

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

Open access books available

186,000

International authors and editors

200M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



The Impact of Olive Oil and Mediterranean Diet on the Prevention of Cardiovascular Diseases

*Muhammad Akram, Rumaisa Ansari, Naheed Akhter,
Olutosin Ademola Otekunrin, Sadia Zafar,
Muhammad Ishaque, Naveed Munir, Luigi Sciarra,
Giulia My, E.C. Gianvito Matarrese, Zefferino Palamà
and Muhammad Riaz*

Abstract

The Mediterranean diet has a lot of health benefits but especially because it lowers the incidence of cardiovascular diseases. It has been shown that food components, certain nutrients and the pattern of the diet lowers the risk of several diseases such as diabetes, certain cancers, obesity, respiratory disorders, mental health and cognitive decline, bone diseases (osteoarthritis), healthy aging and quality of life among more others. It has been concluded from studying the mechanism responsible for lowering these risks that food combinations, food nutrients, presence of non-nutritive substances, lifestyles habits and the cooking techniques all together make the Mediterranean dietary pattern into a tool that can not only prevent but can also be used as a way of treatment for these medical ailments. As part of the essential dietary fat, consumption of extra virgin olive oil is the main feature of Mediterranean diet. Olive oil is noted to have anti-bacterial characteristics, involved in improving the endothelial function in young females, and is hypothesized to have epigenetic effects interplay offering protection from cancers due to the presence of beneficial monounsaturated fats. The presence of antioxidants contributes to the inflammation protecting properties of the olive oil. Olive oil has high quantities of antioxidants and offers numerous benefits for cardiovascular health, such as protection of LDL from oxidation and lowering of the high blood pressure as well as offers protection from diabetes mellitus. The Mediterranean diet and the Olive oil consumption also have a fundamental impact in secondary prevention, such as in patients with atrial fibrillation that underwent catheter ablation.

Keywords: Mediterranean diet, olive oil, cardiovascular diseases, benefits of olive oil consumption, atrial fibrillation

1. Introduction

Native to the Mediterranean region, olive tree also known as *Olea europaea* is considered to be one of the oldest trees still present (**Figure 1**). The fruits and products obtained from the olive tree such as olive oil have been used for a long time for the diet and nutritional demands of the residing population in the Mediterranean regions. As part of the Mediterranean culture olive trees have been cultivated and harvested for a long time. Olives are taken and subsequently used for olive oil extraction. The importance of the use of olive oil in both daily and cultural practices is evident by the fact that the Greek philosophers began to search on its medicinal and nutritional properties by as early as the seventh century BC. Particularly ingestion of olive oil and its use as an ointment for treating ailments related to dermatological ulcers and stomach was recommended by both Hippocrates and Aristotle who recognized the health benefits attributed to the olive oil consumption [1]. Mediterranean countries such as Turkey, Spain, Greece, Morocco, Italy and Tunisia are involved in most (70%) of the olive oil production [2]. Apart from these some other countries such as USA and Australia are also involved in the production of olive oil. Different types of olive oil with different profiles of polyphenol content are being produced by a single country [3] showing that olive oil of different varieties and qualities exists. Nutritional characteristics of different types of olive oil also differ.

Animal fats mainly constitute the saturated fatty acids, while the fats of vegetables mostly contain polyunsaturated fatty acids. Especially, olive oil obtained from the fruits of olive tree consists of both the polyphenols and monounsaturated fatty acids. Even today, the health benefits of consuming olive oil in place of fats of other origins remain unexcelled and is most likely attributed to the extraordinary chemical composition of olive oil [4]. However, the benefits of the olive oil for human health have been mostly evaluated in attribution to the consumption of the Mediterranean diet [5], whereas its individual beneficial impact on human health remains to be confirmed by more research [6].



Figure 1.
Millennial olive tree in Italy, Puglia, San Vito dei Normanni (Mrs. Teresa Village).

There are different types of the marketed olive oil with difference in their potential healthful impacts and include pomace oil, refined olive oil, virgin olive oil and extra virgin olive oil etc. [7]. In context of research the different types of olive oil are often not individually evaluated for their potential health benefits and therefore the difference in their beneficial properties is not properly evaluated. Extra virgin olive oil is the most naturally made olive oil and is produced within the first 24 hours after the harvest and from the very first pressing of the olives. Extra virgin olive oil is obtained by the mechanical means rather than the chemical and no excessive heating is underwent during its extraction as the temperature for extraction is fixed at degrees lesser than 28°C. The acidity or free fatty acid level of the oil is lesser than 0.8 percent contributing to the oil's optimal odor and taste. It should be noted that olive fruit contains different types of hydrophilic phenolic compounds such as simple phenolic compounds, complex phenolic compounds and lignans. Simple phenolic compounds include vanillic, coumaric, galls, caffeic acids, tyrosol and hydroxytyrosol etc. whereas complex phenolic compounds contain secoiridoids such as ligstroside and oleuropein. Lignans found in the olives include pinoresinol and 1-acetoxypinoresinol etc. Extra virgin olive oil has the highest amounts of phenolic compounds as compared to the virgin olive oil [8]. Lignans on the other hand, are not found in any refined olive oils but only found in extra virgin olive oil [9]. Because of these extraordinary compositions extra virgin olive oil is the most beneficial to human health as compared to other refined oils and is used as a precautionary tool against the cardiovascular diseases [10]. Virgin olive oil just like the extra virgin olive oil also arises from the very first pressing of the fruits of olive tree but the acidity levels are a little higher in comparison i.e. lesser than 2 percent. Virgin oil contains in its composition the hydrophilic phenols such as phenolic acids alcohol, lignans, flavonoids and secoiridoids [11]. But because these compounds are present in comparatively lower levels, its consumption is not as healthful as compared to the extra virgin olive oil. But the consumption of virgin olive oil as compared to the other refined oils is still recommended [12]. Another types of marketed olive oil is the refined olive oil which is refined by chemical and thermal means in order to get as much oil from the pulp of olives as possible. This pulp is the leftover of the first pressing of olives. Acids and alkalis are the chemical agents used for the purpose of refinement. This process of oil extraction results in oil with higher fat and acidic content as compared to the extra virgin and virgin olive oil. Therefore, olive oil obtained and refined this way lacks the optimal odor, taste and natural antioxidants. As compared to the olive oils obtained from the first pressing of olives, the refined olive oil has lesser antioxidant potential. Moreover, p-hydroxyphenyl-acetic acid, p-coumaric acid, o-coumaric acid, vanillic acid and p-hydroxybenzoic acid present in the refined olive oil offer very little protection and no antioxidant potential [13]. Pomace oil is another type of the marketed olive oil and is produced as a by-product in the production of extra virgin olive oil. This oil is obtained by heating the olive seeds, skins and pulp. The remaining oil is extracted by the use of hexane as a solvent. The resultant oil obtained is then further refined and therefore it offers very limited beneficial effects on human health as the antioxidant potential is very low. Still more other types of oils produced through more poor practices e.g. glampante oil. These oils, unless refined, are not considered to be suitable for human use [14].

2. Mediterranean diet and cardiovascular diseases

The Mediterranean diet was defined in 1960 by Ancel Keys circa [15] and is one of the most well known and most studied dietary pattern in the world [Medscape,



Figure 2. Oil-Garlic and Pepper. The application of oil in the kitchen leads to this famous dish in the all the Mediterranean diet. On the right-side pure drop of extra virgin olive oil (Gianvito Matarrese EVO Restaurant Alberobello-Italy).

PubMed impact]. The Mediterranean diet has a lot of health benefits but especially because it lowers the incidence of cardiovascular diseases. It has been shown that food components, certain nutrients and the pattern of the diet lowers the risk of several diseases such as diabetes, certain cancers, obesity, respiratory disorders, mental health and cognitive decline, bone diseases (osteoarthritis), healthy aging and quality of life among more others [16]. It has been concluded from studying the mechanism responsible for lowering these risks that food combinations, food nutrients, presence of non-nutritive substances, lifestyles habits and the cooking techniques all together make the Mediterranean dietary pattern into a tool that can not only prevent but can also be used as a way of treatment for these medical ailments [17–20]. As part of the essential dietary fat, consumption of extra virgin olive oil is the main feature of Mediterranean diet. Apart from the healthy proportion of the amount and type of fatty acids present in olive oil [21], it is consumed along with a large amount of vegetables as a salad dressing for cooked or raw legumes and vegetables (**Figure 2**). Even though the inhabitants of the Mediterranean countries lack knowledge regarding the benefits of olive oil for human health, they have believed that the long lives of their populations are attributed to the usage of olive oil in their diets.

3. Impact of olive oil consumption on human health

It has been revealed from the studies by The Global Burden of Disease that the rate of incidence of chronic illnesses such as cardiovascular diseases including coronary artery disease and hypertension have been persistently increasing [22]. It has been revealed that this increase in the rate of these diseases is most likely related to the adoption of unfavorable behaviors and unhealthy dietary patterns [23]. Therefore, the protective qualities of certain dietary patterns such as Mediterranean diet especially its certain components such as olive oil has been studied and evaluated for their beneficial effects on human mortality and morbidity [6]. Olive oil is noted to have anti-bacterial characteristics [11], involved in improving the endothelial function in young females [24], and it has been hypothesized to have epigenetic effects interplay offering protection from cancers [25] due to the presence of healthful monounsaturated fats. The presence of antioxidants contributes to the anti-inflammatory properties of the olive oil. Olive oil has high quantities of antioxidants and offers numerous benefits for cardiovascular health [26], such as protection of LDL from oxidation and lowering of the high blood pressure as well as offers protection from diabetes mellitus [27].

4. Mechanism of actions of virgin olive oil as part of Mediterranean diet to prevent cardiovascular disorders

Atherosclerosis development is becoming one of the major risk factors in people having hypertension, diabetes and hypercholesterolemia [28–30]. During the pathogenesis of hypertension, inflammation causing factors imposes oxidative stress by activating the mononuclear leucocyte by enhancing the production of wide range of cytokines which directly exert oxidative stress on the blood vessels and might lead to the development of atherosclerosis. It was reported that hypertension may develop due to variations in the arterial vasodilation/vasoconstriction particularly due to the modifications of the synthesis of molecules like NO, a potent relaxing factor, and ET1 a potent vasoconstrictor released by endothelium. It was reported in non-smoking women that when Mediterranean diet containing EVOO was given to these women for 1 year, this caused a decrease in hypertension with higher level of serum NO along with changes in gene expression including eNOS upregulation that played important role in the regulation of blood pressure, dilate the blood vessels with a number of vaso-protective and anti-atherosclerotic roles; and caveolin 2 down-regulation was also reported. Caveolin 2 can trap the eNOS and ultimately inhibit the enzyme [31]. Moreover, in patients at high risk of cardiovascular disorders when given EVOO as part of MeDiet, a significantly decrease in the systolic and diastolic blood pressure were reported [31–33] and same effects were also reported in metabolic syndrome patients for giving the MeDiet with EVOO for parallel 2 years [34].

Storniolo et al. [31] explored very interesting findings when used MeDiet containing EVOO both in moderate hypertensive and healthy volunteers and found that EVOO did not decrease the blood pressure in healthy individuals although a drop in blood pressure in moderate hypertensive patients was reported. Approaches to explore the nutritional values of MeDiet supplemented with EVOO is one of the most interesting side as EVOO have potential to reduce the development of chronic disorders like type 2 diabetes, metabolic syndrome an obesity by regulating the metabolism of glucose and lipids in our body. It was reported that hyperglycaemic and hypercholesterolemic conditions are leading cause of the development of cardiovascular disorders or aggravating the atherosclerotic process. Violi et al. [35] explored that administration of MeDiet containing the EVOO significantly regulate the postprandial metabolic profile including the decreased blood glucose, LDL-C and ox-LDL levels and an increased level of insulin was also reported in healthy volunteers. Moreover, the impact of EVOO (10 g) in MeDiet has the potential to normalize the blood glucose level in post-prandial glycaemic patients with impaired fasting glucose. The mechanisms accounting for the positive effect of EVOO are related to increasing up-regulation, as EVOO reduces dipeptidyl peptidase-4 activity with consequent increase in glucagon-like peptide-1 concentration which regulates postprandial glycaemia by up-regulating insulin secretion [36].

High level of lipids contents is one of the second one major risk factor for the development of cardiac disease but MeDiet supplemented with EVOO have significant impact to reduce the total cholesterol, LDL-cholesterol (LDL-C) and non-HDL-cholesterol (non-HDL-C) levels to prevent the cardiovascular risk [36]. Hernáez et al. [37] reported on administering the MeDiet particularly containing EVOO for 1 year to patients at high cardiovascular risk and investigated an improvement in the HDL functions including the cholesterol efflux capacity, modulation in the metabolism of cholesterol, improvement in antioxidant as well as anti-inflammatory properties, and increased vasodilatory properties. Moreover, it was also found by Covas et al. [12] that taking phenolic olive oils increases the HDL-C, decreased the total cholesterol/HDL-C ratio, decreased LDL-C/HDL-C ratio as

well as decrease in triglycerides (TG) level. A study carried out in patients having metabolic syndrome reported that consumption of MeDiet supplemented with EVOO for 2 years significantly reduced the blood glucose level, increase insulin, decrease total cholesterol as well as TG and improved the HDL-C level as compared to control group. Such findings explored that Mediterranean-style diet containing EVOO is an emerging therapeutic strategy to modulate cardiovascular disease risk in metabolic syndrome [34]. During an experimental study it was also found that EVOO along with corn oil have role in improving the total cholesterol, LDL-C, VLDL-C, Apolipoprotein-B, Apolipoprotein-A and LDL particle concentrations and this improvement was observed in more significant individuals given corn oil compared with EVOO intake. Moreover, the findings of some investigations are summarized in **Table 1** and the targets of Me Diet supplemented with EVOO to prevent the cardiovascular diseases risk factors are represented in **Figure 3**.

Mediterranean diet containing extra virgin olive oil and quantity used	Number of volunteers participated	Plan of Study Design with time period used	Targets to manage Cardiovascular disorders	References
8 gram/Day	Having metabolic disorders (n = 180)	All given in parallel upto 2 years	By Decreasing: BMI, waist circumference, Body weight, Blood pressure, Endothelial function score, Blood glucose and insulin, hs-CRP, IL-6, IL-7, Total cholesterol, triglycerides, IL-18, By Increasing: HDL-C,	[34]
50 mL/Day	At high risk of cardiovascular (n = 164)	All given in parallel upto 1 year	By Decreasing: CRP, IL-6, [sICAM-1], [sP-selectin], [sVCAM-1], IL-18/IL-10	[38]
50 mL/Day	At high risk of cardiovascular (n = 165)	All given in parallel upto 3–5 year	By Decreasing: CRP, Interleukin-6, TNF- α , Total cholesterol, LDL-C, Triglyceride, Blood pressure By Increasing: HDL-C	[39]
1 L/ 07 Days	At high risk of cardiovascular (n = 69)	All given in parallel upto 5 years	By Decreasing: IL-6, IL-7, IL-8, IL-18, IL-1 β , IL-5, IL-12p70, IFN- γ , TNF- α , GCSF, GMCSF, ENA78, MCP-1, MIP-1 β ,	[40]
14.8 mL/Day	Given to healthy people (n = 137)	All given in parallel upto 6 months	By Decreasing: Systolic blood pressure By Increasing: FMD	[32]
1 L/07 Days	At high risk of cardiovascular (n = 231)	All given in parallel upto 1 year	By Decreasing: Plasma tryptophan	[41]

Table 1.
Scientific based investigations carried out to investigate the Mediterranean diet containing extra virgin olive oil on preventing the cardiovascular disorders.

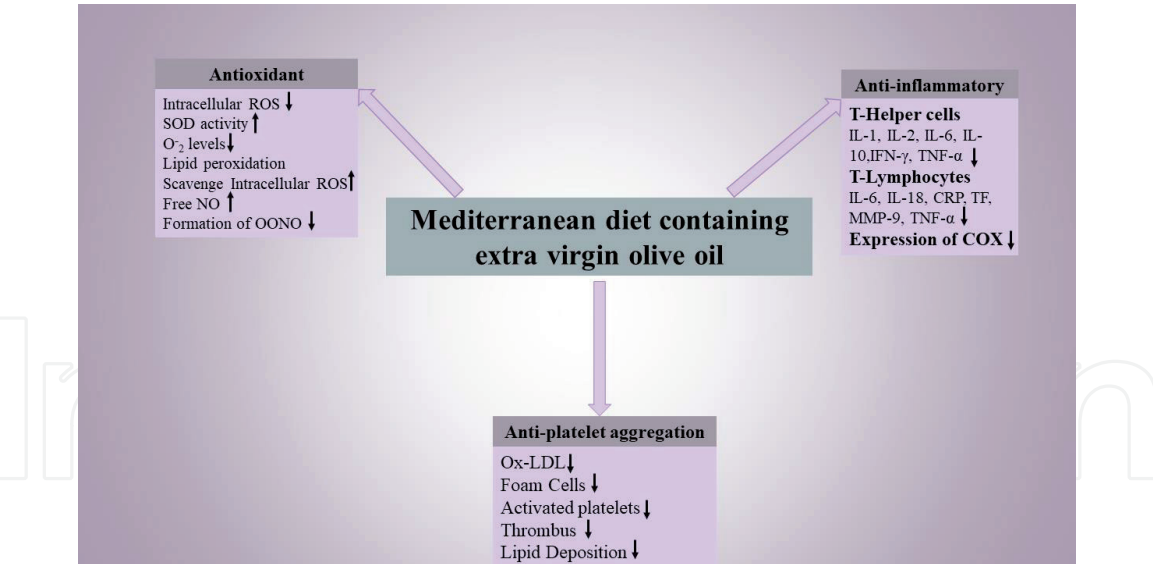


Figure 3.
Major targets of Mediterranean diet containing extra virgin olive oil to prevent the development of cardiovascular diseases.

5. Olive oil for cardiovascular diseases in secondary prevention

If the effect of the Mediterranean diet and olive oil in primary prevention appears almost obvious, it is surprising to be in secondary prevention in cardiovascular diseases. The Lyon Diet Heart Study provided information about outcomes after acute myocardial infarction. This randomized, secondary prevention trial in patients analyzed the incidence of myocardial infarction and cardiovascular deaths. Mediterranean diet was able to significantly reduce the occurrence of all-cause and cardiovascular death [42]. PREDIMED study pointed out the reduction in CD40 expression on monocytes surface, and a further decrease in C-reactive protein and IL-6 in Mediterranean diet group (plus olive oil and plus nuts) with a significant reduction in the expression of adhesion molecules. These molecular changes suggest a protection of atherosclerotic plaques from instability resulting in a reduction in cardiovascular events after a heart attack [38].

However, it is surprising how the effect of olive oil is also protective against the incidence of arrhythmias as demonstrated in the laboratory by Bukhari group [43] and as demonstrated by the sub analysis of the PREDIMED trial suggests that extra virgin olive oil in the context of a Mediterranean dietary pattern may reduce the risk of atrial fibrillation [43].

However, it will be exciting to study the PREDIMAR project, a randomized, single-blind trial testing the effect of a Mediterranean diet enriched with extra virgin olive oil to reduce tachyarrhythmia relapses after atrial fibrillation ablation. If the study hypothesis will be confirmed, the utility of the Mediterranean diet enriched with extra virgin olive oil in slowing the progression of AF will be proven and it could actually become a true healing weapon, on a par with the most recent interventional cardiological technological innovations [44].

6. Conclusion

It has been concluded from studying the mechanism responsible for lowering the cardiovascular risks that food combinations, food nutrients, presence of non-nutritive substances, lifestyles habits and the cooking techniques all together

make the Mediterranean dietary pattern into a tool that can not only prevent but can also be used as a way of treatment for these medical ailments. As part of the essential dietary fat, consumption of extra virgin olive oil is the main feature of Mediterranean diet. Olive oil possess anti-bacterial properties, involved in improving the endothelial function in young females. It has been hypothesized that the olive oil has epigenetic effects offering protection against cancers due to the presence of monounsaturated fats. The presence of antioxidants contributes to the anti-inflammatory properties of the olive oil. Olive oil has high quantities of antioxidants and offers numerous benefits for cardiovascular health, such as protection of LDL from oxidation and lowering of high blood pressure. Various studies have shown that the intake of olive oil offers cardioprotective properties contributed by the high poly phenolic content as well as the presence of antioxidants and its curative effect is not limited to primary prevention, but also to secondary prevention in unexpected fields such as in the treatment of cardiac arrhythmias. Olive oil has many biological activities due to the presence of many important secondary metabolites such as antioxidant and other useful bioactive components that suggests the future use of olive oil in pharmaceutical preparations in pharmaceutical industries.

IntechOpen



Author details

Muhammad Akram^{1*}, Rumaisa Ansari¹, Naheed Akhter²,
Olutosin Ademola Otekunrin³, Sadia Zafar⁴, Muhammad Ishaque¹, Naveed Munir⁵,
Luigi Sciarra⁶, Giulia My⁷, E.C. Gianvito Matarrese^{8,9}, Zefferino Palamà⁷
and Muhammad Riaz¹⁰

1 Department of Eastern Medicine, Government College University Faisalabad,
Pakistan

2 College of Allied Health Professional, Government College University Faisalabad,
Pakistan

3 Department of Agricultural Economics and Farm Management, Federal
University of Agriculture, Abeokuta (FUNAAB), Nigeria

4 Department of Botany, Division of Science and Technology, University of
Education Lahore, Punjab, Pakistan

5 Department of Biochemistry, Government College University Faisalabad, Pakistan

6 Cardiology and Electrophysiology Unit, Policlinico “Casilino”, Rome, Italy

7 Cardiology and Electrophysiology Unit, Villa Verde Hospital, Taranto, Italy


8 University of Bilkent, Ankara, Turkey

9 EVO Restaurant, Alberobello, Italy

10 Department of Allied Health Sciences, University of Sargodha, Pakistan

*Address all correspondence to: makram_0451@hotmail.com

IntechOpen

© 2021 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. 

References

- [1] Nomikos NN, Nomikos GN and Kores DS. The use of deep friction massage with olive oil as a means of prevention and treatment of sports injuries in ancient times. *Archives of medical science: AMS*. 2010; 6: 642.
- [2] Rossi R. The Eu Olive and Olive Oil Sector Main Features, Challenges and Prospects. *European Parliamentary Research Service; European Parliament: Brussels, Belgium*. 2017: 12.
- [3] Vossen P. Olive oil: history, production, and characteristics of the world's classic oils. *HortScience*. 2007; 42: 1093-100.
- [4] La Lastra C, Barranco M, Motilva V and Herrerias J. Mediterranean diet and health biological importance of olive oil. *Current pharmaceutical design*. 2001; 7: 933-50.
- [5] Grosso G, Marventano S, Yang J, et al. A comprehensive meta-analysis on evidence of Mediterranean diet and cardiovascular disease: are individual components equal? *Critical reviews in food science and nutrition*. 2017; 57: 3218-32.
- [6] Buckland G and Gonzalez CA. The role of olive oil in disease prevention: a focus on the recent epidemiological evidence from cohort studies and dietary intervention trials. *British Journal of Nutrition*. 2015; 113: S94-S101.
- [7] Gorzynik-Debicka M, Przychodzen P, Cappello F, et al. Potential health benefits of olive oil and plant polyphenols. *International journal of molecular sciences*. 2018; 19: 686.
- [8] Bianchi G. Lipids and phenols in table olives. *European Journal of Lipid Science and Technology*. 2003; 105: 229-42.
- [9] Tripoli E, Giammanco M, Tabacchi G, Di Majo D, Giammanco S and La Guardia M. The phenolic compounds of olive oil: structure, biological activity and beneficial effects on human health. *Nutrition research reviews*. 2005; 18: 98-112.
- [10] Bogani P, Galli C, Villa M and Visioli F. Postprandial anti-inflammatory and antioxidant effects of extra virgin olive oil. *Atherosclerosis*. 2007; 190: 181-6.
- [11] Servili M, Esposto S, Fabiani R, et al. Phenolic compounds in olive oil: antioxidant, health and organoleptic activities according to their chemical structure. *Inflammopharmacology*. 2009; 17: 76-84.
- [12] Covas M-I, de la Torre R and Fitó M. Virgin olive oil: a key food for cardiovascular risk protection. *British Journal of Nutrition*. 2015; 113: S19-S28.
- [13] Papadopoulos G and Boskou D. Antioxidant effect of natural phenols on olive oil. *Journal of the American Oil Chemists' Society*. 1991; 68: 669-71.
- [14] Bondioli P, Mariani C, Lanzani A, Fedeli E, Mossa A and Muller A. Lampante olive oil refining with supercritical carbon dioxide. *Journal of the American Oil Chemists' Society*. 1992; 69: 477-80.
- [15] Keys A, Mienotti A, Karvonen MJ, et al. The diet and 15-year death rate in the seven countries study. *American journal of epidemiology*. 1986; 124: 903-15.
- [16] Dinu M, Pagliai G, Casini A and Sofi F. Mediterranean diet and multiple health outcomes: an umbrella review of meta-analyses of observational studies and randomised trials. *European journal of clinical nutrition*. 2018; 72: 30-43.
- [17] Corella D, Coltell O, Macian F and Ordovás JM. Advances in understanding the molecular basis of

the mediterranean diet effect. *Annual review of food science and technology*. 2018; 9: 227-49.

[18] Radd-Vagenas S, Kouris-Blazos A, Singh MF and Flood VM. Evolution of Mediterranean diets and cuisine: concepts and definitions. *Asia Pacific journal of clinical nutrition*. 2017.

[19] Vasto S, Buscemi S, Barera A, Di Carlo M, Accardi G and Caruso C. Mediterranean diet and healthy ageing: a Sicilian perspective. *Gerontology*. 2014; 60: 508-18.

[20] Ortega R. Importance of functional foods in the Mediterranean diet. *Public health nutrition*. 2006; 9: 1136-40.

[21] Garcia-Martinez O, Ruiz C, Gutierrez-Ibanez A, Illescas-Montes R and Melguizo-Rodriguez L. Benefits of olive oil phenolic compounds in disease prevention. *Endocrine, Metabolic & Immune Disorders-Drug Targets (Formerly Current Drug Targets-Immune, Endocrine & Metabolic Disorders)*. 2018; 18: 333-40.

[22] Vos T, Barber RM, Bell B, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *The Lancet*. 2015; 386: 743-800.

[23] Wagner K-H and Brath H. A global view on the development of non communicable diseases. *Preventive medicine*. 2012; 54: S38-S41.

[24] Moreno-Luna R, Muñoz-Hernandez R, Miranda ML, et al. Olive oil polyphenols decrease blood pressure and improve endothelial function in young women with mild hypertension. *American journal of hypertension*. 2012; 25: 1299-304.

[25] Menendez JA and Lupu R. Mediterranean dietary traditions for the

molecular treatment of human cancer: anti-oncogenic actions of the main olive oil's monounsaturated fatty acid oleic acid (18: 1n-9). *Current pharmaceutical biotechnology*. 2006; 7: 495-502.

[26] Schwingshackl L, Christoph M and Hoffmann G. Effects of olive oil on markers of inflammation and endothelial function—a systematic review and meta-analysis. *Nutrients*. 2015; 7: 7651-75.

[27] Guasch-Ferré M, Hruby A, Salas-Salvadó J, et al. Olive oil consumption and risk of type 2 diabetes in US women. *The American journal of clinical nutrition*. 2015; 102: 479-86.

[28] Hollander W. Role of hypertension in atherosclerosis and cardiovascular disease. *The American journal of cardiology*. 1976; 38: 786-800.

[29] Choy P, Siow YL, Mymin D, OK. *Lipids and atherosclerosis Biochem Cell Biol*. 2004; 82: 212-24.

[30] Selvin E, Coresh J, Golden SH, Boland LL, Brancati FL and Steffes MW. Glycemic control, atherosclerosis, and risk factors for cardiovascular disease in individuals with diabetes: the atherosclerosis risk in communities study. *Diabetes care*. 2005; 28: 1965-73.

[31] Storniolo CE, Casillas R, Bulló M, et al. A Mediterranean diet supplemented with extra virgin olive oil or nuts improves endothelial markers involved in blood pressure control in hypertensive women. *European journal of nutrition*. 2017; 56: 89-97.

[32] Davis CR, Hodgson JM, Woodman R, Bryan J, Wilson C and Murphy KJ. A Mediterranean diet lowers blood pressure and improves endothelial function: results from the MedLey randomized intervention trial. *The American journal of clinical nutrition*. 2017; 105: 1305-13.

- [33] Medina-Remón A, Tresserra-Rimbau A, Pons A, et al. Effects of total dietary polyphenols on plasma nitric oxide and blood pressure in a high cardiovascular risk cohort. The PREDIMED randomized trial. *Nutrition, Metabolism and Cardiovascular Diseases*. 2015; 25: 60-7.
- [34] Esposito K, Marfella R, Ciotola M, et al. Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. *Jama*. 2004; 292: 1440-6.
- [35] Violi F, Loffredo L, Pignatelli P, et al. Extra virgin olive oil use is associated with improved post-prandial blood glucose and LDL cholesterol in healthy subjects. *Nutrition & diabetes*. 2015; 5: e172-e.
- [36] Reiner Ž, Catapano AL, De Backer G, et al. ESC/EAS Guidelines for the management of dyslipidaemias: the Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). *European heart journal*. 2011; 32: 1769-818.
- [37] Hernáez Á, Castañer O, Goday A, et al. The Mediterranean Diet decreases LDL atherogenicity in high cardiovascular risk individuals: a randomized controlled trial. *Molecular nutrition & food research*. 2017; 61: 1601015.
- [38] Casas R, Sacanella E, Urpi-Sarda M, et al. The effects of the mediterranean diet on biomarkers of vascular wall inflammation and plaque vulnerability in subjects with high risk for cardiovascular disease. A randomized trial. *PloS one*. 2014; 9: e100084.
- [39] Casas R, Sacanella E, Urpí-Sardà M, et al. Long-term immunomodulatory effects of a mediterranean diet in adults at high risk of cardiovascular disease in the PREvención con Dieta MEDiterránea (PREDIMED) randomized controlled trial. *The Journal of nutrition*. 2016; 146: 1684-93.
- [40] Casas R, Urpi-Sardà M, Sacanella E, et al. Anti-inflammatory effects of the Mediterranean diet in the early and late stages of atheroma plaque development. *Mediators of inflammation*. 2017; 2017.
- [41] Yu E, Ruiz-Canela M, Guasch-Ferré M, et al. Increases in plasma tryptophan are inversely associated with incident cardiovascular disease in the Prevencion con Dieta Mediterranea (PREDIMED) Study. *The Journal of nutrition*. 2017; 147: 314-22.
- [42] De Lorgeril M, Salen P, Martin J-L, Monjaud I, Delaye J and Mamelle N. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. *Circulation*. 1999; 99: 779-85.
- [43] Bukhari IA, Mohamed OY, Almotrefi AA, et al. Cardioprotective Effect of Olive Oil Against Ischemia Reperfusion-induced Cardiac Arrhythmia in Isolated Diabetic Rat Heart. *Cureus*. 2020; 12.
- [44] Barrio-Lopez M, Ruiz-Canela M, Ramos P, et al. PREvention of recurrent arrhythmias with Mediterranean diet (PREDIMAR) study in patients with atrial fibrillation: Rationale, design and methods. *American heart journal*. 2020; 220: 127-36.