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

6,300

Open access books available

172,000

International authors and editors

190M

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

Olive Phenomenon from the Mediterranean Diet: Health Promotion via Phytochemicals

Didar Üçüncüoğlu

Abstract

The Mediterranean Diet contains fruits, vegetables, nuts, whole grains, fish and virgin olive oil (VOO) as a key component. It is well explained that those consumption has a number of positive health effects. It has been accepted for a long time that the leading compound in olive was oleic acid as a monounsaturated fatty acid. However, the latter researches were figured out that VOO rich in natural phenolics have multifaceted influence on major diseases including cancer, diabetes, cardiovascular diseases, neurodegenerative disease, and metabolic disorders. Recent medical studies proved that oleocanthal and oleacein, characteristic bioactive biophenol-secoiridoids in VOO, success in the anti-inflammatory and in the antioxidant properties, respectively. It has more recently investigated that oleocanthal and hydroxytyrosol (HT) kills cancer cells (CCs). HT and oleuropein reduces breast cancer and cutaneous melanoma cancer cells both in number and aggressiveness, and inhibits CCs multiplying. It has been declared too many times that nutrition type is the strongest factor can be caused acute and chronic diseases. However, at the same time, nutrition can also prevent some of those heavy symptoms. The main purpose of presented chapter is to meet olive's bioactive molecules and to examine how to improve our health with diet.

Keywords: phytochemicals, health, olive, virgin olive oil, bioactive compounds

1. Introduction

Olea europaea is naturally cultivated in Mediterranean region. It's drupe fruit (olive), flowers & leaves, seeds, fibers and some of by-products (liquid and solid wastes) are used technologically by humans live in there, and also, this is an agricultural & economic culture of Mediterranean populations (Spain, Turkey, Greece, Italy, Morocco, Tunisia, in particular). However, olive oil is also produced in Australia and the USA and basically [1] consumed European Union Countries, United States, Turkey and China (**Figure 1**). The olive oil is the best demonstrated product that examined both its nutritional and medicinal properties. Ancient historical evidence recommended using VOO for stomach health and against to dermatological ulcer.

Nutritional quality of olives depends on various factors. Cultivar, genetic and biologic factors, soil structure, climatic conditions, harvest time, agricultural applications and extraction type are the most effective parameters [2]. These are

Figure 1.
Leading consumers of olive oil worldwide from in 2020/2021.

also influence on the olive oil quality and its chemical composition. Free acidity determines chemical subtype of olive oils such as lampante, virgin, extra virgin, etc.

The edible oils are commonly well-known due to their unsaturated fatty acids and phenolic profiles. In particular, olive oil is rich in both monounsaturated fatty acids and polyphenols. These attributes basically related to consumption of the Mediterranean Diet. One tablespoon of olive oil contains approximately 120 kcal composed of 10 g monounsaturated lipid. The most important of polyphenols are phenolic acids such as ferulic and vanillic acids, phenolic alcohols like hydroxytyrosol and tyrosol, flavonoids and secoiridoids such as oleuropein [3].

Olive oil is contains triacylglycerols as major components (98–99%) and contains small quantities of free fatty acids, glycerol, phosphatides, pigments, flavor compounds, and sterols as minor components (1–2%). Approximate fatty acid composition of olive oil as fallows: 14–15% saturated fats (13% palmitic acid-C16:0 and 1–2% stearic acid-C18:0) and 85% unsaturated fats (60–70% oleic acid-C18:1, also known as ω -9 and 12–15% linoleic acid-C18:2, also known as ω -6 fatty acid, and 3% palmitoleic acid). This profile shows us olive oil composed of more monounsaturated than polyunsaturated fatty acids and it is free of trans (E-) form of fatty acids. Previous researches indicated that a higher proportion of monounsaturated fatty acids in diet cause a strong reduction in the cardiovascular disease (CVD) risks.

The polyphenols are natural antioxidants that link oil's bitter taste and astringency. Moreover, they raise the resistance capacity against to oxidation. The bioactive compounds namely phenolic antioxidants (oleic acid, squalene, terpenoids), simple phenols (hydroxytyrosol, tyrosol), secoiridoids (oleuropein, aglycone of ligstroside, and their respective decarboxylated dialdehyde derivatives, oleacein, oleochantal) and lignin, vitamin E contribute to oil different biologic character such as antitumor, antimicrobial and antioxidant effects via possible pathophysiological pathways generally associated with a decreased risk in breast, colon and skin cancer. It needs to be noted that the quantity of these bioactive molecules depends on many factors such as olive variety, environmental factors (altitude, cultivation practices), harvest time (unripe, semi, ripe olives the extraction and storage conditions [4].

Here, in this chapter, phytoactive compounds found in olive are determined chemically and then biologic mechanisms are described how they prevent us some chronic diseases.

2. Phytochemicals

2.1 Phenolics and tocopherols

The presences of phenolics and tocopherols affect radical scavenging activity and so, antioxidant capacity of olive oil. These chemicals also considered as a functional food component, contains different classes of phenols: simple phenols, phenolic acids, phenolic alcohols, secoiridoids, lignans, and flavonoids. According to EFSA [5], molecules from olive (hydroxytyrosyl and oleuropein complex) have beneficial effects on human health. The consumption of this complex approximately 2–15 mg/day is essential. The vitamin E is a fat-soluble vitamin and is composed by α -, β -, γ and δ -tocopherols and α -, β -, γ - and δ -tocotrienol isomers. α -tocopherol has the highest antioxidant activity in fat-riched foods. Moreover, vitamin E and phenol mixtures are very promising oil stabilizing agent during frying, thanks to its capacity to reduce acrolein and acrylamide production. According to EFSA's current scientific opinion [6] an average requirements of α -tocopherol could be 11–13 mg/day for adults. Extra virgin olive oil contains 100–760 mg/kg α -tocopherol [7, 8].

Mediterranean country peoples demonstrate a long life and lower case of the age-related diseases due to their food habits. Thus, the consumption of extra virgin olive oil has been clinically and experimentally associated with the health promoting properties of the Mediterranean diet. Extra virgin olive oil is characterized by a high amount of polyphenols as miracle pharmanutritional properties against to the development of several chronic diseases such as cardiovascular diseases, diabetes, obesity, metabolic syndrome and cancer. Squalene is a hydrocarbon composed in olive oil and acts as a weak antioxidant affect. Especially, its importance comes from the protective effect under heating against to the oxidative stress. Besides, the squalene quantity varies between 2 and 7 g/kg of olive oil. Scientific papers prove us the health benefits of squalene and its influence capability on cancer cells [9–11]. Meanwhile, tocopherols have attracted tremendous attentions because of their potential roles in preventing aging-associated diseases such as cardiovascular and Alzheimer's disease [12–14]. Oleacein and oleochantal (**Figure 2**) are among the major phenolics determined in virgin olive oil. These are the dialdehydic forms of the elenolic acid deriving from oleuropein and ligstroside, respectively. They have positive role in the treatment of cardiovascular pathologies, certain types of cancers, chronic inflammatory diseases, Alzheimer's disease, *Helicobacter pylori* infection [14]. Cutaneous melanoma is a type of cancer that is spreading in Europe. The relation between melanoma risk and consumption of olive oil has been recently studied. Oleuropein, the main secoiridoid glucoside present in the *Olea europaea* leaves have already been investigated in melanoma *in vitro* and *in vivo* models revealing their cytotoxic activity and anticarcinogenic action. Oleacein, another abundant secoiridoid in olive and leaves show antitumor activity via controlling the altered pattern of gene expression (transcripts and miRNAs) related to mTOR and BCL2 pathways in melanoma cells. Hydroxytyrosol, the most representative simple phenol of *Olea europaea* L. leaves and virgin oils, causes inhibition of melanoma cell proliferation activating caspase-3-dependent apoptosis [15, 16].

2.2 Phytosterols

Phytosterols, in other words plant sterols, are bioactive compounds of seeds, fruits, cereals, and nuts. They can be found in free form, esterified with fatty acids or conjugated with glycosides. Campesterol, β -sitosterol and stigmasterol are the most common phytosterols. Phytosterols are by-products of isoprenoid biosynthesis

Figure 2.
Chemical structure of Oleacein and Oleochantal.

pathway via squalene from acetyl coenzyme A. Its generation cascade involving more than 30 enzymes catalyzed reactions in similar cholesterol biosynthesis within cell membranes. All phytosterols contain one double bond at carbon-5 position and saturation of this double bond occurs either enzymatically in vivo or through hydrogenation. Both β -sitostanol and campestanol are the two most common stanols. In olive oil, they are esterified with fatty acids like esters of sitostanol (sitostanyl oleate) and esters of campestanol (campesteryl oleate). Human cells cannot synthesize those endogenously, so we have to obtain them from our diet. The daily intake of plant stanols (saturated sterols) is about 25 mg/day compared to sterols ranging from 150 to 400 mg/day which include 65% of intake as β -sitosterol, 30% as campesterol and 5% as stigmasterol. The maximum values of campesterol, stigmasterol and β -sitosterol were found in different types of olive oil 34.46 mg, 29.56 mg and 259.46 mg/100 g oil, respectively. Serum phytosterol level in humans should range from between 2.9 and 17.0 mg/L. Phytosterols are alcohols for organic chemistry, resemblance to cholesterol both in structure and in function. Their function in plant cells is to regulate the fluidity and permeability of cell membranes in a way similar to cholesterol in cell membranes of mammals. They can inhibit the absorption of cholesterol by its direct displacement from micelles. This reported as the cholesterol-lowering effect of phytosterols in humans. Additionally, phytosterols and their derivatives have high health benefits related to antiinflammatory, antiulcerative, antitumor, antibacterial, and cardioprotective properties [17–23].

2.3 Chlorophyll and carotenoids

The minor contents in olive oil give to its characteristic organoleptic and nutritional features. Among them, color pigments play an important role in oxidative stability during storage and in the preservation of its quality because of their antioxidant characteristics and prooxidant roles under light. The pigments used as indicators to indicate olive oil freshness or storing conditions. For example, low amount of pheophytins show a fresh, well-stored olive oil, while high presence of those indicate an old, bad-stored oil [24, 25]. Pigments are divided into two main

groups in foods namely carotenoids and chlorophylls. Chlorophylls are responsible for the greenish color of extra virgin olive oil. On the other side, β -carotene, lutein, zeaxanthin and xanthophylls called carotenoids are natural antioxidants found in various amount in olive oil. They have beneficial properties for human health. β -carotene appears to lower the risk of heart diseases, while lutein protects the eye retina from oxidative damage. Some other studies were showed that carotenoids exhibit bioactivities in photosynthesis, special antioxidant properties and produce improvements in cognitive function and cardiovascular health [26–30].

3. Clinical and experimental studies on chronic diseases

The potential health advantages caused by olive oil consumption, particularly within the context of the Mediterranean diet, have been extensively investigated. As mentioned before, olive oil consumption was found to be beneficial for some of chronic non communicable diseases [31]. Below-explained clinical results are also given in **Table 1** with references.

Scope	Outcomes	References
Olive oil consumption and cancer risk	It can decrease the risk of upper digestive and respiratory tract neoplasms, breast and colorectal cancer sites	Pelluchi et al. [32]
Whether olive oil or MUFA intake was associated with the development of cancer	Olive oil intake has a protective role on cancer risk. But, it was not clear which component is responsible for the beneficial effects	Psaltopoulou et al. [33]
MUFA effect on CVD and mortality	VOO reduced risk of all-cause mortality, CV mortality, stroke	Schwingshackl Hoffman [34]
VOO intake and CHD & stroke risks correlation	VOO intake had a significant protective effect	Martinez-Gonzalez et al. [35]
Determine inflammation or endothelial effect of olive oil	Olive oil might be exert beneficial effects on endothelial function and markers of inflammation and endothelial function	Schwingshackl et al. [36]
VOO with high phenolic content, CVD effect and Nutraceutical prevention	Provides small beneficial effect on systolic blood pressure and serum oxidative status. Considered as nutraceutical in CV prevention	Hohmann et al. [37]
Breast cancer risk and dose–response	Olive oil might be a protective factor for the cancer occurrence among case–control studies	Xin et al. [38]
To compare olive and other edible oils effects on blood lipid level	VOO intake decreased serum total cholesterol, LDL and triglycerides less but increased HDL more than other plant oils	Ghobadi et al. [39]
High versus low polyphenol content on CVD risk factors	olive oils contains high polyphenol show some CVD risk reductions	George et al. [40]
To illustrate the impact of olive oil on type II diabetes	Olive oil intake could be beneficial for the prevention and management of type II diabetes	Schwingshackl et al. [41]
to investigate effects of 2 oil blends phytonutrient concentrations on blood lipid profile, compared with refined olive oil as a control	borderline hypercholesterolemia extent as refined olive oil	Haldar et al., [42]

Table 1.
Experimental and clinical studies about olive, nutrition and health [32–42].

3.1 Cardiovascular diseases (CVD)

A comprehensive work included 101,460 cases of Coronary Heart Disease (CHD) and 38,673 cases of stroke participants revealed that after every 25 g increase in olive oil consumption, the risk of CHD was reduced by approximately 4%, while the risk stroke was decrease by 26%. Another research aimed to assess the consumption of monounsaturated fatty acids and olive oil intake on human mortality was applied 32 sample group contains total 841,211 cases. Overall, higher oil intakes lead to a lower risk for all-cause mortality, cardiovascular mortality, cardiovascular events and stroke. On the other hands, the other lipid origin such from animal had no significant positive effect on morbidity and mortality in this work. A research including 3106 individuals search try to detect the potential mediators of the olive oil/CVD relationship. The daily consumption between 1 mg and 50 mg resulted in a significantly more pronounced decrease in C-reactive protein and interleukin-6. The other study examined the effect of high versus low concentration of polyphenol in olive oil on CVD risk factors in clinical trials. It was found that high polyphenol olive oil has beneficial effects on malondialdehyde, oxidized-LDL, total cholesterol and HDL cholesterol, suggesting that olive oil may have cardioprotective properties. A comparative research, which aimed to explain the effects of olive oil or some of other edible oils consumption on blood lipids, showed that olive oil intake significantly diminish total cholesterol, LDL and triglyceride less, but increased HDL more than the others. Chronic kidney disease (CKD) is one of the most common chronic degenerative diseases and it carries a considerable risk factor for CV disorders and mortality. Noce et al., [43] study shows that daily use of high phenolic contents from extra virgin olive oil contributes anti-inflammatory and antioxidant action in nephropathic patients. Consequently, the essential role has been highlighted again here that a well-balanced nutritional-diet therapy plays in the clinical management of CKD cases and the eventual improvements in patient's life style, performing positive effects on CKD symptoms.

3.2 Cancer

There are too actual clinical meta-analysis researches. They are mainly focused between olive oil consumption and various cancer types. 37,140 participants from 19 case-control studies were revealed that extra virgin olive oil intake was associated with low probability to have any type of cancer, compared with the lowest quality of olive oil intake. The other study evaluated the effect of olive oil consumption on breast cancer risk. The results stated that olive oil can decrease the risk of breast cancer as well as other types of cancer. Another comprehensive research, included 150,000 females from 5 cohort and 11 retrospective case control studies, demonstrated that higher olive oils consumption showed a protective effect against breast cancer. Some clinical studies show that the mixtures of phytosterols have inhibitory effect on 5 α -reductase, give rise to apoptosis, alter testosterone metabolism, change urine flow and prostate volume. On the other hand some other experimental studies explain that phytosterols prevent lipoprotein oxidation, inhibit cell growth and the expression of caveolin-1, decrease cell proliferation, reduce or inhibit hyper proliferation of colonocytes, reduce in tumor size. These are the various mechanisms to express anticancer features from phytosterols of olives and olive oils [19, 44]. More recently, Bartolomei [45] provides a huge dataset to characterize of olive oils antioxidant properties, both in vitro by Trolox equivalent antioxidant capacity, oxygen radical absorbance capacity (ORAC value), ferric reducing antioxidant power (FRAP value), and 2,2-diphenyl-1-picrylhydrazyl assays, and at the cellular level in hepatic (HepG2) and intestinal (Caco-2) cells. One of the highlighted results of this

Figure 3.
 Risk factors in diabetes mellitus.

study was to determine the antioxidant effects of phenolic compounds in an extra virgin olive oil (EVOO) extract, using either in vitro assays or liver and intestinal cell models, rather than the effects of single phenols, such as hydroxytyrosol or oleuropein. The selective trans-epithelial transport of some oleuropein derivatives was observed for the first time in differentiated Caco-2 cells in this research.

3.3 Type II diabetes

Risk factors for diabetes Mellitus (DM) has been described [46] as follows: physical inactivity, first degree relative with DM, members of high-risk ethnic populations (such as African Americans, Latinos, Native Americans, Asian American and Pacific Islanders), women who delivered baby, hypertension, HDL cholesterol <35 mg/dL, triglycerides >250 mg/dL, women with polycystic ovary syndrome, HbA1C $\geq 5.7\%$, impaired glucose tolerance, impaired fasting glucose, obesity, insulin resistance and finally history of CVD (**Figure 3**). It was proved that 10 g daily increasing intake of olive oil was caused 9% reduced risk of type-II diabetes, while when the highest quality olive oil intake category was compared to the lowest quality intake category, it was revealed a 16% reduced risk of diabetes. This meta-analysis collected data from 187,068 individuals, participating in 4 cohort studies and 29 trials. Therefore, this meta-analysis provides beneficial evidence concerning the risk of type II diabetes consuming olive oil [42].

4. Conclusion

In biological systems, free radical reactions are associated with aging, cancer, cardiovascular disease, optical disease, and neurodegenerative disease. Antioxidants are used to prevent such reactions and are therefore supporting health. Regular consumption of olive oil has a strong correlation with prevention of cardiovascular disease, immune function, and gastrointestinal (GI) disease. Olive oil improves the curing of mortal diseases like cancer and liver disease. Dietary use of olive oil is therefore helpful in maintaining good health. The present chapter evaluating the effect of olive oil consumption on human health, identified the protective effects

of olive oil on all-cause and cardiovascular mortality, as well as on cardiovascular events. Olive oil consumption exhibits a protective role against overall and particularly breast cancer occurrence, as well as diabetes mellitus type 2. In general, benefits which have been recorded from the intake of pure olive oil have also been recorded from the adoption of a health-promoting lifestyle, based on the principles of the Mediterranean diet. Diets including plants foods, fish, and seafood and preferably including plant oils and low-fat dairy products are associated with a lower risk of most chronic diseases. In conclusion, the aggregated evidence corroborates that the specific impact of olive oil consumption is beneficial for human health, and particularly for the prevention of cardiovascular diseases, several cancers, and diabetes mellitus.

Conflict of interest

The author declares no conflict of interest.

Author details

Didar Üçüncüoğlu
Faculty of Engineering, Department of Food Engineering, Çankırı Karatekin
University, Çankırı, Turkey

*Address all correspondence to: didaru@karatekin.edu.tr

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] International Olive Council (IOC), 2021. Retrieved from <https://www.statista.com/statistics/940532/olive-oil-consumption-worldwide-by-leading-country/> (Accessed in 26.02.2021)
- [2] Martakos I, Kostakis M, Dasenaki M, Pentogennis M, Thomaidis N. Simultaneous Determination of Pigments, Tocopherols, and Squalene in Greek Olive Oils: A Study of the Influence of Cultivation and Oil-Production Parameters. *Foods*. 2019;9(1):31. DOI:10.3390/foods9010031
- [3] Zeb A, Murkovic M. Olive (*Olea europaea* L.) Seeds, From Chemistry to Health Benefits. Chapter 100 - Nuts and Seeds in Health and Disease Prevention 2011; 847-853, Academic Press. DOI: 10.1016/B978-0-12-375688-6.10100-8
- [4] Vita di S. Extra virgin olive oils storage: Effect on constituents of biological significance, Chapter 24. Editor(s): Victor R. Preedy, Ronald Ross Watson, Olives and Olive Oil in Health and Disease Prevention, Academic Press. 2021;291-297, ISBN 9780128195284. DOI:10.1016/B978-0-12-819528-4.00029-8.
- [5] EFSA Panel on Dietetic Products, N. a. A. N. (2011) Scientific Opinion on the substantiation of health claims related to oleic acid intended to replace saturated fatty acids (SFAs) in foods or diets and maintenance of normal blood LDL-cholesterol concentrations (ID 673, 728, 729, 1302, 4334) and maintenance of normal (fasting) blood concentrations of triglycerides (ID 673, 4334) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. *EFSA Journal* 9, 2043.
- [6] EFSA Panel on Dietetic Products, N. a. A. N. (2015) Scientific opinion on the substantiation of health claims related to polyphenols in olive and protection of LDL particles from oxidative damage (ID 1333, 1638, 1639, 1696, 2865), maintenance of normal blood HDL-cholesterol concentrations (ID 1639), maintenance of normal blood pressure (ID 3781), “anti-inflammatory properties” (ID 1882), “contributes to the upper respiratory tract health” (ID 3468), “can help to maintain a normal function of gastrointestinal tract” (3779), and “contributes to body defences against external agents” (ID 3467) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. *EFSA J* 19, 2033.
- [7] Lucci P, Bertoz V, Pacetti D, Moret S, Conte L. Effect of the Refining Process on Total Hydroxytyrosol, Tyrosol, and Tocopherol Contents of Olive Oil. *Foods*. 2020; 9:292. DOI:10.3390/foods9030292
- [8] Dugo L, Russo M, Cacciola F, Mandolino F, et al. Determination of the Phenol and Tocopherol Content in Italian High-Quality Extra-Virgin Olive Oils by Using LC-MS and Multivariate Data Analysis. *Food Analytical Methods*. 2020; 13:1027-1041. DOI: 10.1007/s12161-020-01721-7
- [9] Newmark HL. Squalene, olive oil, and cancer risk: A review and hypothesis. *Cancer Epidemiol. Biomark. Prev.* 1997;6, 1101-1103
- [10] Rodriguez-Rodriguez, R.; Simonsen, U. Natural Triterpenoids from Olive Oil: Potential Activities Against Cancer. In *Natural Compounds as Inducers of Cell Death*; Diederich, M., Noworyta, K., Eds.; Springer: Cham, Switzerland, 2012; Volume 1, pp. 447-461.
- [11] Chira M, Rigane G, Calas-Blanchard C et al. Phenolic, tocopherols and squalene profiles (HPLC-UV) of chemlali-sfax olive oil according to extraction procedure. *Revue Roumaine*

de Chimie 2020; 65:2, 179-190 DOI: 10.33224/rrch.2020.65.2.07

[12] Azzi A. Many tocopherols, one vitamin E. *Molecular Aspects of Medicine*. 2018;61:92-103. DOI: 10.1016/j.mam.2017.06.004

[13] Zhang L, Wang S, Yang R, et al. Simultaneous determination of tocopherols, carotenoids and phytosterols in edible vegetable oil by ultrasound-assisted saponification, LLE and LC-MS/MS. *Food Chemistry* 289 (2019) 313-319. DOI: 10.1016/j.foodchem.2019.03.067

[14] Macciola V, Cuomo F, de Leonardis A. IMPORTANCE OF OLEACEIN and oleochantal on the oxidative stability of extra virgin olive oil measured by Rancimat. *La rivista italiana delle sostanze grasse*. 2020; XCVII. https://www.innovhub-ssi.it/kdocs/1990259/2020_Vol._97_-_Art._03_Macciola.pdfRuzzolini, 2018;

[15] Cirmi S, Celano M, Lombardo GE, Maggisano V, Procopio A, Russo D et al. Oleacein inhibits STAT3, activates the apoptotic machinery, and exerts anti-metastatic effects in the SH-SY5Y human neuroblastoma cells. *Food Funct*. 2020;11 (4), 3271-3279. DOI: 10.1039/d0fo00089b

[16] Carpi S, Polini B, Manera C, Digiacoio M, Salsano JE, Macchia M, Scoditti E, Nieri P. miRNA Modulation and Antitumor Activity by the Extra Virgin Olive Oil Polyphenol Oleacein in Human Melanoma Cells. *Frontiers in Pharmacology* 2020;11. DOI:10.3389/fphar.2020.574317

[17] Uddin MS, Sarker MZI, Ferdosh S, et al. Phytosterols and their extraction from various plant matrices using supercritical carbon dioxide: a review, *J. Sci. Food Agric*. 2015;95:7, 1385-1394.

[18] Ogbe RJ, Ochalefu DO, Mafulul SG, Olumide OB. A review on

dietary phytosterols: their occurrence, metabolism and health benefits, *Asian J. Plant Sci. Res*. 2015;5:4, 10-21.

[19] Shahzad N, Khan W, Shadab MD, Ali Asgar et al. Phytosterols as a natural anticancer agent: Current status and future perspective. *Biomedicine & Pharmacotherapy* 88 (2017) 786-794. DOI: 10.1016/j.biopha.2017.01.068

[20] de Figueiredo LC, Bonafe EG, Martins JG, Martins, AF et al. Development of an ultrasound assisted method for determination of phytosterols in vegetable oil. *Food Chemistry*. 2018; 240:441-447. DOI:10.1016/j.foodchem.2017.07.140

[21] Huang J, Xu M, Fang YJ, Lu MS, Pan ZZ, Huang WQ, Chen YM, Zhang CX, Association between phytosterol intake and colorectal cancer risk: a case-control study, *Br. J. Nutr*. 2017; 117:6, 839-850.

[22] Wang H, Liu H, Guo B, Lan D et al. A novel poly (NMA-co-DEA-co-EDMA) monolithic column as a sorbent for online solid-phase extraction and its application in the determination of beta-sitosterol in plant oil samples, *Food Chem*. 2019; 278:594-600.

[23] Silva ACA, Baggio SR, Mariutti LRB, Bragagnola N. One-step rapid extraction of phytosterols from vegetable oils. *Food Research International* 2020;130:108891 DOI:10.1016/j.foodres.2019.108891

[24] Giuliani A, Cerretani L, Cichelli A. Chlorophylls in olive and in olive oil: Chemistry and occurrences. *Crit. Rev. Food Sci. Nutr*. 2011;51, 678-690.

[25] Cayuela JA, Yousfi K, Carmen Martínez M, García, JM. Rapid Determination of Olive Oil Chlorophylls and Carotenoids by Using Visible Spectroscopy. *J. Am. Oil Chem. Soc.* 2014;91, 1677-1684

- [26] Tapiero H, Townsend DM, Tew KD. The role of carotenoids in the prevention of human pathologies. *Biomed Pharm.* 2004;58, 100-110.
- [27] Fieor J, Bra K. Potential role of carotenoids as antioxidants in human health and disease. *Nutrients*, 2014;6, 466-488.
- [28] Hashimoto H, Sugisaki M, Yoshizawa M. Ultrafast time resolved vibrational spectroscopies of carotenoids in photosynthesis. *Biochimica et Biophysica Acta (BBA) – Bioenergetics*. 2015;1847(1), 69-78. DOI: 10.1016/j.bbabi.2014.09.001
- [29] Egeland ES. Carotenoids. In *The Physiology of Microalgae*; Borowitzka M, Beardall J, Raven J. *Developments in Applied Phycology*; Springer International Publishing: Cham, Switzerland, 2016;6.
- [30] Eggersdorfer M, Wyss A. Carotenoids in human nutrition and health. *Archives of Biochemistry and Biophysics*, 2018; 652, 18-26.
- [31] Foscolou A, Critselis E, Panagiotakos D. Olive oil consumption and human health: A narrative review. *Maturitas* 2018;11860:66. DOI:10.1016/j.maturitas.2018.10.013
- [32] Pelucchi C, Bosetti C, Negri E, Lipworth L, La Vecchia C. Olive oil and Cancer risk: an update of epidemiological findings through 2010. *Curr. Pharm. Des.* 2011; 17, 8: 805-812, DOI: 10.2174/138161211795428920
- [33] Psaltopoulou T, Kostis RI, Haidopoulos D, Dimopoulos M, Panagiotakos DB. Olive oil intake is inversely related to cancer prevalence: a systematic review and a meta-analysis of 13800 patients and 23340 controls in 19 observational studies. *Lipids Health Dis.* 2011; 127. DOI: 10.1186/1476-511X-10-127
- [34] Schwingshackl L, Hoffmann G. Monounsaturated fatty acids, olive oil and health status: A systematic review and meta-analysis of cohort studies, *Lipids Health Dis.* 2014; 13:154. DOI: 10.1186/1476-511X-13-154
- [35] Martínez-González MA, Dominguez LJ, Delgado-Rodríguez M. Olive oil consumption and risk of CHD and/or stroke: a meta-analysis of case-control, cohort and intervention studies. *Br. J. Nutr.* 2014; 112, 2:248-259. DOI: 10.1017/S0007114514000713
- [36] Schwingshackl L, Christoph M, Hoffmann G. Effects of olive oil on markers of inflammation and endothelial function-a systematic review and meta-analysis. *Nutrients* 2015; 7, 9: 7651-7675, DOI: 10.3390/NU7095356
- [37] Hohmann CD, Cramer H, Michalsen A, Kessler C, Steckhan N, Choi K, Dobos G. Effects of high phenolic olive oil on cardiovascular risk factors: a systematic review and meta-analysis, *Phytomedicine* 2015; 22, 6:631-640, DOI: 10.1016/j.phymed.2015.03.019
- [38] Xin Y, Li XY, Sun SR, Wang LX, Huang T. Vegetable oil intake and breast cancer risk: a meta-analysis. *Asian Pac. J. Cancer Prev.* 2015;16, 12: 5125-5135. DOI: 10.7314/apjcp.2015.16.12.5125
- [39] Ghobadi S, Hassanzadeh-Rostami Z, Mohammadian F, Nikfetrat A, negar H Ghasemifard, Raeisi Dehkordi, Faghih S. Comparison of blood lipid-lowering effects of olive oil and other plant oils: a systematic review and meta-analysis of 27 randomized placebo-controlled clinical trials. *Crit. Rev. Food Sci. Nutr.* 2018; 8: 1-15. DOI: 10.1080/10408398.2018.1438349
- [40] George ES, Marshall S, Mayr HL, Trakman GL, Tatucu-Babet OA, Lassemillante A-CM, Bramley A,

Reddy AJ, Forsyth A, Tierney AC, Thomas CJ, Itsiopoulos C, Marx W. The effect of high-polyphenol extra virgin olive oil on cardiovascular risk factors: a systematic review and meta-analysis, *Crit. Rev. Food Sci. Nutr.* 2018; 30, 1-138, DOI: 10.1080/10408398.2018.1470491

[41] Schwingshackl L, Lampousi AM, Portillo MP, Romaguera D, Hoffmann G, Boeing H. Olive oil in the prevention and management of type 2 diabetes mellitus: a systematic review and meta-analysis of cohort studies and intervention trials, *Nutr. Diabetes* 2017; 7, 4:e262. DOI: 10.1038/nutd.2017.12

[42] Haldar S, Long Hui Wong, Shia Lyn Tay, Jörg J Jacoby, Pengfei He, Farhana Osman, Shalini Ponnalagu, Yuan Rong Jiang, Hwee Peng Rebecca Lian, Christiani Jeyakumar Henry, Two Blends of Refined Rice Bran, Flaxseed, and Sesame Seed Oils Affect the Blood Lipid Profile of Chinese Adults with Borderline Hypercholesterolemia to a Similar Extent as Refined Olive Oil, *The Journal of Nutrition*, 2020;150:12, 3141-3151, DOI:10.1093/jn/nxaa274

[43] Noce A, Marrone G, Urciuoli S, Di Daniele F, Di Lauro M, Pietroboni Zaitseva A, Di Daniele N, Romani A. Usefulness of Extra Virgin Olive Oil Minor Polar Compounds in the Management of Chronic Kidney Disease Patients. *Nutrients*. 2021; 13(2):581. DOI:10.3390/nu13020581

[44] Stark AH, Madar Z, Olive oil in the prevention of breast and colon carcinogenesis, Chapter 28. Editor(s): Victor R. Preedy, Ronald Ross Watson, *Olives and Olive Oil in Health and Disease Prevention*, Academic Press. 2021;337-345. ISBN 9780128195284. DOI: 10.1016/B978-0-12-819528-4.00047-X.

[45] Bartolomei M, Bollati C, Bellumori M, Cecchi L, Cruz-Chamorro I, Santos-Sánchez G,

Ranaldi G, Ferruzza S, Sambuy Y, Arnoldi A, Mulinacci N, Lammi C. Extra Virgin Olive Oil Phenolic Extract on Human Hepatic HepG2 and Intestinal Caco-2 Cells: Assessment of the Antioxidant Activity and Intestinal Trans-Epithelial Transport. *Antioxidants*. 2021; 0(1):118. DOI:10.3390/antiox10010118

[46] Msopa E, Mwanakasale V. Identification of risk factors of diabetes mellitus in bank employees of selected banks in Ndola town. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*. ISSN 1871-4021, 2019; 13, Issue 2: 1497-1504. DOI:10.1016/j.dsx.2018.11.062