks, fast foods and processed meat, and genetically modified foods modified to increase certain types of cancer (such as colorectal cancer) by modification in the nucleic acids thus causing changes in enzymatic activity [219, 220, 223, 224].

IV. Discussion

Adopting a healthy lifestyle is the cornerstone of chronic disease prevention and treatment, and healthy eating is a major lifestyle change. Various studies show that dietary treatment is most effective for reducing the average body weight of people suffering from overweight or obesity, and a statistically significant reduction in BMI, and thus showing beneficial effects on health [172, 173, 179].

The traditional MD is a plant-based diet, where vegetables, fruits, cereals (preferably whole grains), legumes and nuts, fish and shellfish, white meat is consumed in large quantities and frequently. The main source of dietary fat in MD is olive oil and adequate daily water intake must be ensured. The Mediterranean diet also includes a moderate consumption of eggs and dairy products,
on the contrary, the consumption of red meats, processed meats and foods rich in sugars and fats is reduced in quantity and frequency. Seasonality, biodiversity, the use of traditional and local food products are also important elements of this trend. In addition, the Mediterranean diet also includes qualitative cultural and living elements, such as conviviality, culinary activities, physical activity and adequate rest [40]. Thus MD is known as one of the healthiest diets [39].

The critical importance of food and nutrition in cancer prevention is widely recognized, due to an impressive amount of data from epidemiological, clinical and laboratory research [199]. So, the issues of diet and cancer and the problems of diet, nutrition and cancer come from different types of research, including animal and mechanical studies, ecological studies in humans (correlation studies at the level of population, useful for generating hypotheses), observational analytical epidemiology studies (ie, case-control and cohort studies) and dietary intervention trials. In laboratory studies using cell cultures and experimental animal models, nutrients and other bioactive food components have been shown to affect key biological processes involved in the regulation of cell growth and carcinogenesis. Foods are naturally complex and provide many bioactive substances that can act individually and/or synergistically to influence processes such as cell differentiation and apoptosis, as well as the hormonal regulation of cellular functions. Hypocaloric diet is still the main and essential step in the treatment of obesity, associated with increased physical activity and lifestyle changes [170]. Also, the dose-response relationship: For example, squamous cell carcinoma of the esophagus is very different from esophageal adenocarcinoma: the former is more strongly related to smoking and alcohol consumption in Western populations [207] [208], or human papillomavirus (HPV) infection in other populations, such as those in China [209] [210]; the latter is more closely associated with obesity and/or reflux disease [211]. In addition, the dietary factors associated with these two cancers have some overlap, but are also quite distinct [212] [213]. Similarly, an analysis of the NIH-AARP study on diet and health [214] pointed out that the high risk of endometrial cancer in obese compared to non-obese women was higher for subtypes. Type I tumors (endometrioid). With respect to nutrients, increased consumption of phytoestrogens was associated with a reduced risk of mucinous ovarian cancer, but no other subtypes of ovarian cancer, in the Australian ovarian cancer [215]. For example, in the large-scale long-term pooling of prospective studies on diet and cancer [212, 213], a protective effect of fruit and vegetable consumption on esophageal breast cancer (ER Negative but not breast cancer has been consistently demonstrated in 20 studies [216, 217]. Several factors and their interactions, namely tobacco, dietary protein, and alcohol [221] increase the risk of cancer of various types of cancer [221] and exposures experienced by a person during his life including: metabolism, hormones, body composition, physical activity, gut microbiome, inflammation, oxidative stress, aging, diet, and alcohol, and broader psychosocial and environmental [222].

Bacteria can either promote or suppress cell growth and metastasis through bacterial toxins induced by the secretion of bacterial proteins leading to changes in gene expression, altering the tumor (inflammation, immune functions, or by altering host metabolism [229], and by promoting the production of endogenous factors that cause carcinogenesis (such as bile acids and steroid hormones) [230], and since diet influences both the type and the number of intestinal microorganisms [230] [231] the microbiome in the development of cancer, including host genome interactions with microbiota [232]. Thus, one of the main intermediate step in the link between diet and cancer remain in research, and require technologies in the prevention and development of cancer to provide ideas and data relevant to the relationship between food intake and cancer risk and progression.

The total antioxidant capacity of biological samples can also be evaluated in clinical studies that measure the end products of degradation of endogenous compounds such as lipids or DNA. Changes from baseline levels of these products could then be attributed to changes in the antioxidant capacity of the diet, so the antioxidant capacity of the biological samples can be controlled by a variety of tests, which do not
necessarily reflect the physiological mechanisms in humans vivo [248].

Several studies describe insulin and leptin resistance in obese subjects. The relationships between these two hormones are complex and poorly understood, and there is evidence that they are associated with body fat through different mechanisms [186, 187]. Other studies with comparable or even larger samples had similar results and found a statistically significant decrease in leptin levels and not adiponectin in weight loss [188] [189]. Several nutrients characterize MD and protect against various chronic diseases, such as olive oil, and prospective studies have shown that olive oil significantly improves cognitive function [130, 131].

V. Conclusion

The traditional Mediterranean diet has a protective effect against cardiovascular diseases, oxidative stress, dyslipidemia, diabetes mellitus, blood pressure, cancer, neurodegenerative diseases and obesity, this protective effect of the Mediterranean diet is provided by antioxidants, anti-inflammatories and bioactive components of foods characteristic of the Mediterranean basin, reducing the risk of development of chronic diseases.

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