

Olive oil: maternal and pediatric health

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Abstract

The new base of the pyramid that represents the Mediterranean Diet (MD) includes a balanced lifestyle, healthy cooking methods, traditional, local and eco-friendly products, conviviality, physical activity with an adequate amount of rest, as well as caloric restriction and food frugality. Moreover, it has been confirmed that the main source of MD fat is Extra Virgin Olive Oil (EVOO). EVOO is considered a key feature of the healthy properties of the MD, due to its fatty acid, vitamin and polyphenol composition. However, these components need to be bioavailable to allow EVOO to exert its nutraceutical properties, which include antioxidant, anti-inflammatory, anti-cancer, antimicrobial, antiviral and hypoglycemic properties, as well as protective effects on the heart and brain, and during pregnancy and breast feeding. The main phenolic components responsible for the nutraceutical properties of EVOO are hydroxytyrosol, tyrosol and oleuropein. The adopted oil production and extraction technologies, such as extraction at low oxidative stress, determine the final polyphenol content in virgin olive oil.

Limited information on the epigenetic effects of olive polyphenols is presently available, although the epigenetic effects of many other plant polyphenols have been well documented. In this context, it has been found that, if mothers consume an adequate amount of olive oil during pregnancy, their children will be exposed to a lower risk of wheezing in the first period of their lives.

In addition, EVOO, because of its oleochemical content, a natural anti-inflammatory substance, may have an effect on many inflammatory diseases, even in the early period of life.

Keywords

Extra Virgin Olive Oil, polyphenols, epigenetic effects, oleochemical, pregnancy, childhood.

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Introduction

The new base of the pyramid that represents the Mediterranean diet (MD) includes a balanced lifestyle, healthy cooking methods, traditional, local and eco-friendly products, conviviality, physical activity with an adequate amount of rest, caloric restriction and food frugality. The MD pyramid confirms the importance of a daily food intake of vegetables, cereals, fruit, legumes, as well as nuts and seeds, which are rich in micronutrients; the daily consumption of water and herbal infusions is also considered of fundamental importance [1].

The MD has been indicated as being very important in the prevention of Non Communicable Diseases (NCDs) [2], which are also known as chronic diseases that are not transmissible. According to the World Health Organization (WHO) definition, these include: cardiovascular diseases, cancer, chronic respiratory diseases and diabetes [3].

The main dietary fat in the MD is Extra Virgin Olive Oil (EVOO) [1].

EVOO is considered a key feature of the healthy properties of the MD, due to its fatty acid, vitamin and polyphenol contents. Sureda and colleagues from the Balearic Island University have recently shown, within the PREDIMED study, that an MD supplemented with EVOO, nuts or with a low-fat diet can enhance the plasma antioxidant capabilities and decrease the xanthine oxidase activity in patients suffering from metabolic syndrome [4].

What affects the nutritional characteristics of EVOO

The nutritional and chemical characteristics of EVOO are influenced by many/several different parameters (**Tab. 1**). First, environmental factors (such as altitude, cultivation practices and irrigation) have an effect on the final quality of EVOO. For example, the polyphenol, oleic and stearic acid contents of different Ortime olive cultivars grown in Campania (Italy) were found to be different when grown at 50 m a.s.l. (above sea level) and at 500 m a.s.l. The oil obtained from the

Table 1. Parameters affecting EVOO nutritional and chemical characteristic.

- Cultivar
- Altitude
- Irrigation
- Cultivation practices
- Degree of ripeness
- Oil extraction technologies (malaxation, pressure or centrifugation system, low oxidative stress extraction technology)
- Procedures and timing of the olive conservation
- Procedure for transporting
- Storage condition before use (industry and home)

olives grown at 500 m a.s.l. showed a higher total biofenol and fatty acid content than those grown at 50 m a.s.l. [5]. Irrigation practices may also affect the biophenol oil content. Water deficit has been found to enhance the phytoprostane content in EVOO from the Cornicabra cultivar (Toledo, Spain) [6].

A study on the effect of different irrigation treatments applied to the Chemlali olive tree cultivar (East Coast of Tunisia) showed that different irrigation practices affected some aspects of the olive oil composition, as the palmitic acid, linoleic acid, total phenols and α -tocopherol contents were modified significantly [7]. The polyphenol content of olives is highest during the “veraison” period (the spotted olives, grape berry colouring), and it then decreases until complete ripening [8]. Moreover, different cultivars have different total polyphenol contents (**Tab. 2**), and the chemical characteristics of olive oils are influenced by the harvest time and the malaxation temperature. The oil extracted from Ayvalik and Memecik olives (Turkish monocultivars), by means of an industrial two-phase continuous system, showed higher hydroxytyrosol, tyrosol and pigment concentrations at early harvest than at mid-harvest; moreover, the malaxation temperature affected the hydroxytyrosol, tyrosol, and peroxide values [9]. A positive relationship has been observed in a recent study between the malaxation temperature and the phenolic concentration in olive pastes and in virgin olive oils from four Italian olive cultivars for two different initial atmospheric composition conditions [10]. A study concerning two typical Sardinian cultivars, Bosana and Semidana, showed that an extraction technology, with a low oxygen contact during malaxation, using a plant equipped with a vertical-axis malaxator and with a low oxidative stress impact, allowed oil to be obtained

Table 2. Total polyphenol contents of different olive cultivars.

Cultivars containing phenols > 600 mg/kg oil	Cultivars containing phenols 500-200 mg/kg oil	Cultivars containing phenols < 200 mg/kg oil
Chetoui Picual Coratina Manzanilla Cornicabra Ogliarola Moraiolo	Manzanilla Koroneiki Leccino Hojiblanca Arbequina Frantoiana	Nocellara Tanche Leccino Taggiasca Hojiblanca Arbequina Sevillano

with significantly higher antioxidant activity values, and a higher phenol content [11].

Nutraceutical properties of EVOO

The nutraceutical properties of EVOO include antioxidant, anti-inflammatory, anti-cancer, antimicrobial, antiviral and hypoglycemic properties, and have a protective effect on the heart and brain, as well as during pregnancy and breast feeding [12]. The high oleic acid content of EVOO was once believed to be responsible for the benefits obtained from consuming EVOO. Currently, the known benefits are considered to be due to a combination of several nutrient and non-nutrient phytochemicals. EVOO contains a series of phenolic components that induce important antioxidant activities [13].

The main EVOO phenolic compound classes are flavonoids, lignans, simple phenols and secoiridoids, with the latter two groups predominating. The phenolic compounds present in EVOO are shown in **Tab. 3**. The hydroxytyrosol, tyrosol, oleuropein and ligostride phenolic compounds are those that are mainly responsible for the health benefits, for the antioxidant activity, for the protection from blood lipid oxidation, for the anti-inflammatory activity, the anticarcinogenetic potential, the oxidative stress resistance, and numerous other health benefits [14].

In addition, EVOO contains decarboxymethyl ligostride aglycone (oleochantal), a natural anti-inflammatory substance, which may have an effect on several inflammatory diseases [15], even in the early period of life. Decarboxymethyl ligostride aglycone was first isolated by Montedoro in 1992 [16], and in 2005 was named, by Beauchamp, oleochantal, which stands for, *oleo* for olive, *canth* for sting, and *al* for aldehyde. The oleochantal of EVOO has the same anti-inflammatory charac-

Table 3. Phenolic compounds contained in EVOO.

- Benzoic acids and derivatives: 3-hydroxybenzoic acid, *p*-hydroxybenzoic acid, 3,4-dihydroxybenzoic acid, gentisic acid, vanillic acid, gallic acid, syringic acid
- Cinnamic acids and derivatives: *o*-coumaric acid, *p*-coumaric acid, caffeic acid, ferulic acid, sinapic acid
- Phenyl ethyl alcohols: tyrosol ([*p*-hydroxyphenyl] ethanol), hydroxytyrosol ([3,4-dihydroxyphenyl] ethanol)
- Other phenol acids and derivatives: *p*-hydroxyphenylacetic acid, 3,4-dihydroxyphenylacetic acid, 4-hydroxy-3-methoxyphenylacetic acid, 3-(3,4-dihydroxyphenyl), propanoic acid
- Dialdehydic forms of secoiridoids: decarboxymethyl oleuropein aglycon (oleacin), decarboxymethyl ligostride aglycon (oleocanthal)
- Secoiridoid aglycons: oleuropein aglycon, ligostride aglycon, aldehydic form of oleuropein aglycon, aldehydic form of ligostride aglycon
- Flavonoids: taxifolin, apigenin, luteolin
- Lignans: pinoresinol, (+)-1-acetoxypinoresinol, (+)-1-hydroxypinoresinol
- Other categories like the hydroxyisochromans 1-phenyl-6,7-dihydroxyisochroman, 1-(3-methoxy-4-hydroxy)phenyl-6,7-dihydroxy-isochroman

teristics as ibuprofen (the dose-dependent inhibition of COX-1 and COX-2 activities) [17].

The health benefits of continuous virgin olive oil consumption, as part of the Mediterranean diet, derive from its natural pharmacological qualities and its ability to reduce the diseases that cause inflammation, such as joint-degenerative and neurodegenerative diseases and cancer [12].

Natural plant, fruit and vegetable polyphenols play a role in the prevention and treatment of chronic diseases, as they modulate the effect of epigenetic-related enzymes [18]. This effect has been demonstrated for cancer and in other NCDs.

Despite the limited information on the epigenetic effects of olive polyphenols that is presently available, the similarities between many effects of different plant polyphenols at the molecular level suggest that the well documented epigenetic effects reported for many other plant polyphenols could also be hypothesized for olive polyphenols. However, data on the epigenetic effects of olive polyphenols are still scarce, and further research is needed to increase the information necessary to propose the possible use of these substances as epigenome modulators in humans [19].

How much EVOO?

In order to have an effect on the metabolism, the currently recommended dietary intake of EVOO is

20 g per day, with at least 5 mg of hydroxytyrosol and its derivatives. In order to bear the health claim, consumers should be informed that the beneficial effect is only obtained with a daily intake of 20 g of olive oil [20, 21]. This quantity of oil includes EVOO used both for cooking and to dress vegetables.

Influence of EVOO on maternal, neonatal and pediatric health

A recent study has proved that a healthy diet is capable of influencing the health at different life stages, that is, as a fetus, a newborn and/or during adult life. This research showed that a diet rich in monounsaturated fats (20% of olive oil/EVOO enriched diet) was able to influence the oxidative parameters and ameliorate the neurotrophic factor gene expression in different brain areas of rats at different stages of life, even during the prenatal period. The diet period was also found to be able to influence the body weight of pups in a significant way. When, after weaning, the diet rich in EVOO was changed with the control diet, the body weight of the adults increased. The same increase was not observed when the enriched EVOO diet was maintained over the whole period, thus showing an inverse relationship between the Mediterranean diet and overweight or obesity. This effect is due to the monounsaturated fatty acids present in EVOO, which play a role on body weight regulation [18].

Pase and colleagues showed that an EVOO enriched diet could reduce oxidative damage in the total brain areas of rats at weaning, by decreasing the lipid peroxidation levels and the reactive species production, by eliciting significant free-radical scavenging effects, and by enhancing the antioxidant defense system, which was estimated on the basis of the reduced glutathione levels in the cortex of adult rats [22, 23]. Furthermore, EVOO consumption could increase Brain-Derived Neurotrophic Factor gene expression in the prefrontal cortex of rats [18, 24]. Fibroblast Growth Factors are trophic factors in the central nervous system that have an important influence on neuronal protection, plasticity, development and repair. Fibroblast Growth Factor 2 (FGF-2) mediates synaptogenesis and neurite branching [25]. These are able to induce the proliferation of neuronal progenitor cells in the hippocampus and in the subventricular zones [26]. If there is a reduced expression of FGF-2, it is possible that the vulnerability of a selected

neuronal population will increase (altered mood disorders) [27]. Pase and colleagues [22] showed that the constant consumption of EVOO in pregnancy and breastfeeding may increase FGF-2 mRNA expression. It is therefore possible to infer that nutritional interventions during critical developmental windows produce enduring effects on brain functions as well as an enhanced resilience toward pathologic conditions. These findings open a pioneering line of investigation on dietary adjunctive therapeutic strategies and the potential of healthy dietary habits to prevent neonatal conditions and their influence in adulthood [18].

New technologies to create super healthy oils at a low cost [28, 29], obtained by adding microalgae or polyphenols to improve EVOO stability, are currently being advertised on the Internet. Using this approach, olive oil can achieve the same beneficial effects as standard EVOO in reducing rheumatoid arthritis and anti-inflammatory processes. In animals, the supplementation of refined olive oil with hydroxytyrosol has been shown to significantly decrease paw edema, histological damage, cyclooxygenase-2 and inducible nitric oxide synthase expression, bone resorption and osteophyte formation. The improvement in the inflammatory status improves the articular function, and is therefore beneficial for chronic and acute inflammation [30]. However, the protective effects of MD are due to the nutritional food complex, rather than to individual macronutrients and micronutrients [31], and refined olive oil is not EVOO, even when polyphenols have been added.

A study that compared the effects of fish oil and olive oil supplementation in sows and their piglets, in late pregnancy and during lactation, on oxidative stress and inflammation showed that that oxidative stress indicators and cytokines can be carried over from mothers through the colostrum and milk. The oxidative stress of sows fed with fish oil can be reduced by adding extra antioxidants at a level of 2% during late gestation and 4.8% during lactation. In this study, lower cytokine levels in the colostrum and milk of sows and the plasma of piglets were observed in the olive oil treated group, thus showing that the maternal diet can decrease the plasma pro-inflammatory cytokine levels of piglets due to a lower transfer from the maternal colostrum and milk [32].

A mother-child study, named “Rhea project”, conducted in Heraklion, Crete, prospectively studied a cohort of pregnant women (Greek and immigrants) and their offspring. The study was

the first to prospectively examine, in a general population, the relationship between dietary patterns during pregnancy and post partum depression (symptoms). It showed that women who followed a “healthy” diet (MD) during pregnancy (a diet comprising vegetables, fruit, nuts, pulses, fish and seafood, EVOO and dairy products) had a reduced risk of postpartum depressive symptoms [33]. It has also been found that if mothers have consumed an adequate amount of olive oil as the main source of fat for cooking or salad dressing during pregnancy, their children are exposed to a lower risk of wheezing in the first period of their lives [34].

It is also interesting to note that in this study, when an infant did not suffer from wheezing during the first year of life, the mothers had a significantly higher MD score. When the effect of MD vanished, after removing the potential confounders, only the use of EVOO remained as a protective factor against wheezing during the first year of life. The results could suggest that an increase in olive oil consumption during pregnancy and the first 1,000 days of life might be a primary prevention measure to reduce wheezing early in life [35].

In addition, it has been shown that dietary supplements with n-3 long chain polyunsaturated fatty acids (LCPUFA), which are also present in EVOO, may change the developing immune system of a newborn baby before allergic responses are established, particularly for those with a genetic predisposition to the production of the immunoglobulin E (IgE) antibody [36].

It has been shown that the urinary metabolome can be affected by the MD [37], with variations in the compounds of the metabolism of carbohydrates, creatine, creatinine, amino acids, lipids and the cometabolites of bowel microbes. An appropriate quantity of EVOO can influence the urinary metabolome [38]. It could therefore be interesting to evaluate how the MD, with a suitable quantity of EVOO, can influence the urinary metabolome of nursing mothers and the health of breastfed children.

Conclusion

It has been demonstrated that a high level of adherence to the MD early on in life protects against the development of asthma and atopy in children, and helps prevent wheezing in children. Olive oil is an important pillar of the MD, as it is the main and highest quality source of fat. If taken at

an early age (the first 1,000 days of life) childhood and adolescence, it plays an important role in the prevention of adulthood diseases. Studies recently conducted on model animals have opened new and interesting perspectives on the efficacy of a diet integrated with EVOO for children. For this reason, it is important that olive oil producers should put more effort into increasing the phenolic content of olives, by selecting more suitable cultivars and more suitable degrees of ripeness, as well as by improving oil extraction technologies.

I want to conclude by citing a few verses from the Ode to Olive Oil by Pablo Neruda: “... It’s not only wine that sings/Olive oil sings too/It lives in us with its ripe light/And among the good things of the earth/I set apart/Olive oil,/Your ever-flowing peace, your green essence/Your heaped-up treasure which descends/In streams from the olive tree”.

Declaration of interest

The Authors declare that there is no conflict of interest.

References

1. Willett WC, Sacks F, Trichopoulos A, Drescher G, Ferro-Luzzi A, Helsing E, Trichopoulos D. Mediterranean diet pyramid: a cultural model for healthy eating. *Am J Clin Nutr.* 1995;61(6 Suppl):1402S-1406S.
2. Bloomfield HE, Kane R, Koeller E, Greer N, MacDonald R, Wilt T. Benefits and harms of the mediterranean diet compared to other diets. Washington (DC): Department of Veterans Affairs (US), 2015.
3. <http://www.who.int/mediacentre/factsheets/fs355/en/>, last access: September 2016.
4. Sureda A, Del Mar Bibiloni M, Martorell M, Buil-Cosiales P, Marti A, Pons A, Tur JA, Martinez-Gonzalez MÁ; PREDIMED Study Investigators. Mediterranean diets supplemented with virgin olive oil and nuts enhance plasmatic antioxidant capabilities and decrease xanthine oxidase activity in people with metabolic syndrome: The PREDIMED study. *Mol Nutr Food Res.* 2016;60(12):2654-64.
5. Di Vaio C, Nocerino S, Paduano A, Sacchi R. Influence of some environmental factors on drupe maturation and olive oil composition. *J Sci Food Agric.* 2013;93(5):1134-9.
6. Collado-González J, Pérez-López D, Gil-Izquierdo A. Water deficit during pit hardening enhances phytoprostanes content, a plant biomarker of oxidative stress, in extra virgin olive oil. *J Agric Food Chem.* 2015;15(14):3784-92.
7. Ben Brahim S, Gargouri B, Marrakchi F, Bouaziz M. The effects of different irrigation treatments on olive oil quality and composition: a comparative study between treated and olive mill wastewater. *J Agric Food Chem.* 2016;64(6):1223-30.

8. <http://phenol-explorer.eu/reports/45#olive>, last access: October 2016.
9. Jolayemi O, Tokatli F, Ozen B. Effects of malaxation temperature and harvest time on the chemical characteristics of olive oils. *Food Chem.* 2016;211:776-83.
10. Taticchi A, Esposito S, Veneziani G, Urbani S, Selvaggini R, Servili M. The influence of the malaxation temperature on the activity of polyphenoloxidase and peroxidase and on the phenolic composition of virgin olive oil. *Food Chem.* 2013;136(2):975-83.
11. Del Caro A, Fadda C, Sanguinetti AM, Urgeghe PP, Vacca V, Arca PP, Piga A. Influence of low oxidative stress extraction technology on in vitro antioxidant capacity and quality of two extra virgin monovarietal oils of Sardinia (Italian). *Rivista Italiana Sostanze Grasse.* 2012;89(4):247-52.
12. Cicerale S, Lucas L, Keast R. Biological activities of phenolic compounds present in virgin olive oil. *Intern J Mol Sci.* 2010;11(2):458-79.
13. de la Torre-Carbot K, Jauregui O, Gimeno E, Castellote A, Lamuela-Raventós R, López-Sabater M. Characterization and quantification of phenolic compounds in olive oils by solid-phase extraction, HPLC-DAD, and HPLC-MS/MS. *J Agric Food Chem.* 2005;53(11):4331-40.
14. Kalogeropoulos N, Tsimidou M. Antioxidants in Greek Virgin Olive Oils. *Antioxidants (Basel, Switzerland).* 2014;3(2):387-413.
15. Parkinson L, Keast R. Oleocanthal, a Phenolic Derived from Virgin Olive Oil: A Review of the Beneficial Effects on Inflammatory Disease. *Intern J Mol Sci.* 2014;15(7):12323-34.
16. Montedoro G, Servili M, Baldioli M, Miniati E. Simple and hydrolyzable phenolic compounds in virgin olive oil. 1. Their extraction, separation, and quantitative and semiquantitative evaluation by HPLC. *J Agric Food Chem.* 1992;40:1571-6.
17. Beauchamp G, Keast R, Morel D, Lin J, Pika J, Han Q, Lee CH, Smith AB, Breslin PA. Phytochemistry: ibuprofen-like activity in extra-virgin olive oil. *Nature.* 2005;437(7055):45-6.
18. Ayissi V, Ebrahimi A, Schluesener H. Epigenetic effects of natural polyphenols: a focus on SIRT1-mediated mechanisms. *Mol Nutr Food Res.* 2014;58(1):22-32.
19. Rigacci S, Stefani M. Nutraceutical Properties of Olive Oil Polyphenols. An Itinerary from Cultured Cells through Animal Models to Humans. *Intern J Mol Sci.* 2016;17(6):E843.
20. EFSA, Commission Regulation (EU) 432/2012.
21. <http://www.1life63.com/en/research-recommended-literature-olive-oil-efsa-health-claim-olive-oil-polyphenols/efsa-regulation-health-claim-for-olive-oil-polyphenols>, last access: October 2016.
22. Pase CS, Teixeira AM, Roversi K, Dias VT, Calabrese F, Molteni R, Franchi S, Panerai AE, Riva MA, Burger ME. Olive oil-enriched diet reduces brain oxidative damages and ameliorates neurotrophic factor gene expression in different life stages of rats. *J Nutr Biochem.* 2015;26(11):1200-7.
23. Jacomelli M, Pitozzi V, Zaid M, Larrosa M, Tonini G, Martini A, Urbani S, Taticchi A, Servili M, Dolaro P, Giovannelli L. Dietary extra-virgin olive oil rich in phenolic antioxidants and the aging process: long-term effects in the rat. *J Nutr Biochem.* 2010;21(4):290-6.
24. Zrelli H, Matsuoka M, Kitazaki S, Araki M, Kusunoki M, Zarrouk M, Miyazaki H. Hydroxytyrosol induces proliferation and cytoprotection against oxidative injury in vascular endothelial cells: role of Nrf2 activation and HO-1 induction. *J Agric Food Chem.* 2011;59(9):4473-82.
25. Reuss B, von Bohlen und Halbach O. Fibroblast growth factors and their receptors in the central nervous system. *Cell Tissue Res.* 2003;313(2):139-57.
26. Vaccarino F, Ganat Y, Zhang Y, Zheng W. Stem cells in neurodevelopment and plasticity. *Neuropsychopharmacology.* 2011;25(6):805-15.
27. Riva M, Molteni R, Bedogni F, Racagni G, Fumagalli F. Emerging role of the FGF system in psychiatric disorders. *Trends Pharmacol Sci.* 2005;26(5):228-31.
28. Limón P, Malheiro R, Casal S, Ación-Fernández FG, Fernández-Sevilla JM, Rodrigues N, Cruz R, Bermejo R, Pereira JA. Improvement of stability and carotenoids fraction of virgin olive oils by addition of microalgae *Scenedesmus almeriensis* extracts. *Food Chem.* 2015;175:203-11.
29. <http://www.teatronaturale.it/strettamente-tecnico/l-arca-olearia/23230-se-i-polifenoli-fanno-bene-alla-salute-basta-aggiungerli-all-olio-d-oliva.htm>. last access: October 2016.
30. Silva S, Sepodes B, Rocha J, Direito R, Fernandes A, Brites D, Freitas M, Fernandes E, Bronze MR, Figueira ME. Protective effects of hydroxytyrosol-supplemented refined olive oil in animal models of acute inflammation and rheumatoid arthritis. *J Nutr Biochem.* 2015;26(4):360-8.
31. Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, Gómez-Gracia E, Ruiz-Gutiérrez V, Fiol M, Lapetra J, Lamuela-Raventós RM, Serra-Majem L, Pintó X, Basora J, Muñoz MA, Sorlí JV, Martínez JA, Martínez-González MA; PREDIMED Study Investigators. Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med.* 2013;368(14):1279-90.
32. Shen Y, Wan H, Zhu J, Fang Z, Che L, Xu S, Lin Y, Li J, Wu D. Fish Oil and Olive Oil Supplementation in Late Pregnancy and Lactation Differentially Affect Oxidative Stress and Inflammation in Sows and Piglets. *Lipids.* 2015;50(7):647-58.
33. Chatzi L, Melaki V, Sarri K, Apostolaki I, Roumeliotaki T, Georgiou V, Vassilaki M, Koutis A, Bitsios P, Kogevas M. Dietary patterns during pregnancy and the risk of postpartum depression: the mother-child 'Rhea' cohort in Crete, Greece. *Public Health Nutr.* 2011;14(9):1663-70.
34. Castro-Rodriguez J, Garcia-Marcos L, Sanchez-Solis M, Pérez-Fernández V, Martínez-Torres A, Mallol J. Olive oil during pregnancy is associated with reduced wheezing during the first year of life of the offspring. *Pediatr Pulmonol.* 2010;45(4):395-402.
35. Chatzi L, Kogevas M. Prenatal and childhood Mediterranean diet and the development of asthma and allergies in children. *Public Health Nutr.* 2009;12:1629-34.
36. Chatzi L, Torrent M, Romieu I, Garcia-Esteban R, Ferrer C, Vioque J, Kogevas M, Sunyer J. Mediterranean diet in

pregnancy is protective for wheeze and atopy in childhood. *Thorax*. 2008;63:507-13.

37. Vázquez-Fresno R, Llorach R, Urpi-Sarda M, Lupianez-Barbero A, Estruch R, Corella D, Fitó M, Arós F, Ruiz-Canela M, Salas-Salvadó J, Andres-Lacueva C. Metabolomic pattern analysis after Mediterranean diet intervention in a nondiabetic

population: a 1- and 3-year follow-up in the PREDIMED study. *J Proteome Res*. 2015;14(1):531-40.

38. Silva S, Combet E, Figueira M, Koeck T, Mullen W, Bronze M. New perspectives on bioactivity of olive oil: evidence from animal models, human interventions and the use of urinary proteomic biomarkers. *Proc Nutr Soc*. 2015;74(3):268-81.