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Hazelnuts as Source of Bioactive Compounds and Health Value Underestimated Food

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Abstract

Hazelnut (HN) has found its way into nontraditional foods due to the recognition of its nutritional and nutraceutical properties. Among nut species, hazelnut plays a major role in human nutrition and health because of its special composition of fat (mainly oleic acid), dietary fibre, vitamins (vitamin E), minerals, phytosterols (mainly β-sitosterol), and antioxidant phenolics.

In particular, lipids represent 60% of its dry weight and are mainly represented by triacylglycerols where the main fatty acids are oleic and linoleic acids. Furthermore, HN oil is an exceptional source of specific bioactive compounds as tocopherols, mainly α-tocopherol. Besides a favourable fatty acid profile and high tocopherols content, HNs are also a source of minerals and phytosterols, where potassium and β-sitosterol are the major ones. In addition, the presence of several phenolic antioxidants such as mono- and oligomeric flavan 3-ols has been reported.

HNs represent a very interesting food, and their nutritional and health value need to be further evidenced in intervention trials. In addition, the use of HN by-products as new functional ingredient represents an important challenge for the sector and the food industry.

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Introduction

Corylus avellana L., the European HN, is the second most popular nut worldwide just after almonds and production ranges from North Africa and Europe to the Asia Minor and Caucasus region. Countries around the Black Sea account for the majority of production in the world: Turkey (610,264 tons, average for the period 2009–2011), Azerbaijan

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(28,564 tons), and Georgia (20,567 tons). Other important producers are Italy (114,991 tons), the USA (35,079 tons), and Spain (16,988 tons).[1]

In Turkey, the principal HN producer providing around 72% of the HN production in the world, the major HN cultivar is Tombul, followed by Çakıldak, Mincane and İncekara, which are located mainly in the provinces of Ordu and Giresun.[2] Italy, the world's second largest producer, possess numerous traditional cultivars, which are mostly growth in the regions Campania, Latium and Piedmont. Recently, some of the major cultivars (Tonda Romana from Latium, Tonda di Giffoni from Campania and Tonda delle Langhe from Piedmont) obtained the European Community quality stamp for their traditional peculiarity.[3] Today exists a variety of almost 400 HN cultivars, but only about 20 of them represents the basis of world production. Nut chemical, physical and morphological characteristics are highly dependent on interactions with the environment and genotype, postharvest management and cultural techniques.[4]

Thanks to their sensory properties, HNs are consumed not only as a ripe or "green" fruit but also in a variety of manufactured food such as chocolate spread, cereal bar, cookie, nougat, pastry, ice cream and cooking oil production. HNs are consumed roasted or raw, chopped, intact, or processed into a praline paste; they are typically processed integrally into food products, although HN oil is also frequently used for cooking.[5,6]

Among nuts, HN plays a key role in human nutrition and health because of its special content of macronutrients (lipids and fibre), micronutrients (minerals and vitamins), fat-soluble bioactives (tocols, phytosterols, phytostanols and squalene) and phytochemicals (flavonoids and phenolic and hydroxycinnamic acids).[7-9] A list of each class of nutrients and their quantity is reported in table 1.

Lipids and Fatty Acids

The main nutrient of the HN kernel is the lipid portion, which has the biggest impact on kernel flavour, especially after roasting. For many years the edible vegetable oils composition has been evaluated with the objective to obtain knowledge to improve product quality in terms of flavour, taste, nutrition, storage stability and guaranteeing the legitimacy of the material.[10]

Lipids may constitute more than 60% of the HN kernel dry weight and are constituted of 98.8% triacylglycerols (TAG) and 1.2% polar lipids (PL). Within PL, phosphatidylcholine, phosphatidylethanolamine and phosphatidylinositol are present at 56.4%, 30.8% and 11.7%, respectively.[11] Among fatty acids, oleic acid (C18:1n9) is by far the most predominant ranging from 76.7% to 82.8%, followed by linoleic (C18:2n6), palmitic (C16:0), stearic (C18:0) and vaccenic (C18:1n7) acids with mean values of 9.2%, 5.6%, 2.7% and 1.4%, respectively.[12] This is very similar in composition to fatty acids of olive oil and generally recommended for a healthy diet.[13] Moreover, due to the high level of mono-unsaturated fatty acids (MUFA) and tocopherols/tocotrienols content, HN oils have an oxidative stability similar to the value of olive oil, and higher compared to rapeseed oil.[14] As consequence, it is present only a minor increase of the possibly harmful trans fatty acids during the thermal treatment of nuts (roasting) and, although some minor changes occurred in the TAG and fatty acid compositions, the corresponding profiles basically remained identical to that of raw HNs.[12]

Moreover, various studies reported as lipids content increased continuously during the development of the kernel, from 6.38 g/100g dry matter to 68 g/100g dry matter.[13,14] Regarding fatty acids, from early to harvest stage a reducing and an increasing trend in the amount of polyunsaturated fatty acids (from 31 to 10.3 g/100g of oil) and MUFA (from 22 g/100g oil to 79.2 g/100g oil) was detected, respectively. No significant changes were observed in total saturated fatty acids at different maturation stage.[14,15]

From the nutritional viewpoint, various studies have confirmed that a diet with a low amount of saturated fatty acids and high content of MUFA can effectively reduce the risk of coronary heart disease amending blood lipid levels and blood pressure ameliorating metabolic syndrome and insulin sensitivity.[18-21]

Dietary Fibre

In the simple terms, dietary fibre can be considered as a 'roughage' material of carbohydrates (beta-glucans,

lignin, cellulose, pectin and hemicellulose) resistant to small intestine digestion, requiring microbiota fermentation situated in the large intestine.[22,23] Types of dietary fibre may be categorized according to their sources, solubility, fermentability, physiological effects, and they can be obtained from cereals, legumes, fruit and vegetables.[24-25]

After cereals, nuts are the vegetables most reach in fibre. Among tree nuts, the highest content in dietary fibre were measured in almonds (9.2%), followed by HNs (8.7%), walnuts (6.8%), macadamia nuts (5.5%) and pistachios (4.2%).[26] Moreover, Silva *et al.*[27] compared the fibre in six cultivars of HNs harvested in Portugal. The fibre content, expressed as g/100g, ranged from 12.07 to 8.05 for Butler and Merveille de Bollwille varieties respectively, indicating consistent variations of dietary fibre among HN cultivars.

Today, recent and persuasive evidences confirmed that high dietary fibre intake promotes overall health and associates with lower mortality through preventing and mitigating of cardiovascular disease, colon cancer and type 2 diabetes mellitus,[28] suggesting an adequate intake for the Italian adult in the amount of 25 g/day.[29] Although the mechanisms that underline the described effects of dietary fibre on health are not well-known, it is supposed to be a consequence of changes in nutrient absorption, production of short chain fatty acids, gut hormones secretion and intestinal viscosity.[30-32]

Minerals

Minerals are normally divided into macro-minerals and micro-minerals. Major minerals include Ca, Mg, K, Na, Cl, P and S; while trace minerals are I, Zn, Se, Fe, Mn, Cu, Co, Mo, F, Cr and B. Different plant and animal sources can be consumed to obtain a number of essential minerals for a healthy nutrition.[33]

In HN, at least a total of 24 minerals have been stated so far with an extremely high variability depending on genotypes, geographical origin, year of harvesting, climate, soil composition, irrigation, use of fertilizer and method of cultivation.[34,35] Generally, K is the most present mineral with a concentration ranging from 147 mg/100g to 761 mg/100g, followed by P (from 256 mg/100g to 458 mg/100g), Ca (from 65 mg/100g to 328 mg/100g) and Mg (from 34 mg/100g to 335 mg/100g). HNs serve also as an excellent source of trace minerals as Cu (from 0.94 mg/100g to 3.47 mg/100g), Mn (from 1.4 mg/100g to 19 mg/100g), and Se (from 5.5 µg/100g to 60 µg/100g).[35-40] With regard to the trace minerals, a standard portion of HN (30g) supplies, as percentage of the Population Reference Intake (PRI) or Adequate Intake (AI) for Italian adult males (aged 30-59 years), 31-116% of Cu, 16-211% of Mn, and 3-33% of Se.[29]

Even though each essential mineral has its own health benefits, Se in particular is an essential trace mineral of central importance to human health. As part of L-selenocysteine, selenium is needed for the

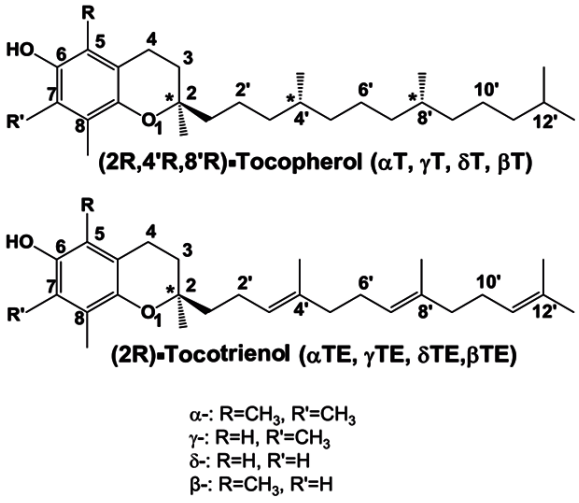

Fig. 1: Natural forms of vitamin E.[44]

synthesis of selenoproteins, a class of proteins with important functions including skeletal and cardiac muscle function, T-cell immunity, thyroid hormone metabolism and antioxidant defense.[41]

Tocols

Tocopherols and tocotrienols are monophenols having the identical main chemical structure constituted by a long chain attached at 2-position of a chromane ring. Tocotrienols diverge from tocopherols because they have a farnesyl rather than a saturated isoprenoid C16 side chain[42] and exist as four homologues (α, β, γ, δ) which differ from each other by the number and location of methyl groups in their chemical structures.[43]

Various nuts have been reported to show significant tocopherols and tocotrienols differences, ranging from approximately 1.6 mg/100g of kernel for macadamia to 32 mg/100g of kernel for black walnut. Among them, α- and γ-tocopherol are the most represented isoforms.[45] HN oil is an exceptional source of vitamin E, where α-tocopherol being the dominant form with a content up to 41.9 mg/100g extracted oil,[8,34] corresponding at 96% of total tocols.[46] Differences in vitamin E content in HN oil depend on the variety and geographical origin, where the Tombul variety grown in Turkey seems to have the highest tocols content.[41] Moreover, roasting and removal of the pellicle (peeling) have shown to reduce considerably tocopherol content.[46]

The high α-tocopherol content represents a peculiar characteristic, since of the eight naturally occurring forms, α-tocopherol is the most active homologues retained in human plasma with the highest antioxidant activity.[47] In addition to its activity as an antioxidant in the prevention of potentially harmful phospholipid oxidation events at plasma membrane,[48] vitamin E is also involved in various metabolic processes such as regulation of gene expression, cell signalling and immune function.[49] Moreover, vitamin E forms suppress pro-inflammatory signalling such as STAT3/6 and NF-κB and inhibit eicosanoids catalysed by cyclooxygenase- and 5-lipoxygenase.[44] Consistent with mechanistic findings, assumption of vitamin E contributes to the prevention of various diseases as cardiovascular, neurodegenerative, non-alcoholic fatty liver diseases and some kind of cancer.[50]

Phytosterols and Phytostanols

HNs are also rich in plant sterols (phytosterols and phytostanols). Phytosterols are comparable in structure to cholesterol, possessing the same basic cyclopentanoperhydrophenanthrene ring structure but differentiating in the side chain at C24 and/or the position and configuration of unsaturated double bonds and the optical rotation at chiral carbons.[51,52] Phytostanols are produced by hydrogenating phytosterols.

Sterols include a major percentage of the unsaponifiable matter of most vegetable oils and they exist as free sterols and sterol esters of fatty acids.

In HN, the total phytosterols content ranges from 133.8 mg/100g to 263 mg/100g of oil. Among them,

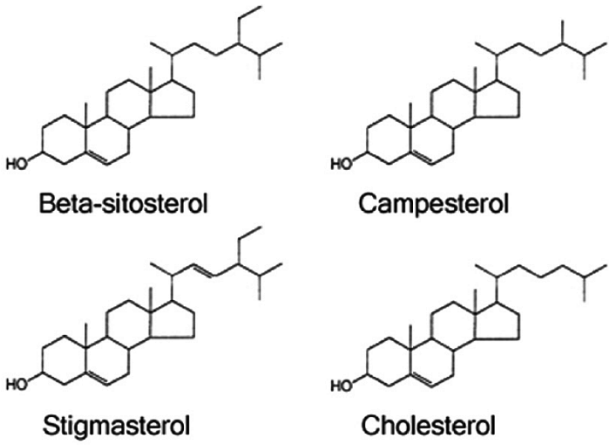

Fig. 2: Structures of common dietary phytosterols and cholesterol.[53]

β-sitosterol is the major one with a mean percentage of 83.6%, while Δ^5-avenasterol and campesterol are the second and the third components of the group with mean values of 6.1% and 5.8%, respectively.[12] Other minor phytosterol/phytostanol found in HN are sitostanol, stigmasterol, cholestenol, campestanol, Δ^7-campesterol, $\Delta^{5,23}$-stigmastadienol, $\Delta^{5,24}$-stigmastadienol, clerosterol, Δ^7-stigmastenol, and Δ^7-avenasterol.[10] The HN oil sterol composition is influenced by agronomic and environmental conditions, crop season, cultivar as well as storage conditions and oil extraction methods.[2] In particular, the percentage of sterol esters ranged from 11% to 75%, mainly depending on the refined process and geographical origin. It is remarkable that sterol esters of Turkish HN oils (either crude or refined) included more than 40%, while they were less than 35% in HN oils from Franch, Italy and Spain, the lowest values being for roasted crude HN oils (11–16%).[16]

Phytosterols are well-known for their ability of reducing blood cholesterol. In fact, many studies have demonstrated that phytosterols induce clinically significant reductions in low-density lipoprotein cholesterol (LDL-C) levels.[54] In particular, daily dose of 1.5 g - 3 g of phytosterols, phytostanols and their esters have been suggested for lowering total cholesterol (TC) and LDL-C concentration significantly.[34] One of the most suggested mechanisms of action of phytosterols in lowering plasma cholesterol concentration is their capacity to reduce cholesterol absorption at intestinal level. In fact, phytosterols are structurally similar to cholesterol and are assimilated into micelles in the intestinal tract. Since plant sterols are more hydrophobic than cholesterol, they possess a higher inclination for micelles than they have for cholesterol. Consequently, they displace cholesterol from mixed micelles and determine a reduction in the duodenal cholesterol absorption and a higher fecal excretion of cholesterol.[55] Furthermore, *in vitro* and *in vivo* studies suggest that phytosterols content in diet promotes a decrease in various cancers including colon, breast and prostate cancer by slowing cell cycle progression, inducing apoptosis, and inhibiting tumor metastasis.[53,56-58]

Squalene

Squalene is a highly unsaturated all-trans linear terpenoid hydrocarbon which comports as the biochemical precursor of terpenoids and sterols with their central role in human, animal and plant functions.[59,60]

It is extensively present in nature, and considerable quantities are found in oil from shark and whale liver, wheat-germ, palm, rice bran, olive and amaranth.[61]

Among nuts, squalene content was higher in HN > macadamia > peanuts > almonds > walnut,[62] with a value in HN ranging from 93 mg/kg to 885 mg/kg oil, depending by cultivar, environmental conditions, geographical origin, fruit development and the method of squalene extraction.[2,63-65] In particular for the latter, squalene contents appeared higher in HN oil extracted with solvent compared to cold pressed one, probably due to higher squalene solubility in hexane.[2]

From a nutritional perspective, squalene has important beneficial effects on health, mainly related to its hypolipidemic, anticancer, antioxidant and detoxifying activity.[66] Enriched squalene diet significantly increased paraoxonase 1and high-density lipoprotein cholesterol (HDL-C) and reduced oxidative damage in animals.[67]

In parallel to its plasma lipids lowering effect, experimental studies have revealed that squalene may efficiently prevent chemically-induced skin, lung

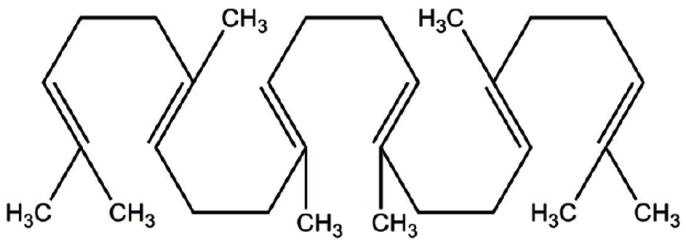

Fig. 3: Structure of squalene in coiled form.[60]

and colon tumorigenesis in rats. The mechanisms implicated for the chemopreventive action of squalene can comprise modulation of carcinogen activation, anti-oxidative activities and inhibition of Ras farnesylation.[68,69] Furthermore, various *in vivo* and *in vitro* studies suggested that squalene possesses an antioxidant activity, principally acting as radical scavenger, and may protect different biological molecules as DNA, lipids and protein against oxidative stress.[70-74]

Phenols

The health effects of diets rich in fruits and vegetables are due not only to minerals, vitamins and fibre but also to a variety of plant secondary metabolites referred collectively as polyphenols,[75] to which many biological effects have been attributed.[76-78] The preponderance of polyphenols in plants exist as glycosides with diverse sugar units at different positions of the polyphenol skeletons and have been categorized by their biological function, source of origin and chemical structure.[79-80] According to the chemical structures of aglycones, polyphenols may be classified in flavonoids, stilbenes, lignans, flavonoids, hydrobenzoic and hydroxycinnamic acids.[81]

The presence of several phenolic and hydroxycinnamic acids (sinapic acid, gallic acid, p-coumaric acid, caffeic acid, vanillic acid, protocatechuic acid, ferulic acid,), and flavonoids (catechin, quercetin, myricetin, kaempferol) have been reported in HNs. In particular, the main polyphenolic subclass comprises of mono- and oligomeric flavan 3-ols, which accounts between 34.2 and 58.3% in HN kernels, with a total phenolic content ranging from 491.2 to 1700.4 mg of gallic acids equivalent/kg.[82]

Moreover, roasting increase the phenolic content in a time and temperature dependent manner compared to raw HNs.[83] Numerous epidemiological and nutritional evidences suggest that natural polyphenols play a key role in prevention of cancer,[84] and in particular Li & Parry have shown that extract of HN roasted skin cultivated in Oregon significantly reduce the proliferation of a human colon cancer cell line.[85]

Table 1. HS Nutrient Composition

Total lipids	> 60% d.w.
Oleic acid	76.7% - 82.8%
Linoleic acid	9.2%
Palmitic acid	5.6%
Stearic acid	2.7%
Vaccenic acid	1.4%
Fibre	8.05 g/100g - 12.07 g/100g
K	147 mg/100 – 761 mg/100mg
P	256 mg/100g – 458 mg/100g
Ca	65 mg/100g – 328 mg/100g
Mg	34 mg/100g – 335 mg/100g
Cu	0.94 mg/100g – 3.47 mg/100g
Mn	1.4 mg/100g – 19 mg/100g
Se	5.5 µg/100 – 60 µg/100
Tocols	41.9 mg/100g extracted oil
Total phytosterols	133.8 mg/100g – 263 mg/100g
Total sterol esters	11% - 75%
β-Sitosterol	83.6%
Δ5-Avenasterol	6.1%
Campesterol	5.8%
Squalene	93 mg/kg oil – 885 mg/kg oil
Total polyphenols	0.491 g/kg oil – 1.7 g of gallic acid equivalent/kg
Flavan 3-ols	34.2% - 58.3%

Health Effects of HNs Consumption

Even though a significant number of clinical studies on various tree nuts have been realized, only few studies specifically related to HN have been conducted. In a recent systematic review and bayesian meta-analysis, Perna *et al.* evidenced that HN-enriched diet is associated with a decrease of LDL-C and TC equal to -0.150 mmol/L and -0.127 mmol/L, respectively, in favour of a HN-enriched diet.[86] More recently, this trend was also confirmed by Deon *et al.*, who reported in adolescents with primary hyperlipidemia a significant effect on serum LDL-C, HDL-C/LDL-C ratio and non-HDL-C.[87] Similar results in the reduction of serum LDL-C were also observed by Santi et al. in healthy volunteers.[88] At the same time, HN consumption was able to decrease LDL oxidation (-15.7%) in normolipidemic healthy volunteers[89] and plasma inflammatory markers such as high-sensitivity C-reactive protein (-35.9%), soluble vascular cell adhesion molecule-1 (-10.6%) and soluble intercellular adhesion molecule-1 (-8.08%) in hypercholesterolemic subjects, compared to a control diet.[90]

Future Directions

At present, considering the world production of HNs, another relevant challenge for the sector could be to turn food processing by-products and wastes into new ingredients. In fact, during processing of HN, by-products arise as waste materials. Among them, none has any commercial value except the HN hard shell, which is currently used as a heating source upon burning. HN wastes could represent functional ingredients to take advantage of to improve nutritional and health value of foods. To do it, comprehensive studies of their chemical composition, physical structure, sensorial properties and nutritional characteristics are necessary.

Conclusion

The expansion of studies and investigations intended to exam the effectiveness of functional nutrients and food components has illuminated many parts of the multifaceted connection between nutrition and health. Despite, we have to take in mind that our diet is based on foods and not on individual compounds. Consequently, it is fundamental to demonstrate that certain nutrients have a positive effect in the prevention of a disease, and to recognize which foods possess them at relevant concentration.[91] Moreover, foods are complex matrices in which those components could have synergistic effects, and bioaccessibility may be influenced by both gastrointestinal conditions and chemical characteristics of the food matrix.[92-97]

HN is an example of synergism among nutrients that can be transformed into a large variety of products consumed by a wide range of population every day. Studies reported in this review underscore the health-promoting effects of HN nutrients and consumption. At present, more scientific confirmations are needed to regard HNs as functional food, but results are auspicious and there are various elements of great attention that push the researchers to expand the scientific acquaintance about nuts in general and HNs in particular.

Conflict of Interest

The Author reports no potential conflict of interest.

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References

1. Boccacci P., Aramini M., Valentini N., Bacchetta L., Rovira M., Drogoudi P., Silva A.P., Solar A., Calizzano F., Erdoğan V., Cristofori V., Ciarmiello L.F., Contessa C., Ferreira J.J. Marra F.P., Botta R. Molecular and morphological diversity of on-farm HN (*Corylus avellana* L.) landraces from southern Europe and their role in the origin and diffusion of cultivated germplasm. *Tree Genet Genomes*. 2013; 9:1465-1480.
2. Gumus C.E., Yorulmaz A.; Tekin A. Differentiation of Mechanically and Chemically Extracted HN Oils Based on their Sterol and Wax Profiles. *J Am Oil Chem Soc*. 2016 93:1625-1635.
3. Bacchetta L., Aramini M., Bernardini C., Rugini

E. In Vitro Propagation of Traditional Italian HN Cultivars as a Tool for the Valorization and Conservation of Local Genetic Resources. *HortScience*. 2008; 43(2):562-566.

4. Cristofori V., Ferramondo S., Bertazza G., Bignami C. Nut and kernel traits and chemical composition of HN (*Corylus avellana* L.) cultivars. *J Sci Food Agric*. 2008;88:1091-1098.
5. Platteau C., De Loose M., De Meulenaer B., Taverniers I. Quantitative detection of HN (*Corylus avellana*) in cookies: ELISA versus real-time PCR. *J Agric Food Chem*. 2011;59(21):11395-11402.
6. Moscetti R., Frangipane M.T., Monarca D., Cecchini M., Massantini R. Maintaining the quality of unripe, fresh hazelnuts through storage under modified atmospheres. *Postharvest Biol Technol.* 2012;65:33-38.
7. Oliveira I., Sousa A., Morais J.S., Ferreira I.C., Bento A., Estevinho L., Pereira J.A. Chemical composition, and antioxidant and antimicrobial activities of three HN (*Corylus avellana* L.) cultivars. *Food Chem Toxicol*. 2008;46(5):1801-1807.
8. Alasalvar C., Bolling B.W. Review of nut phytochemicals, fat-soluble bioactives, antioxidant components and health effects. *Br J Nutr*. 2015;113 Suppl 2:S68-78.
9. Glei M., Fischer S., Lamberty J., Ludwig D., Lorkowski S., Schlörmann W. Chemopreventive Potential of In Vitro Fermented Raw and Roasted HNs in LT97 Colon Adenoma Cells. *Anticancer Res.* 2018;38(1):83-93.
10. Crews C., Hough P., Godward J., Brereton P., Lees M., Guiet S., Winkelmann W. Study of the main constituents of some authentic HN oils. *J Agric Food Chem*. 2005;53(12):4843-4852.
11. Miraliakbari H., Shahidi F. Oxidative stability of tree nut oils. *J Agric Food Chem.* 2008;56 (12):4751-4759.
12. Amaral J.S., Casal S., Citová I., Santos A., Seabra R.M., Oliveira B.P.P. Characterization of several HN (Corylus avellana L.) cultivars based in chemical, fatty acid and sterol composition. *Eur Food Res Technol.* 2006;222:274-280.
13. Cristofori V., Bertazza G., Bignami C. Changes in kernel chemical composition during nut development of three Italian hazelnut cultivars. Fruits. 2015;70:(5):311-322.
14. Ciemniewska-Zytkiewicz H., Pasini F., Verardo V., Bryś J., Koczoń P., Caboni M.F. Changes of the lipid fraction during fruit development in hazelnuts (*Corylus avellana* L.) grown in Poland. *Eur. J. Lipid Sci. Technol.* 2015:117;710–717.
15. Seyhan F., Ozay G., SaklarS., Ertaş E., Satır G., Alasalvar C. Chemical changes of three native Turkish hazelnut varieties (*Corylus avellana* L.) during fruit development. *Food Chem*. 2007;105:590-596.
16. Benitez-Sánchez P.L., León-Camacho M., Aparicio R. A comprehensive study of HN oil composition with comparisons to other vegetable oils, particularly olive oil. *Eur Food Res Technol*. 2003;218:13–19.
17. Ciemniewska-Żytkiewicz H., Verardo V., Pasini F., Bryś J., Koczoń P., Caboni M.F. Determination of lipid and phenolic fraction in two HN (*Corylus avellana* L.) cultivars grown in Poland. *Food Chem.* 2015;168:615-622.
18. Bos M.B., de Vries J.H., Feskens E.J., van Dijk S.J., Hoelen D.W., Siebelink E., Heijligenberg R., de Groot L.C. Effect of a high monounsaturated fatty acids diet and a Mediterranean diet on serum lipids and insulin sensitivity in adults with mild abdominal obesity. *Nutr Metab Cardiovasc Dis.* 2010;20(8):591-598.
19. Gillingham L.G., Harris-Janz S., Jones P.J. Dietary monounsaturated fatty acids are protective against metabolic syndrome and cardiovascular disease risk factors. Lipids. 2011;46(3):209-228.
20. Finucane O.M., Lyons C.L., Murphy A.M., Reynolds C.M., Klinger R., Healy N.P., Cooke A.A., Coll R.C., McAllan L., Nilaweera K.N., O'Reilly M.E., Tierney A.C., Morine M.J., Alcala-Diaz J.F., Lopez-Miranda J., O'Connor D.P., O'Neill L.A., McGillicuddy F.C., Roche H.M. Monounsaturated fatty acid-enriched high-fat diets impede adipose NLRP3 inflammasome-mediated IL-1β secretion and insulin resistance despite obesity. *Diabetes*. 2015;64(6):2116-2128.
21. Shatwan I.M., Weech M., Jackson K.G., Lovegrove J.A., Vimaleswaran K.S. Apolipoprotein E gene polymorphism modifies

fasting total cholesterol concentrations in response to replacement of dietary saturated with monounsaturated fatty acids in adults at moderate cardiovascular disease risk. *Lipids Health Dis*. 2017;16(1):222.

22. Lattimer J.M., Haub M.D. Effects of Dietary Fiber and Its Components on Metabolic Health. *Nutrients*. 2010;2(12):1266-1289.
23. Stephen A.M., Champ M.M., Cloran S.J., Fleith M., van Lieshout L., Mejborn H., Burley V.J. Dietary fibre in Europe: current state of knowledge on definitions, sources, recommendations, intakes and relationships to health. *Nutr Res Rev.* 2017;30(2):149-190.
24. Mudgil D., Barak S. Composition, properties and health benefits of indigestible carbohydrate polymers as dietary fiber: a review. *Int J Biol Macromol*. 2013;61:1-6.
25. Dreher M.L. Whole Fruits and Fruit Fiber Emerging Health Effects. *Nutrients*. 2018;10(12):E1833.
26. Schlörmann W., Birringer M., Böhm V., Löber K., Jahreis G., Lorkowski S., Müller A.K., Schöne F., Glei M. Influence of roasting conditions on health-related compounds in different nuts. *Food Chem*. 2015;180:77-85.
27. Silva, A.P., Santos A., Cavalheiro J., Ribeiro C., Santos F., Gonçalves B. Fruit chemical composition of HN cultivars grown in Portugal. *Journal of Applied Horticulture*, 2007;9(2):157-161.
28. Liu L., Wang S, Liu J. Fiber consumption and all-cause, cardiovascular, and cancer mortalities: a systematic review and meta-analysis of cohort studies. *Mol Nutr Food Res*. 2015;59(1):139-46.
29. Società Italiana di Nutrizione Umana, SINU. Livelli di Assunzione di Riferimento di Nutrienti ed energia per la popolazione italiana, IV revision. Milan: SICS Editore, 2014.
30. Grundy M.M., Edwards C.H., Mackie A.R., Gidley M.J., Butterworth P.J., Ellis P.R. Re-evaluation of the mechanisms of dietary fibre and implications for macronutrient bioaccessibility, digestion and postprandial metabolism. *Br J Nutr*. 2016;116(5):816-833.
31. Koh A., De Vadder F., Kovatcheva-Datchary P., Bäckhed F. From Dietary Fiber to Host Physiology: Short-Chain Fatty Acids as Key Bacterial Metabolites. Cell. 2016;165(6):1332-1345.
32. Nilsson A.C., Johansson-Boll E.V., Björck I.M. Increased gut hormones and insulin sensitivity index following a 3-d intervention with a barley kernel-based product: a randomised cross-over study in healthy middle-aged subjects. *Br J Nutr*. 2015;114(6):899-907.
33. Gharibzahedi S.M.T., Jafari S.M. The importance of minerals in human nutrition: Bioavailability, food fortification, processing effects and nanoencapsulation. *Trends Food Sci Technol*. 2017;62:119-132.
34. Alasalvar C., Shahidi F., Amaral J.S., Oliveira B.P.P. Compositional Characteristics and Health Effects of HN (Corylus avellana L.): An Overview. In: Alasalvar C., Shahidi F. Tree Nuts. Composition, Phytochemicals, and Health Effects. Boca Raton, FL, USA: CRC Press; 2009:340.
35. Alasalvar C., Amaral J.S., Satir G., Shahidi F. Lipid characteristics and essential minerals of native Turkish HN varieties (*Corylus avellana* L.). *Food Chem*. 2009;113(4):919-925.
36. Alasalvar C., Shahidi F., Liyanapathirana C.M., Ohshima T. Turkish Tombul HN (Corylus avellana L.). 1. Compositional characteristics. *J Agric Food Chem*. 2003;51(13):3790-3796.
37. Ozdemir F., Akinci I. Physical and nutritional properties of four major commercial Turkish HN varieties. *J Food Eng*. 2004;63(3):341-347.
38. Cosmulescu S., Botu M., Trandafir I. The mineral source for human nutrition of nuts in different HN (*corylus avellana* L.) cultivars. *Not Bot Horti Agrobo*. 2013;41(1):250-254.
39. Özdemir M., Açkurt F., Kaplan M., Yildiz M., Löker M., Gürcan T., Biringen G., Okay A., Seyhan F.G. Evaluation of new Turkish hybrid HN (Corylus avellana L.) varieties: Fatty acid composition, α-tocopherol content, mineral composition and stability. *Food Chem.* 2001;73(4):411-415.
40. Köksal A.I., Artik N., Şimşek A., Güneş N. Nutrient composition of HN (*Corylus avellana* L.) varieties cultivated in Turkey. *Food Chem*. 2006;99:509-515.
41. Di Nunzio M., Bordoni A., Aureli F., Cubadda F., Gianotti A. Sourdough Fermentation Favorably Influences Selenium Biotransformation and

the Biological Effects of Flatbread. *Nutrients*. 2018;10(12):E1898.
42. Colombo M.L. An update on vitamin E, tocopherol and tocotrienol-perspectives. *Molecules*. 2010;15(4):2103-2113.
43. Azzi A. Many tocopherols, one vitamin E. *Mol Aspects Med*. 2018;61:92-103.
44. Jiang Q. Natural forms of vitamin E: metabolism, antioxidant, and anti-inflammatory activities and their role in disease prevention and therapy. *Free Radic Biol Med*. 2014;72:76-90.
45. Robbins K.S., Shin E.C., Shewfelt R.L., Eitenmiller R.R., Pegg R.B. Update on the healthful lipid constituents of commercially important tree nuts. *J Agric Food Chem*. 2011;59(22):12083-12092.
46. Lucchetti S., Ambra R., Pastore G. Effects of peeling and/or toasting on the presence of tocopherols and phenolic compounds in four Italian HN cultivars. *Eur Food Res Technol.* 2018;244(6):1057-1064.
47. Péter S., Friedel A., Roos F.F., Wyss A., Eggersdorfer M., Hoffmann K., Weber P. A Systematic Review of Global Alpha-Tocopherol Status as Assessed by Nutritional Intake Levels and Blood Serum Concentrations. *Int J Vitam Nutr Res.* 2015;85(5-6):261-281.
48. Howard A.C., McNeil A.K., McNeil P.L. Promotion of plasma membrane repair by vitamin E. *Nat Commun*. 2011;2:597.
49. Galli F., Azzi A., Birringer M., Cook-Mills J.M., Eggersdorfer M., Frank J., Cruciani G., Lorkowski S., Özer N.K. Vitamin E: Emerging aspects and new directions. *Free Radic Biol Med*. 2017;102:16-36.
50. Shahidi F., de Camargo A.C. Tocopherols and Tocotrienols in Common and Emerging Dietary Sources: Occurrence, Applications, and Health Benefits. *Int J Mol Sci.* 2016;17 (10):E1745.
51. Phillips K.M., Ruggio D.M., Ashraf-Khorassani M. Phytosterol composition of nuts and seeds commonly consumed in the United States. *J Agric Food Chem*. 2005;53(24):9436-9445.
52. Moreau R.A., Nyström L., Whitaker B.D., Winkler-Moser J.K., Baer D.J., Gebauer S.K., Hicks K.B. Phytosterols and their derivatives: Structural diversity, distribution, metabolism, analysis, and health-promoting uses. *Prog Lipid Res*. 2018;70:35-61.
53. Bradford P.G., Awad A.B. Phytosterols as anticancer compounds. *Mol Nutr Food Res.* 2007;51(2):161-170.
54. AbuMweis S.S., Marinangeli C.P., Frohlich J., Jones P.J. Implementing phytosterols into medical practice as a cholesterol-lowering strategy: overview of efficacy, effectiveness, and safety. *Can J Cardiol.* 2014;30(10):1225-1232.
55. Plat J., Mensink R.P. Plant stanol and sterol esters in the control of blood cholesterol levels: mechanism and safety aspects. *Am J Cardiol*. 2005;96(1A):15D-22D.
56. Shahzad N., Khan W., Md S., Ali A., Saluja S.S., Sharma S., Al-Allaf F.A., Abduljaleel Z., Ibrahim I.A.A., Abdel-Wahab A.F., Afify M.A., Al-Ghamdi S.S. Phytosterols as a natural anticancer agent: Current status and future perspective. *Biomed Pharmacother*. 2017;88:786-794.
57. Danesi F., Ferioli F., Caboni M.F., Boschetti E., Di Nunzio M., Verardo V., Valli V., Astolfi A., Pession A., Bordoni A. Phytosterol supplementation reduces metabolic activity and slows cell growth in cultured rat cardiomyocytes. *Br J Nutr.* 2011;106(4):540-548.
58. López-García G., Cilla A., Barberá R., Alegría A. Antiproliferative effect of plant sterols at colonic concentrations on Caco-2 cells. *J Funct Foods*. 2017;39:84-90.
59. Naziri E., Mantzouridou F., Tsimidou M.Z. Squalene resources and uses point to the potential of biotechnology. *Lipid Technol.* 2011;23(12):270-273.
60. Ghimire G.P., Thuan N.H., Koirala N., Sohng J.K. Advances in Biochemistry and Microbial Production of Squalene and Its Derivatives. *J Microbiol Biotechnol*. 2016;26(3):441-451.
61. Spanova M., Daum G. Squalene – biochemistry, molecular biology, process biotechnology, and applications. *Eur. J. Lipid Sci. Technol*. 2011;113:1299-1320.
62. Maguire L.S., O'Sullivan S.M., Galvin K., O'Connor T.P., O'Brien N.M. Fatty acid profile, tocopherol, squalene and phytosterol content of walnuts, almonds, peanuts, HNs and the macadamia nut. *Int J Food Sci Nutr.* 2004;55(3):171-178.
63. Bada J.C., León-Camacho M., Prieto M.,

Alonso L. Characterization of oils of HNs from Asturias, Spain. *Eur. J. Lipid Sci. Technol*. 2004;106:294-300.

64. Vujević P., Petrović M., Vahčić N., Milinović B., Čmelik Z. Lipids and minerals of the most represented HN varieties cultivated in Croatia. *Ital J Food Sci.* 2014;26(1):24-30.
65. Fernandes G.D., Gómez-Coca R.B., Pérez-Camino M.D.C., Moreda W., Barrera-Arellano D. Chemical Characterization of Major and Minor Compounds of Nut Oils: Almond, HN, and Pecan Nut. *J Chem.* 2017; 2609549.
66. Vadalà M., Laurino C., Palmieri L., Palmieri B. Shark derivatives (Alkylglycerols, Squalene, Cartilage) as putative nutraceuticals in oncology. *Eur J Oncol.* 2017;22(1):5-20.
67. Gabás-Rivera C., Barranquero C., Martínez-Beamonte R., Navarro M.A., Surra J.C., Osada, J. Dietary Squalene Increases High Density Lipoprotein-Cholesterol and Paraoxonase 1 and Decreases Oxidative Stress in Mice. PLoS One. 2014; 9(8):e104224.
68. Kim .SK., Karadeniz F. Biological importance and applications of squalene and squalane. *Adv Food Nutr Res*. 2012;65:223-233.
69. Smith T.J. Squalene: potential chemopreventive agent. Expert Opin Investig Drugs. 2000;9(8):1841-1848.
70. Dessì M.A., Deiana M., Day B.W., Rosa A., Banni S., Corongiu F.P. Oxidative stability of polyunsaturated fatty acids: Effect of squalene. *Eur J Lipid Sci Technol.* 2002;104(8):506-512.
71. Warleta F., Campos M., Allouche Y., Sánchez-Quesada C., Ruiz-Mora J., Beltrán G., Gaforio J.J. Squalene protects against oxidative DNA damage in MCF10A human mammary epithelial cells but not in MCF7 and MDA-MB-231 human breast cancer cells. *Food Chem Toxicol.* 2010;48(4):1092-1100.
72. Narayan B.H., Tatewaki N., Giridharan V.V., Nishida H., Konishi T. Modulation of doxorubicin-induced genotoxicity by squalene in Balb/c mice. *Food Funct.* 2010;1(2):174-179.
73. Wang H., Wang H., Yang L., Zu Y.-G., Liu F., Liu T.-T. Comparative effect of carnosic acid, BHT and α-tocopherol on the stability of squalene under heating and UV irradiation. *Food Res Int.* 2011; 44(9),2730-2734.
74. Lou-Bonafonte J.M., Martínez-Beamonte R., Sanclemente T., Surra J.C., Herrera-Marcos L.V., Sanchez-Marco J., Arnal C., Osada J. Current Insights into the Biological Action of Squalene. *Mol Nutr Food Res.* 2018;e1800136.
75. Kay C.D., Pereira-Caro G., Ludwig I.A., Clifford M.N., Crozier A. Anthocyanins and Flavanones Are More Bioavailable than Previously Perceived: A Review of Recent Evidence. *Annu Rev Food Sci Technol.* 2017;8:155-180.
76. Di Nunzio M., Toselli M., Verardo V., Caboni M.F., Bordoni A. Counteraction of oxidative damage by pomegranate juice: influence of the cultivar. *J Sci Food Agric.* 2013;93(14):3565-73.
77. Di Nunzio M., Valli V., Tomás-Cobos L., Tomás-Chisbert T., Murgui-Bosch L., Danesi F., Bordoni A. Is cytotoxicity a determinant of the different in vitro and in vivo effects of bioactives? BMC Complement Altern Med. 2017;17(1):453.
78. Di Nunzio M., Picone G., Pasini F., Caboni M.F., Gianotti A., Bordoni A., Capozzi F. Olive oil industry by-products. Effects of a polyphenol-rich extract on the metabolome and response to inflammation in cultured intestinal cell. *Food Res Int.* 2018;113:392-400.
79. Tsao R. Chemistry and biochemistry of dietary polyphenols. *Nutrients*. 2010;2(12):1231-1246.
80. Tresserra-Rimbau A., Lamuela-Raventos R.M., Moreno J.J. Polyphenols, food and pharma. Current knowledge and directions for future research. *Biochem Pharmacol.* 2018;156:186-195.
81. Bulgakov V.P., Vereshchagina Y.V., Veremeichik G.N. Anticancer Polyphenols from Cultured Plant Cells: Production and New Bioengineering Strategies. *Curr Med Chem*. 2018;25(36):4671-4692.
82. Slatnar A., Mikulic-Petkovsek M., Stampar F., Veberic R., Solar A. HPLC-MSn identification and quantification of phenolic compounds in HN kernels, oil and bagasse pellets. *Food Res Int.* 2014;64:783-789.
83. Marzocchi S., Pasini F., Verardo V., Ciemniewska-Żytkiewicz H, Caboni M.F., Romani S. Effects of different roasting

conditions on physical-chemical properties of Polish HNs (*Corylus avellana* L. var. Kataloński). *LWT-Food Sci Technol*. 2017;77:440-448.

84. Zhou Y., Zheng J., Li Y., Xu D.P., Li S., Chen Y.M., Li H.B. Natural Polyphenols for Prevention and Treatment of Cancer. *Nutrients.* 2016;8(8):E515.
85. Li H., Parry J.W. Phytochemical Compositions, Antioxidant Properties, and Colon Cancer Antiproliferation Effects of Turkish and Oregon HN. *Food Nutr Sci.* 2011;2:1142-1149.
86. Perna S., Giacosa A., Bonitta G., Bologna C., Isu A., Guido D., Rondanelli M. Effects of HN Consumption on Blood Lipids and Body Weight: A Systematic Review and Bayesian Meta-Analysis. *Nutrients*. 2016;8(12):E747.
87. Deon V., Del Bo' C., Guaraldi F., Abello F., Belviso S., Porrini M., Riso P., Guardamagna O. Effect of HN on serum lipid profile and fatty acid composition of erythrocyte phospholipids in children and adolescents with primary hyperlipidemia: A randomized controlled trial. *Clin Nutr.* 2018;37(4):1193-1201.
88. Santi C., Giorni A., Terenzi C.T., Altavista P., Bacchetta L. Daily HN Intake Exerts Multiple Reversible Effects on Plasma Profile of Healthy Subjects. *Food Nutr Sci*. 2017;8:633-646.
89. Yücesan F.B., Orem A., Kural B.V., Orem C., Turan I. HN consumption decreases the susceptibility of LDL to oxidation, plasma oxidized LDL level and increases the ratio of large/small LDL in normolipidemic healthy subjects. Anadolu Kardiyol Derg. 2010;10(1):28-35.
90. Orem A., Yucesan F.B., Orem C., Akcan B., Kural B.V., Alasalvar C., Shahidi F. HN-enriched diet improves cardiovascular risk biomarkers beyond a lipid-lowering effect in hypercholesterolemic subjects. *J Clin Lipidol.* 2013;7(2):123-131.
91. Bordoni A., Danesi F., Di Nunzio M., Taccari A., Valli V. Ancient wheat and health: a legend or the reality? A review on KAMUT khorasan wheat. *Int J Food Sci Nutr.* 2017;68(3):278-286.
92. Bordoni A., Picone G., Babini E., Vignali M., Danesi F., Valli V., Di Nunzio M., Laghi L., Capozzi F. NMR comparison of in vitro digestion of Parmigiano Reggiano cheese aged 15 and 30 months. *Magn Reson Chem.* 2011;49 Suppl 1:S61-70.
93. Ferranti P., Nitride C., Nicolai M.A., Mamone G., Picariello G., Bordoni A., Valli V., Di Nunzio M., Babini E., Marcolini E., Capozzi F. In vitro digestion of Bresaola proteins and release of potential bioactive peptides. *Food Res Int.* 2014;63:157-169.
94. Bordoni A., Laghi L., Babini E., Di Nunzio M., Picone G., Ciampa A., Valli V., Danesi F., Capozzi F. The foodomics approach for the evaluation of protein bioaccessibility in processed meat upon in vitro digestion. *Electrophoresis*. 2014;35(11):1607-1614.
95. Marcolini E., Babini E., Bordoni A., Di Nunzio M., Laghi L., Maczó A., Picone G., Szerdahelyi E., Valli V., Capozzi F. Bioaccessibility of the Bioactive Peptide Carnosine during in Vitro Digestion of Cured Beef Meat. *J Agric Food Chem*. 2015;63(20):4973-4978.
96. Valli V., Danesi F., Gianotti A., Di Nunzio M., Taneyo Saa D.L., Bordoni A. Antioxidative and anti-inflammatory effect of in vitro digested cookies baked using different types of flours and fermentation methods. *Food Res Int.* 2016; 88(Part B):256-262.
97. Antognoni F., Mandrioli R., Bordoni A., Di Nunzio M., Viadel B., Gallego E., Villalba MP., Tomás-Cobos L., Taneyo Saa D.L., Gianotti A. Integrated Evaluation of the Potential Health Benefits of Einkorn-Based Breads. *Nutrients* 2017;9(11):E1232.