Pecan nuts: A review of reported bioactivities and health effects

Article *in* Trends in Food Science & Technology · November 2017

DOI: 10.1016/j.tifs.2017.10.019

10 authors, including:

Atanas G Atanasov
Medical University of Vienna
309 PUBLICATIONS **5,058** CITATIONS
SEE PROFILE

Shefali Sabharanjak
Tata Institute of Fundamental Research
6 PUBLICATIONS **1,235** CITATIONS
SEE PROFILE

Gokhan Zengin
Selcuk University
471 PUBLICATIONS **3,886** CITATIONS
SEE PROFILE

Adriano Mollica
Università degli Studi G. d'Annunzio Chieti e Pescara
215 PUBLICATIONS **2,651** CITATIONS
SEE PROFILE

Trends in Food Science & Technology 71 (2018) 246–257

Contents lists available at ScienceDirect

Trends in Food Science & Technology

journal homepage: www.elsevier.com/locate/tifs

Review

Pecan nuts: A review of reported bioactivities and health effects

Atanas G. Atanasov[a,b,*,1], Shefali M. Sabharanjak[c,1], Gokhan Zengin[d], Adriano Mollica[e], Agnieszka Szostak[a,f], Mario Simirgiotis[g], Łukasz Huminiecki[a], Olaf K. Horbanczuk[h], Seyed Mohammad Nabavi[i], Andrei Mocan[j,**]

[a] Institute of Genetics and Animal Breeding of the Polish Academy of Sciences, 05-552 Jastrzebiec, Poland
[b] Department of Pharmacognosy, University of Vienna, 1090 Vienna, Austria
[c] Phase 1, Royal Enclave, Jakkur P.O., Bangalore 560064, India
[d] Department of Biology, Science Faculty, Selcuk University, Konya, Turkey
[e] Department of Pharmacy, University "G. d'Annunzio" of Chieti-Pescara, Chieti 66100, Italy
[f] Faculty of Animal Sciences, Warsaw University of Life Sciences, 02-786 Warsaw, Poland
[g] Instituto de Farmacia, Facultad de Ciencias, Universidad Austral de Chile, Valdivia, Chile
[h] Faculty of Human Nutrition and Consumer Sciences, Warsaw University of Life Sciences, 02-776 Warsaw, Poland
[i] Applied Biotechnology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran
[j] Department of Pharmaceutical Botany, Iuliu Haţieganu University of Medicine and Pharmacy, 400012 Cluj-Napoca, Romania

ARTICLE INFO

Keywords:
Pecan nuts
Polyphenols
Epigallocatechin-3-gallate (EGCG)
Cardiovascular disease
Polyunsaturated fatty acids (PUFA)
Monounsaturated fatty acids (MUFA)

ABSTRACT

Background: Food choices represent a highly significant approach to combat human obesity. Dietary intake of lipids, especially polyunsaturated and monounsaturated fatty acids, is gaining popularity in the effort to reduce or eliminate the occurrence of obesity. Pecan (*Carya illinoinensis*) nuts are an abundant source of these dietary fatty acids. Moreover, they are a rich source of epigallocatechin-3-gallate (EGCG), a polyphenol with a variety of health-beneficial properties.

Scope and approach: In this review, we summarize the literature reports examining physiological effects associated with pecan nuts consumption and described effects of their bioactive constituents.

Key findings and conclusions: The growing body of evidence suggests including pecan nuts into obesity management strategies. The consumption of pecan nuts can mitigate inflammation by reducing the extent of the synthesis of inflammatory mediator molecules. Pecan nuts can also counteract the pro-inflammatory effects of a diet rich in commonly overconsumed saturated fatty acids, characteristic of the Western diet. Additionally, consumption of pecans and other nuts has been linked to reduced risk of physiological parameters associated with cardiovascular disease or metabolic disorders. Diets enriched with tree nuts and peanuts can modulate the blood level of cholesterol, adiposity, and insulin resistance. Almonds and walnuts have been so far the most studied nuts, and studies with them have led to a greater understanding of the protective effects of diverse tree nuts on human physiology. In this review, we summarize the available data indicating that pecan nuts exert similar health-promoting benefits.

1. Introduction

According to the World Health Organization (WHO), obesity has been a globally prevalent health problem for the past several decades, with the worldwide prevalence of obesity more than doubling between 1980 and 2014 (http://www.who.int/mediacentre/factsheets/fs311/en/). According to statistics compiled by the WHO, 600 million adults were documented to be obese and 1.9 billion adults were overweight in 2014. Forty-one million children under the age of five were also classified as overweight or obese in 2014. A complex health condition associated with risks of developing diabetes and cardiovascular disease, obesity is a multifactorial health syndrome that results from a complex interplay of genetics, lifestyle choices, food choices, and low physical exertion (Adamo, Ferraro, & Brett, 2012; Han, Lawlor, & Kimm, 2010; Loos & Yeo, 2014). Strategies to manage or reduce obesity are a blend of proper medical attention, adequate physical exercise, and management of food choices. Food choices have taken center stage in the worldwide debate about the causes of obesity and ways to combat it.

* Corresponding author. Institute of Genetics and Animal Breeding of the Polish Academy of Sciences, 05-552 Jastrzebiec, Poland.
** Corresponding author. Department of Pharmaceutical Botany, Iuliu Haţieganu University of Medicine and Pharmacy, 400012 Cluj-Napoca, Romania.
E-mail addresses: a.atanasov.mailbox@gmail.com (A.G. Atanasov), amocanm@gmail.com (A. Mocan).
[1] These authors contributed equally to this study.

https://doi.org/10.1016/j.tifs.2017.10.019
Received 24 July 2017; Received in revised form 11 October 2017; Accepted 30 October 2017
Available online 07 November 2017
0924-2244/

There have been numerous discussions about managing food intake, drugs for weight loss, and diet regimens for overcoming obesity and controlling the gain of body fat.

The inclusion of “healthy natural foods” in the diet is now being recommended as one of the measures to control obesity, in conjunction with others such as physical exercise and diverse lifestyle modifications. In general, many recommendations related to food choices revolve around restricting the intake of fatty foods, especially processed foods to which fats have been added during food processing and preparation. High-carbohydrate, high-fat-containing processed food preparations (often referred as “junk food”) are linked to overweight and obesity via several mechanisms. The total caloric value of meals enriched with such products directly contributes to obesity by modifying the glucose and cholesterol homeostatic processes in the human body. Interestingly, whereby carbohydrate and fat density of foods is directly linked to energy content, high salt content, another characteristic of junk foods, has also been indicated as a potential risk factor for obesity independent of energy intake (Ma, He, & MacGregor, 2015). Additionally, junk foods also have addictive effects, leading to cravings and repeated cycles of the consumption of such foods, accelerating the development of obesity (Oginsky, Goforth, Nobile, Lopez-Santiago, & Ferrario, 2016; Park et al., 2010). The intake of junk food has a “priming” effect on the nucleus accumbens area of mammalian brains, brought about by increased activity of the calcium-permeable AMPA-receptor (Oginsky et al., 2016). In rats prone to obesity, this priming effect has been shown to persist for weeks after the consumption of junk foods, and result in enhanced motivation to choose similar foods. In C57Bl/6 mice, Park et al. demonstrated that prolonged consumption of high-fat foods result in suppression of the level of brain-derived nerve growth factor (BDNF) and consequent loss of neuroregenerative capacity in the hippocampal area (Park et al., 2010). In another study, a diet rich in saturated fatty acids (SFA), supplied as lard, was also found to impair cognition, reduce BDNF levels and increase inflammation in the brain, in mice (Pistell et al., 2010). Suppression of BDNF levels, a concomitant decrease in hippocampal synaptic plasticity, and reduction in new learning abilities have also been associated with the consumption of a diet rich in saturated fat and refined sugar in rats (Molteni, Barnard, Ying, Roberts, & Gomez-Pinilla, 2002). A reduction in the production of BDNF has been associated with a decrease in the levels of cyclic-AMP-response element binding protein (CREB) as well as those of growth-associated protein 43 (GAP-43), which is involved in neurite outgrowth and in release of neurotransmitters. Clearly, the amount and the type of dietary fats can have profound long-lasting effects on food choices, metabolic health as well as cognitive processes. These findings also indicate how consumption of foods high in saturated fat and refined carbohydrates can be an addictive process and result in a vicious cycle of consumption of foods that lead to obesity. Findings from these studies with animal models are corroborated by studies in human subjects, as well. Consumption of a high-fat, high-carbohydrate diet has been linked to the breakdown of the blood-brain barrier, thereby contributing to the onset of neurodegenerative conditions like Alzheimer's disease and dementia (Kanoski & Davidson, 2011). A pilot study with Hispanic women indicated that abdominal obesity is associated with higher stimulation of selected areas of the brain when visual cues, like high-calorie foods, were shown to the participants. The participants of this study also indicated a greater desire to eat sweet and savory foods, after being shown images of high-calorie foods. The stimulation of appetite and preference towards high-calorie foods was positively correlated with increasing abdominal obesity (Luo et al., 2013). A long-term, population-based study has also highlighted the link between consumption of elevated levels of SFA in midlife with the development of mild cognitive impairments (MCI), later in life after an average follow-up of 21 years (Eskelinen et al., 2008).

The effect of a diet rich in SFA on the development of obesity and its co-morbidities is evident from these and other comparable studies. The perception of foods rich in natural fats, such as nuts, fruits like avocados, and oilseeds, as high-fat and, therefore, undesirable food is also a factor that hampers the inclusion of these foods in the diet. Nevertheless, the consumption of nuts and oilseeds has been associated with a reduced risk of the development of cardiovascular disease and restoration of favorable blood lipid profiles (Sabate & Wien, 2010; Sabaté, Oda, & Ros, 2010; Salas-Salvadó, Guasch-Ferré, Bulló, & Sabaté, 2014). It is evident that choice of dietary sources of foods enriched with appropriate natural fats is a crucial factor in the management of health and prevention of obesity and the metabolic syndrome, which is often associated with obesity and involves a clustering of other medical conditions such as hypertension, hyperglycemia, and dyslipidemia. Furthermore, aside from lipid composition, secondary metabolites present in diverse plant-derived food sources have also been reported to display a variety of bioactivities with the potential to counteract obesity and the metabolic syndrome (Atanasov et al., 2015; Waltenberger, Mocan, Šmejkal, Heiss, & Atanasov, 2016; Wang et al., 2014).

Tree nuts are an abundant source of unsaturated fatty acids and secondary metabolites with diverse bioactivities. Potential health benefits from the inclusion of tree nuts into the diet have been investigated in several clinical trials (Del Gobbo, Falk, Feldman, Lewis, & Mozaffarian, 2015; Sabate & Wien, 2010). The hickory family of tree nuts (Juglandaceae) includes walnuts and pecan (*Carya illinoinensis* (Wangenh.) K.Koch, family Juglandaceae) nuts. Pecan nuts are widely consumed in North America as a popular snack and a dessert ingredient. In this review, we summarize studies that have examined the various biochemical constituents of pecan nut kernels and review the potential health benefits of consumption of pecans and their principal constituents.

Table 1
Comparison of important bioactive constituents and antioxidant activity (expressed as Trolox equivalents) of pecan nuts and walnuts.

Constituent	Pecans (*Carya illinoinensis*)	Walnuts (*Juglans regia*)	Reference
Total fat	58.1–66.18 g oil/100 g nut meat	64.5 g/100 g nut meat	(Ryan et al., 2006; Venkatachalam & Sathe, 2006)
Total PUFAs	24.92 g/100 g lipid	72.96 g/100 g lipid	(Venkatachalam & Sathe, 2006)
Total MUFAs	66.73 g/100 g lipid	15.28 g/100 g lipid	(Venkatachalam & Sathe, 2006)
Linoleic acid (C18:2n6) (PUFA)	23.68 g/100 g lipids	59.79 g/100 g lipid	(Venkatachalam & Sathe, 2006)
Alpha-linolenic acid (C18:3n3) (PUFA)	1.24 g/100 g lipids	13.17 g/100 g lipids	(Venkatachalam & Sathe, 2006)
Oleic acid (C18:1n9) (MUFA)	66.66 g/100 g lipids	15.19 g/100 g lipids	(Venkatachalam & Sathe, 2006)
Total polyphenols (gallic acid equivalents)	2016 (mg GAE/100 g) – USDA database 1284.00 (mg GAE/100 g) – Phenol Explorer database	1556 (mg GAE/100 g) – USDA database 1574.82 (mg GAE/100 g) – Phenol Explorer database	(Wu et al., 2004)
EGCG	2.1 mg/90 g	–	(Hudthagosol et al., 2011)
Antioxidant activity (Trolox equivalents)	58 μmol/g	120 μmol/g	(Abe et al., 2010)

2. The composition of pecan nuts

Pecan nuts are the seeds of *C. illinoinensis*. They are rich in fats, with a net yield of around 58.1–66.18 g oil/100 g of nut mass, which is in a similar range as walnuts, as indicated in Table 1 (Ryan, Galvin, O'connor, Maguire, & O'brien, 2006; Venkatachalam & Sathe, 2006). Among five compared types of nuts, brazil, pecan, pine, pistachio and cashew nuts, it was found that pecan nuts have the highest ratio of unsaturated/saturated fatty acids (13.54), with the total content of unsaturated fatty acids in the oil extracted from pecan nuts reaching as high as 93%. The unsaturated fatty acids are a group of lipids characterized by the presence of one or more double bonds in the structure. Unsaturated fatty acids containing one double bond in the fatty acid chain are referred to monounsaturated fatty acids (MUFAs), and if two or more double bonds are present, the respective molecule is regarded as a representative belonging to the group of the polyunsaturated fatty acids (PUFAs). The presence and numbers of double bonds has a significant impact on the main functions of the fatty acids as components of cells membranes. Saturated fatty acids (SFAs) do not contain double bonds in their structure. The low ratio of saturated to unsaturated fatty acids in the cell membranes increase membrane fluidity and permeability and further affect the activity of embedded enzymes (Schachter, 1984). Venkatachalam *et al.* found that pecan nuts contain more MUFAs than PUFAs (Table 1) (Venkatachalam & Sathe, 2006), whereby another study indicated a similar amount of PUFAs and MUFAs in oil gained from pecan nuts (Ryan et al., 2006). Specifically, linoleic acid (C18:2n6) (Fig. 1) has been found to be the most abundant PUFA in pecan nuts (Ryan et al., 2006). Additionally, pecan nuts contain a small amount of alpha-linolenic acid (C18:3n3). Furthermore, oleic acid (C18:1n9) (Fig. 1) is the most significant MUFA present in pecan nuts (Ryan et al., 2006). Other studies have also shown that oleic acid (52.52–74.09%) and linoleic acid (17.69–37.52%) are the predominant MUFA and PUFAs in pecan nut meat (Venkatachalam et al., 2007). Omega-6 linoleic acid and omega-3 alpha-linolenic are essential fatty acids, that cannot be synthesized endogenously by most of animals, therefore their constant dietary intake is crucial (El-Badry, Graf, & Clavien, 2007). One of the best sources of PUFAs in the world is the Inca nuts or Sacha inchi (*Plukenetia volubilis* L.), which contain a high quantity of edible oil (41–54%) with a really high proportion of unsaturated fatty acids (Niu, Li, Chen, & Xu, 2014).

The low peroxide value of pecan oil (0.15 mEq O_2 per kg oil), indicative of a reduced tendency towards auto-oxidation (development of rancidity) also helps to maintain the taste and, therefore, food value of pecan nuts in storage (Ryan et al., 2006). Pecan nuts are also a dietary source of alpha-tocopherol (12.2 ± 3.2 mg/g), gamma-tocopherol (168.5 ± 15.9 mg/g) and squalene (151.7 ± 10.8 mg/g) (Fig. 2) (Ryan et al., 2006). Alpha-tocopherol and gamma-tocopherol help to prevent the oxidation of unsaturated fatty acids, which are especially prone to oxidation process by presence of unsaturated bonds in their structure. In regards to tannin content, with the exception of a high tannin (2.7%) Texas seedling, the pecan tannin content was reported to be in the narrow range 0.6–1.85% (Venkatachalam et al., 2007).

According to the United States Department of Agriculture National Nutrient Database for Standard Reference Release 28 (https://ndb.nal.usda.gov/ndb/foods), pecan nuts are also a source of thiamine, folate, niacin, riboflavin and vitamin B6 (Fig. 2), as well as minerals like calcium, iron, magnesium, phosphorus, and zinc (Haddad, 2011). Pecans also contain phytosterols (Fig. 3), specifically, beta-sitosterol (1572.4 ± 41.0 mg/g oil), campesterol (52.2 ± 7.1 mg/g oil), and stigmasterol (340.5 ± 29.5 mg/g oil) (Ryan et al., 2006). The presence of Δ^5-avenasterol (14.6 mg/100 g nuts) and smaller amounts of sitostanol and campestanol have also been reported (Phillips, Ruggio, & Ashraf-Khorassani, 2005).

Pecans are also a rich source of polyphenolic compounds, which are reported to have beneficial effects on human health (Table 1 and Fig. 3). Interestingly, pecan nuts are reported to have the highest total polyphenol content among ten diverse types of reviewed nuts, in particular, almonds, brazil nuts, cashews, hazelnuts, macadamias, peanuts, pecans, pine nuts, pistachios, and walnuts (Wu et al., 2004).

Medicinal plant extracts and ethnobotanical formulations containing plant-derived polyphenolic compounds, have been integral components of traditional healing systems, such as the traditional Chinese medicine and Ayurveda. Ellagic acid is one of the significant polyphenols found in pecan nuts, and it was reported to be present at 301 ± 7 mg/100 g (Abe, Lajolo, & Genovese, 2010). Polyphenolic compounds are also known to act as anti-oxidants or free radical scavengers, in addition to having other biochemical attributes. The total anti-oxidant capacity of polyphenolic extracts from pecan nuts has been reported to be 58 μmol Trolox equivalents/g (Abe et al., 2010). Amongst the studied edible nuts and oilseeds, this anti-oxidant capacity of pecans is second only to that of walnuts (120 μmol Trolox equivalents/g). Pecans also contain epigallocatechin-3-gallate (EGCG), a polyphenolic molecule that is also known as one of the prominent bioactive constituents of green tea (Hudthagosol et al., 2011). Pecan nuts were also reported to have the highest amount of flavonoids (34 mg/100 g nut meat) amongst several reviewed kinds of nuts, including almonds, pistachios, and hazelnuts (Chen & Blumberg, 2008). Pecan nuts shells have also a high content of polyphenolics (93 mg gallic acid equivalents and 46 mg catechin equivalents per gram), and high antioxidant activity (1257 μmol TEAC per gram and 293 mg TEAC per gram in the ABTS and DPPH methods, respectively) which were mainly due to the presence of chlorogenic acids, procyanidins and other phenolic acids (Engler Ribeiro, de Britto Policarpi, Dal Bo, Barbetta, & Block, 2017).

3. Bioavailability of anti-oxidants from pecans

The presence of supercharged free radicals in biological systems can contribute to processes like oxidation of LDL particles and, consequently, to the generation of atherosclerotic plaques. The link between the presence of free radicals and inflammatory processes leading to cardiovascular disease and metabolic syndrome has been sufficiently described in recent literature (Ceriello & Motz, 2004; Thomas, Sibui, & Debabrata, 2016). Plant-derived polyphenolic compounds exhibit beneficial free radical scavenging effects, and pecan nuts are a good source of polyphenolic compounds that are also bioavailable. Hudthagosol *et al.* studied the post-prandial availability of anti-oxidants from pecan nuts (Hudthagosol et al., 2011). Sixteen healthy men and women were provided with test meals of whole pecans, blended pecans or isocaloric meals made with refined ingredients. In the follow-up period, the plasma concentrations of tocopherols, and oxygen radical absorbance capacity (ORAC), as well as the presence of oxidized LDL, were assessed. Within two hours of ingesting of a pecan meal, hydrophilic and lipophilic ORAC increased by 12% and 10%, respectively. The concentrations of plasma gamma-tocopherols doubled from that seen at baseline within eight hours of consumption of pecan nuts. A concomitant decrease in the levels of oxidized LDL - 29.6% at 2 h post-meal, 33.3% at 3 h post-meal and 26.3% at 8 h post-meal – was also observed following whole pecan consumption (Hudthagosol et al., 2011). As discussed above, pecans are also a source of epigallocatechin-3-gallate (EGCG). Plasma concentrations of EGCG following the pecan intake were noted to be 95.1 ± 30.6 nmol/L after 1 h and 116.3 ± 80.5 nmol/L after 2 h. These values are significantly different from those seen at the same time-points in individuals fed with an isocaloric control meal ($P < 0.05$). Consumption of pecans can, therefore, release significant amounts of anti-oxidant substances into the bloodstream (Hudthagosol et al., 2011).

4. The consumption of nuts and cardiovascular disease

Accumulation of atherosclerotic plaques on the blood vessel walls is a hallmark of cardiovascular disease (CVD). Formation of these plaques

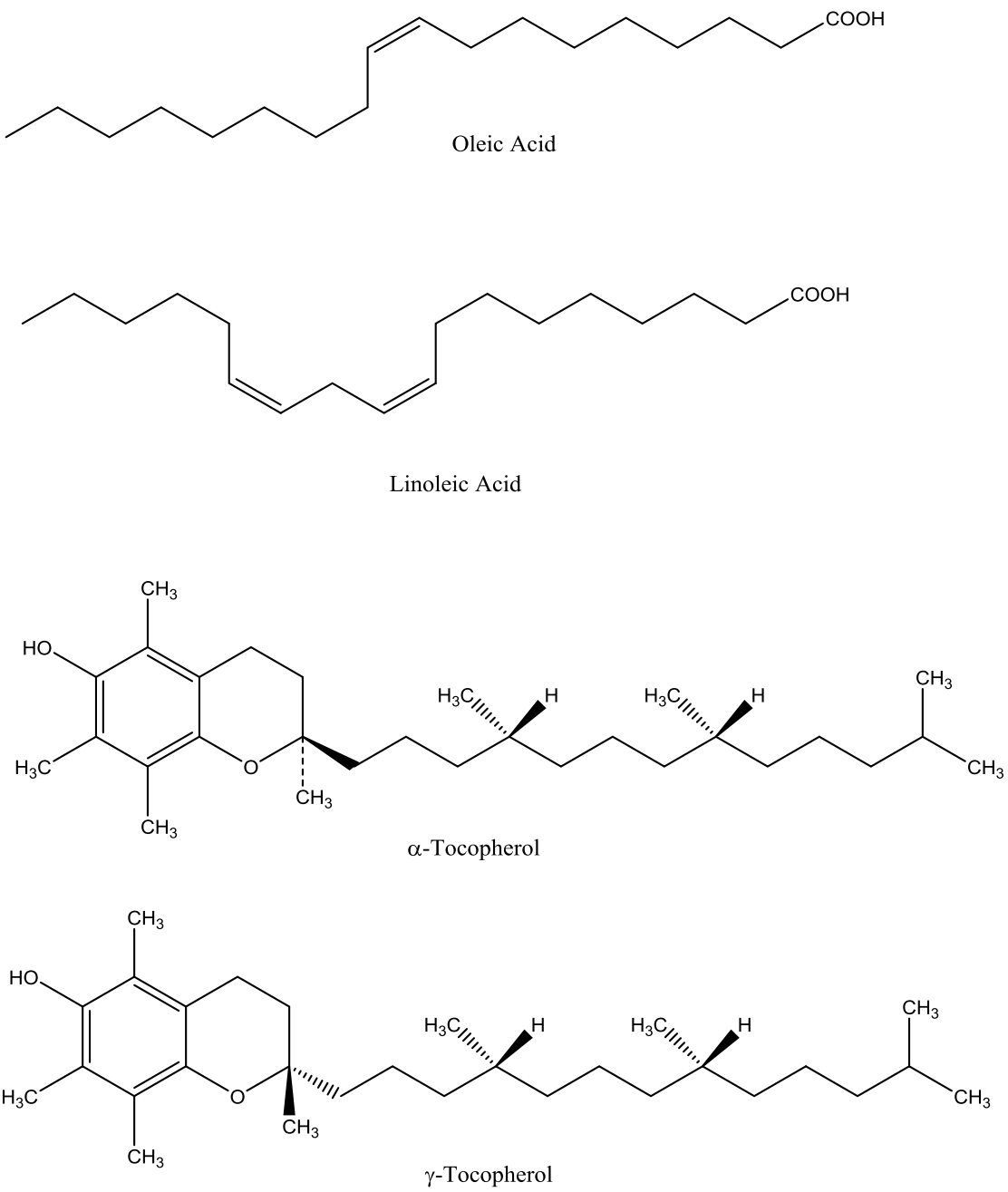
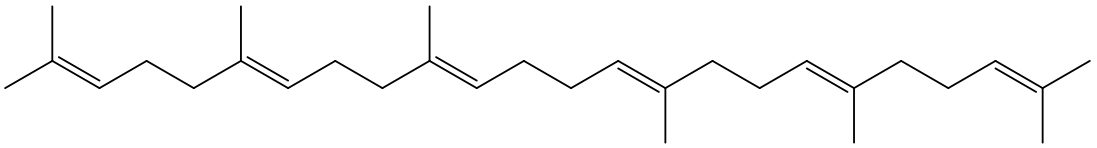


Fig. 1. Chemical structures of tocopherol and selected significant lipids contained in pecan nuts.

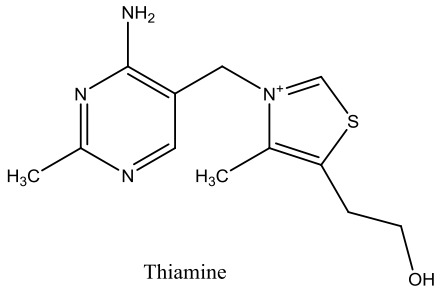
is dependent on several factors; one amongst them is the dysregulation of the balance between low-density lipoprotein (LDL) and high-density lipoproteins (HDL) in circulation. Appropriate strategies to maintain the ideal ratios between LDL and HDL include the prescription of statin drugs, diet modifications, and exercise. Overview of human studies assessing the consumption of pecans/nuts on parameters related to cardiovascular disease and metabolic syndrome is presented in Table 2.

The Mediterranean diet is a food pattern that is complemented by the practice of physical exercise and the climate of countries bordering the Mediterranean Sea, and which has multiple health benefits that might be partially linked to some of the prominent used fat sources (olive oil, fish and nuts). Results from one cohort of the PREDIMED (prevention with Mediterranean diet) trial, which examines the effect of a Mediterranean diet supplemented with mixed nuts (walnuts, hazelnuts, almonds) on cardiovascular health parameters, suggest that inclusion of nuts reduces the risk of atherosclerosis (Damasceno et al., 2013). A Mediterranean diet supplemented with mixed nuts resulted in a significant loss of waist circumference (−5 cm, range −7 to −3 cm; CI [confidence interval] of 95%). Interestingly, the loss of truncal obesity was also accompanied by a decreased LDL particle number and increased LDL particle size in peripheral circulation, which prevents from atherosclerotic plaque formation in blood vessels. These results show that nuts, despite the relatively high content of fats, might help counteract abdominal obesity and aid in the restoration of the normal homeostasis of blood lipid constituents. These effects, in turn, manifest as a reduction in the risk of cardiovascular disease.

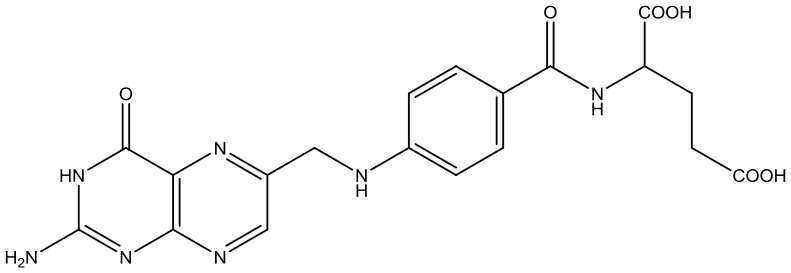
A link between the consumption of products rich in unsaturated fats, including nuts, and the restoration of homeostasis of blood lipid levels was reported as early as 1960 (Pilkington, Stafford, Hankin, Simmonds, & Koerselman, 1960). In this study, the inclusion of nuts in a diet regimen that was intentionally biased towards the inclusion of unsaturated fatty acids was instrumental in reducing serum LDL-



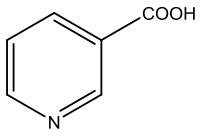
Squalene



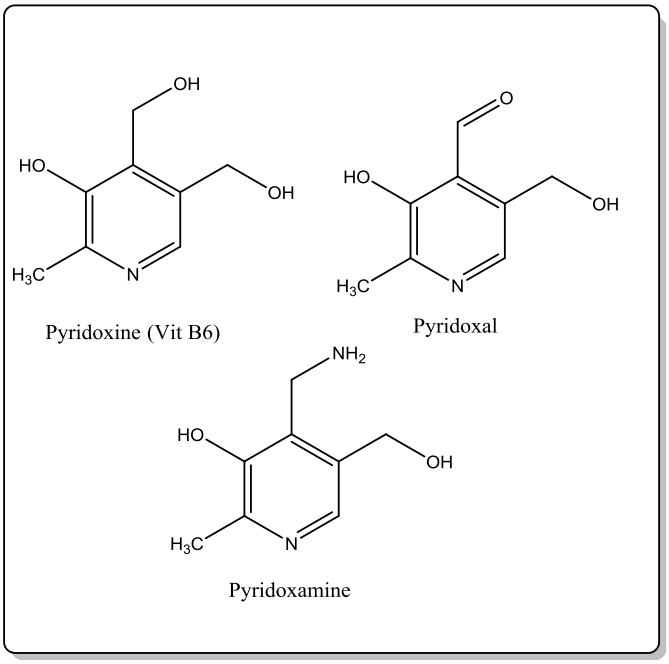
Thiamine



Folic Acid



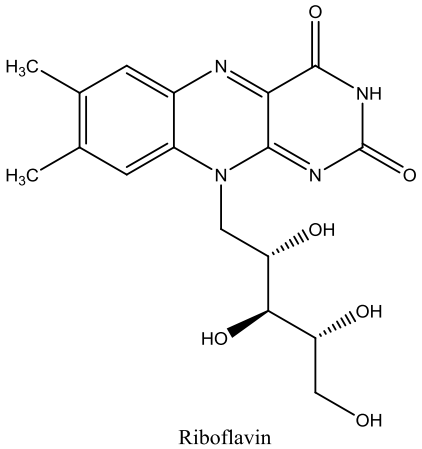
Niacin



Pyridoxine (Vit B6)

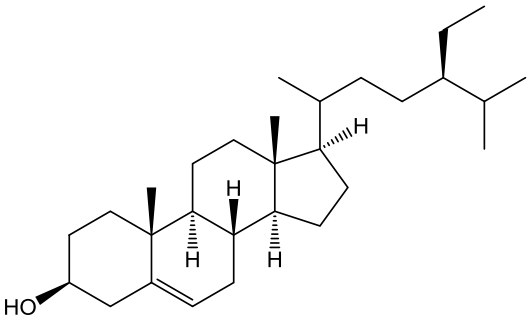
Pyridoxal

Pyridoxamine

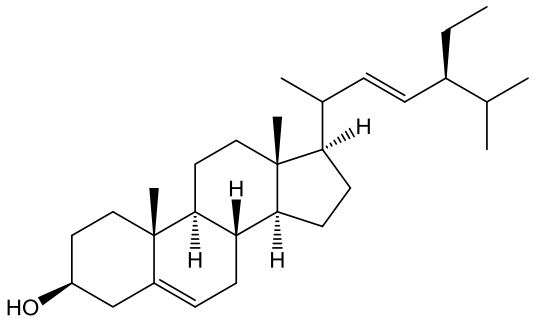


Riboflavin

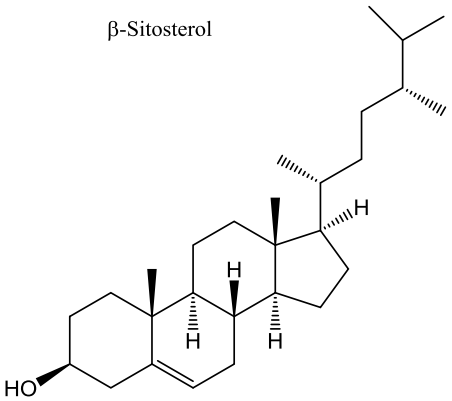
Fig. 2. Vitamins and other micronutrients from pecan nuts.



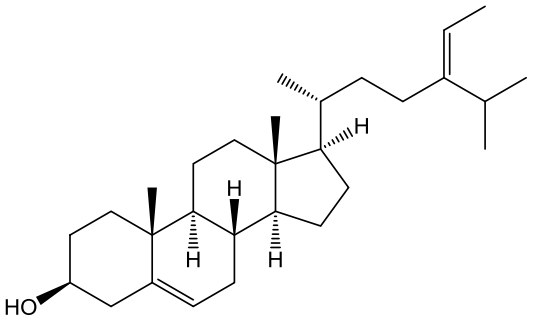
β-Sitosterol



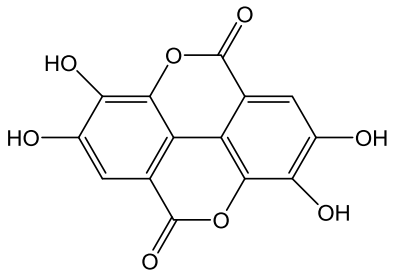
Stigmasterol



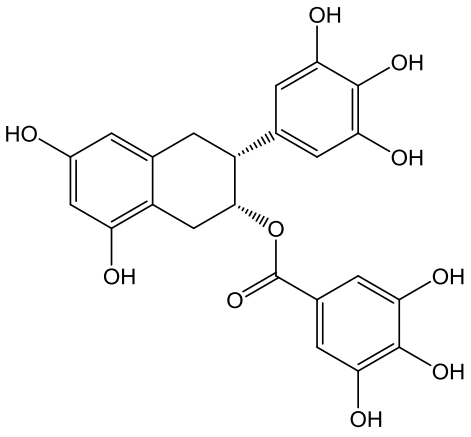
Campesterol



5-Δ–Avenasterol



Ellagic acid



Epigallocatechin-3-gallate

Fig. 3. Chemical structures of selected phytosterols and polyphenols found in pecan nuts.

cholesterol levels. Reduction of serum LDL-cholesterol was greater than that seen in participants who were given a low-fat diet, which included sources of saturated fatty acids. Although the diets were isocaloric, the total amount of fats in the unsaturated fatty acids meals was three times the amount of fats in a low-fat diet containing saturated fatty acids. Although these results were preliminary, the reduction of serum LDL-cholesterol levels was attributed to the inclusion of unsaturated fatty acids in the diet.

Results from the Adventist Health Study conducted in 1992, show that non-Hispanic, Caucasian individuals who consumed at least four helpings of nuts per week had a reduced risk of developing coronary heart disease (relative risk, 0.52; CI of 95%, 0.36 to 0.76). The relative risk of such individuals suffering from non-fatal myocardial infarction was also lower (relative risk, 0.49; 95% CI, 0.28 to 0.85), compared to people who consumed nuts less than once a week (Fraser, Sabate, Beeson, & Strahan, 1992).

In a controlled randomized feeding trial with 19 volunteers, Morgan and Clayshulte reported that inclusion of pecans (68 g per person per day) to a self-selected diet can help to lower serum levels of LDL-cholesterol in the peripheral circulation (Morgan & Clayshulte, 2000). The limitation of the study was the small number of subjects/participants. However, the results are comparable with those reported in the

Table 2
Human studies assessing the consumption of pecans/nuts on parameters related to metabolic syndrome and cardiovascular disease.

Study design and pecans/nuts consumption details	Outcomes
The PREDIMED trial studied the effects of Mediterranean diet supplemented with hazelnuts, almonds, and walnuts in 169 subjects (Damasceno et al., 2013).	Reduction in waist circumference (−5 cm, range −7 to −3 cm; CI 95%) and decrease in the LDL particle number and increase in the LDL particle size was observed.
Eight-week, randomized, controlled study with 19 human volunteers consuming 68 pecans per day (Morgan & Clayshulte, 2000).	Pecan consumption was associated with lower levels of total cholesterol, LDL-cholesterol and HDL-cholesterol.
The Adventist Health Study examined the effects of 4 helpings of nuts per week in 31208 subjects (self-reported consumption, the amounts of nuts and the types of nuts consumed were variable) (Fraser et al., 1992).	Nut consumption of more than four times per week resulted in reduced risk for developing coronary artery disease (relative risk, 0.52; 95% CI, 0.36 to 0.76). Lower risk was observed of developing non-fatal myocardial infarction (relative risk, 0.49; 95% CI, 0.28 to 0.85) when compared against people who had lower or negligible nut consumption.
Single-blind, randomized, crossover, controlled trial with 23 human volunteers comparing for 4 weeks a Step I diet and a pecan-enriched diet (accomplished by proportionately reducing all food items in a Step I diet by one fifth for a 20% isoenergetic replacement with pecans). The pecans-intake group consumed 72 g of pecans per 10,032 kJ energy intake (Rajaram et al., 2001).	Both diets improved the lipid profile, however, the pecan-enriched diet decreased both serum total and LDL-cholesterol by 0.32 mmol/L (6.7% and 10.4%, respectively) and triglyceride by 0.14 mmol/L (11.1%) beyond the Step I diet, while increasing HDL cholesterol by 0.06 mmol/L (2.5 mg/dL).
The NHANES survey (National Health and Nutrition Examination Survey 2005–2010) examining the consumption of ≥0.25 ounce per day of mixed nuts (Brazil nuts, pecans, almonds, walnuts, hazelnuts, pine nuts, pistachios, cashews and macadamia nuts) in 14386 subjects (51% male) (O'Neil & Nicklas, 2015; O'Neil et al., 2015).	Tree nut consumption was associated with lower BMI ($p = 0.004$), waist circumference ($p = 0.008$) and systolic blood pressure ($p = 0.001$). Insulin resistance (HOMA-IR) was also lower ($p = 0.043$), and higher serum levels of high-density lipoprotein-cholesterol ($p = 0.022$), was detected compared with no consumption, as well as lower likelihood of obesity (−25%), obesity/overweight (−23%), and elevated waist circumference (−21%).
Meta-analysis of 12 trials examining effects of the consumption (56 g/day median consumption) of tree nuts (predominantly almonds and walnuts, but also pecans, cashew nuts, pistachio, mixed nuts, and hazelnuts), by 450 diabetic subjects (Viguiliouk et al., 2014).	Reduction in HbA1c (mean difference (MD) = −0.07% [95% CI: −0.10, −0.03%]; $P = 0.0003$) and in fasting glucose (MD = −0.15 mmol/L [95% CI: −0.27, −0.02 mmol/L]; $P = 0.03$) were observed in comparison to the control diets.

PREDIMED trial, suggesting that the consumption of nuts rich in PUFAs can help to reduce serum levels of LDL-cholesterol.

Rajaram et al. reported a single-blind, randomized, crossover, controlled trial with 23 volunteers wherein the volunteers were given two feeding interventions. The control group received a Step I diet, whereas the other group received a Step I diet that was modified to include pecans (72 g per 10,032 kJ energy intake). Whereby the diets were isoenergetic, the percentage of energy received from fat was higher in the pecan group (39.6%) than in the Step I diet (28.3%) (Rajaram, Burke, Connell, Myint, & Sabaté, 2001). At the end of the 4-week trial, the lipid profiles of volunteers fed with the pecan-supplemented diet showed a significant reduction in total serum (−6.7%) and LDL-bound cholesterol (−10.4%). Interestingly, serum triglyceride levels were also reduced by 0.14 mmol/L (11.1%) beyond the Step I diet, while the HDL cholesterol increased by 0.06 mmol/L (2.5 mg/dL). One must note that the Step I diet was different from the standard daily diet of the volunteers, and produced a favorable lipid profile (although the improvements were smaller in comparison to the pecans-supplemented group) in the volunteers of this trial, as well. However, the results of the inclusion of pecans in this crossover trial indicate a significant difference and, thereby, a trend towards a lower atherogenic profile (Rajaram et al., 2001).

Domínguez-Avila et al. examined the lipid profile of male Wistar rats when administered a high-fat diet, or a high-fat diet supplemented with pecan oil, pecan polyphenolic fractions, or whole pecan nuts (Domínguez-Avila et al., 2015). In the 9-week intervention period, the total body weights of the animals remained at comparable levels. The whole pecans and pecan fractions were able to reverse some of the unfavorable alterations induced by the high-fat diet. The diet supplemented with whole pecans was effective in preventing hyperleptinemia and reduced the concentration of blood lipids (total cholesterol, HDL cholesterol, LDL cholesterol, and triacylglycerols), in some cases, to values lower than those of the control group. Interestingly, the pecan oil and the pecan polyphenolic fractions also displayed some of the mentioned beneficial effect, or had distinct activities; nevertheless, the consumption of whole pecans induced the most beneficial profile of biochemical changes, which could not be fully replicated by the consumption of pecan oil or pecan polyphenols alone (Domínguez-Avila et al., 2015).

Serum markers, such as levels of inflammatory molecules like C-reactive protein (CRP) and interleukin-6 (IL-6), in addition to serum hyperlipidemia, can be examined for the assessment of predisposition towards cardiovascular disease. Consumption of nuts and seeds can lead to reduction in the serum levels of some inflammatory molecules (Ros, 2009). Nut-enriched diets, such as the Mediterranean diet, can also be instrumental in increasing the circulatory levels of adiponectin, a cytokine that can reduce inflammation, control glucose metabolism and fatty acid oxidation (Nigro et al., 2014; Ros, 2009). Serum concentrations of adiponectin are inversely correlated with obesity (degree of adiposity) with obese people having significantly reduced adiponectin levels. Obesity is often accompanied by chronic inflammatory state in adipose tissue. The hypertrophied adipocytes in obese individuals release increase amount of pro-inflammatory adipokines (leptin, TNF, IL-6) and decreased amount of anti-inflammatory adiponectin (González-Muniesa et al., 2017). The available data suggests that factors that lead to increased levels of serum adiponectin are likely to produce favorable metabolic outcomes in the adipose tissue. A recent study has presented evidence to show that acute intake of walnuts (1 g fat/kg bodyweight) increases the post-prandial production of adiponectin better than meals supplemented with either olive oil or butter. The increase in serum adiponectin levels was higher with the walnut-meals than with the other two fat sources for up to six hours. The free fatty acids in circulation were also reduced with the walnut supplementation in comparison to the supplementation with olive oil or butter (Lozano et al., 2013).

Endothelial dysfunction is also a hallmark of cardiovascular disease (Favero, Paganelli, Buffoli, Rodella, & Rezzani, 2014; Matsuzawa, Guddeti, Kwon, Lerman, & Lerman, 2015). Human trials have suggested that dietary supplementation with walnuts attenuates endothelial dysfunction (gauged as improvement of endothelium-dependent vascular reactivity) better than the application of the isoenergetic healthy Mediterranean diet or the inclusion of olive oil in the diet (Ros, 2009). Given the high degree of similarity between pecans and walnuts, similar physiological benefits might be expected also upon inclusion of pecans in the diet.

These results obtained with pecans or related nuts offer insight into the possible mechanisms by which they can exert health benefits in the context of metabolic syndrome and cardiovascular diseases. Polyphenolic compounds from pecans exhibit anti-oxidant activity and can possibly contribute to serum cholesterol homeostasis via

independent mechanisms. Whole pecan nuts bring together the benefits of the "healthy" fat composition together with the protective effects associated with present polyphenolics.

As already discussed above, pecans are a significant source of linoleic acid (C18:2n6), an important PUFA. A cohort study with 2792 participants examined the correlation between fatty acids in circulation and coronary heart disease (CHD) and revealed that high levels of linoleic acid in peripheral circulation were inversely associated with mortality resulting from CHD (Wu et al., 2014).

Data from the NHANES survey (National Health and Nutrition Examination Survey 2005–2010) also highlights the importance of inclusion of tree nuts in the management of obesity and the risk for cardiovascular disease (O'Neil, Fulgoni, & Nicklas, 2015). Regular consumption of tree nuts, including pecans, was associated in this study with a lower Body Mass Index (BMI) ($p = 0.004$), lower waist circumference ($p = 0.008$), systolic blood pressure ($p = 0.001$), and lower Homeostatic Model Assessment Insulin Resistance (HOMA-IR) ($p = 0.043$). The risk for development of obesity was also 25% lower with consumption of ≥1/4th ounce of nuts per day. Additionally, the risk for an increase in waist circumference (truncal/omental obesity) was also reduced by 21% in people who included nuts in their overall diet. Interestingly, the overall availability of other micronutrients, such as vitamins A, E, C, folate, and minerals like zinc, calcium, iron and magnesium was also higher in diets that included tree nuts versus those that were deficient in tree nuts. The overall Healthy Eating Index (HEI)-2005 score was also higher for diets that included tree nuts (O'Neil & Nicklas, 2015). Dietary intake of PUFAs has been inversely associated with all-cause mortality, as seen from the data of 83,349 women from the Nurses' Health Study (1980–2012) and 42,884 men from the Health Professionals' Follow-Up Study (1986–2012) (Wang et al., 2016). The mortality hazard ratios for fat intake were 1.08 (95% CI, 1.03–1.14) for SFAs, 0.81 (95% CI, 0.78–0.84) for PUFAs, 0.89 (95% CI, 0.84–0.94) for MUFAs, and 1.13 (95% CI, 1.07–1.18) for *trans*-fats ($P < 0.001$ for trend for all calculations). These analyses also showed that the substitution of SFAs with PUFAs or MUFAs can reduce the hazard ratio for mortality. A 5% substitution of SFAs with PUFAs can reduce the hazard ratio for all-cause mortality by 27%, and 5% substitution of SFAs with MUFAs results in a 13% reduction of the mortality hazard ratio (Wang et al., 2016). A meta-analysis of twelve clinical trials (n = 450) indicates that dietary inclusion of tree nuts (including pecans) can reduce the levels of glycosylated hemoglobin (HbA1c; [HbA1c mean difference (MD = −0.07% [95% CI: −0.10, −0.03%]; P = 0.0003) and the fasting glucose levels [glucose MD = −0.15 mmol/L [95% CI: −0.27, −0.02 mmol/L]; P = 0.03) in diabetic people who consumed about 56 g of nuts per day (Viguiliouk et al., 2014). Although some of the studies included in this meta-analysis were of poor quality and short duration, a clear tendency was observed, which indicates that dietary inclusion of tree nuts like pecans can help to control relevant metabolic parameters in type 2 diabetes patients.

Beneficiary effects of linoleic acid on cholesterol homeostasis are also evident from the ERA-JUMP clinical trial (Choo et al., 2010). In this study examining 1098 men (40–49 years) an inverse association was observed between the prevalence of linoleic acid in the serum and large VLDL (very low density lipoprotein; $P < 0.001$), total LDL ($P < 0.001$), and small LDL ($P < 0.001$) particle concentrations and the VLDL size ($P < 0.001$). High serum levels of linoleic acid were also positively correlated with large HDL particle concentration ($P < 0.001$) and HDL size ($P < 0.001$) (Choo et al., 2010). These studies show that inclusion of sources of linoleic acid, the most abundant PUFA in pecan nuts, in dietary intake can reduce the overall risk for cardiovascular disease by regulating cholesterol homeostasis.

5. Use of pecans and their constituents in diabetes

Unsaturated fatty acids like linoleic acid (PUFA) and oleic acid (MUFA) have been associated with a lower risk of type 2 diabetes mellitus. Unsaturated fatty acids were demonstrated to act as natural agonists of peroxisome proliferator-activated receptors (PPARs, a group of several transcription factors that are key regulators in the catabolism of fatty acids) and inhibitors of the protein tyrosine phosphatase 1B (PTP1B), a major negative regulator in the insulin signalling pathway (Steinmann et al., 2012; Wang et al., 2014). In this context, linoleic acid, the most abundant PUFA in pecan nuts, was shown to stimulate insulin secretion in rat pancreatic cells (Lai, Teng, & Yang, 2013; Zhao et al., 2013).

Dietary polyphenolic compounds are also capable of exerting antidiabetic effects (Kim, Keogh, & Clifton, 2016). Polyphenolic compounds can inhibit intestinal digestion of starch, enhance the peripheral tissue uptake of the blood glucose and improve the insulin sensitivity of liver and muscle tissues. Polyphenolic compounds from dietary sources can also promote the growth of symbiotic *Lactobacilli* and *Bifidobacterium* spp, thereby contributing to overall gut health. Pecans are a good source of polyphenolic compounds which are also easily bioavailable (Hudthagosol et al., 2011). Since pecans and other tree nuts have a low carbohydrate content, they might be a suitable food supplement for diabetic individuals. A human study involving 1984 participants also indicated that consuming ≥4 servings per week of nuts significantly reduces the risk of developing type 2 diabetes, compared with the consumption of < 1 serving per week (Asghari, Ghorbani, Mirmiran, & Azizi, 2017).

6. EGCG and its bioeffects

EGCG has been also shown to exert diverse favorable bioeffects, including but not limited to the area of obesity, cardiovascular and neurological health, and cancer. Formation of aging-associated products like lipofuscin (an aggregate of oxidized proteins, lipids and metals, a marker for cellular senescence) (Georgakopoulou et al., 2013), in rat pheochromocytoma cells, can be inhibited by treatment with EGCG (Cai et al., 2016). Formation of lipofuscin is linked with the formation amyloidogenic β-sheet structures in this cell model, and treatment with EGCG also counteracted the deposition of amyloid aggregates and lipofuscin in D-galactose-induced brain-ageing mice model (Cai et al., 2016).

In balb/C mice, treatment with EGCG (2.5 mg/kg of body weight) supported neurogenesis and survival of hippocampal neurons in the dentate gyrus of the hippocampus (Ortiz-López et al., 2016). Increased neurogenesis in the dentate gyrus is known to be associated with enhanced memory and learning abilities, and the authors found that the effects of EGCG were caused by the inhibition of apoptosis without affecting neuronal cell proliferation.

Administration of EGCG (effective dosage 100 mg/kg of body weight in rats) has been shown to protect the brain from physical trauma by reducing edema and oxidative stress (Zhang, Wang, Cao, & Wang, 2015). Expression of aquaporin 4 and glial fibrillary acidic protein were found to be attenuated along with an increase in the activities of superoxide dismutase and glutathione peroxidase, in animals that were given EGCG immediately after the induction of trauma. The observed activity pattern suggests that EGCG might have therapeutic potential, if administered early, to treat traumatic brain injuries.

In an *in vitro* model, downregulation of inflammatory responses of EOC 13.31 mouse immortalized microglia cells upon exposure to the amyloid β Alzheimer's disease-associated peptide has been attributed to treatment with EGCG (Wei et al., 2016).

EGCG can enhance the sensitivity of cancer cells towards chemotherapeutic agents. Resistance to chemotherapy drugs in successive rounds of treatment abets the development of resistant and highly malignant cancer cells (McDermott et al., 2015; Silva & Gatenby, 2010). Administration of EGCG to chemotherapy-resistant cancer cells, *in vitro*, resulted in enhanced sensitivity to 5-fluorouracil (5FU) as well as the induction of cell death (Toden, Tran, Tovar-Camargo, Okugawa, & Goel, 2016). Enhancement of cisplatin sensitivity of ovarian cancer cells

was also observed upon treatment with EGCG. The increased sensitivity is attributed to the enhanced expression of copper transporter 1 (CTR1) (Wang et al., 2015). In the same line, aqueous extracts from pecan nut shells (rich of EGCG, gallic, 4-hydroxybenzoic, vanillic, chlorogenic, caffeic and ellagic acid) were shown to induce apoptotic cell death and cell cycle arrest in breast cancer MCF-7 cells, as well as increased with 67% the survival time in Balb-C mice with Ehrlich ascites tumors (Hilbig et al., 2017).

EGCG has also been examined for its role in combating various physiological phenomena associated with the metabolic syndrome, a complex disorder often associated with several conditions from the tetrad of hyperlipidemia, hyperglycemia, obesity, and hypertension. EGCG is a potent anti-oxidant agent owing to its potential for electron transfer as well as its ability to chelate metal ions (Legeay, Rodier, Fillon, Faure, & Clere, 2015). EGCG has also been shown to control hyperlipidemia as well as hyperglycemia in experimental animal models of obesity. A proposed mechanism to explain the role of EGCG in controlling hyperlipidemia is that this molecule can inhibit pancreatic lipase. The inhibition of digestion of fats can lead to postprandial oxidation and breakdown of stored body fats, thereby leading to a reduction in adiposity (Legeay et al., 2015). In addition to promotion of the catabolism of fats, EGCG is also thought to inhibit the anabolism of fatty tissues, overall shifting the lipid metabolism towards a weight loss condition (Wang et al., 2014).

Possible anti-diabetic effects of EGCG are supported by epidemiological studies as well (Keske et al., 2015). Consumption of green tea has been also found to be associated with favorable improvement in the levels of serum cholesterol (Tian et al., 2016).

In addition to green tea, pecans can serve as a significant source of EGCG. The dietary inclusion of pecans as a significant source of EGCG also enhances variety in food choices. Additionally, consumption of a significant portion of solid foods (capable of delivering physiologically relevant quantities of EGCG) is a viable alternative to drinking several cups of beverages like green tea. Bioavailability of EGCG in circulation has been assessed in population studies that have examined long-term repetitive intake of EGCG from foods sources such as green tea (Yuan, 2011, 2013). However, it should be noted that bioaccumulation of EGCG is not evident from several studies and the absorbed EGCG is rapidly cleared from the plasma (Tachibana, 2011). Therefore, serum levels of EGCG must be maintained with adequate regular dietary intake in order to elicit the multiple and tissue-specific physiological modifications that this polyphenolic compound can facilitate. Prolonged and regular intake of foods rich in EGCG is therefore indicated as a desired dietary modification. Along with green tea, pecan nut kernels can also serve as a dietary source of EGCG.

7. Oleic acid and its bioeffects

Oleic acid forms a significant fraction of the MUFAs from pecan nut kernels. Oleic acid is also the major fatty acid species in virgin olive oil (accounting for 49%–83% of its total fatty acids), and significant beneficial effects on cardiovascular health have been demonstrated to be associated with the intake of both olive oil and oleic acid (Piroddi et al., 2017).

In post-menopausal women, intake of oleic acid along with other unsaturated fatty acids, like omega-3 fatty acids and calcium (in the forms of fortified milk), has been linked to reduction in total serum cholesterol (5.78% decrease) and serum LDL-cholesterol (9.79% decrease) (Fonolla-Joya, Reyes-García, García-Martín, López-Huertas, & Muñoz-Torres, 2016). In this 12-month long, controlled study with women aged 45 $\pm$ 7.7 years ($n = 63$ in the intervention group and $n = 54$ in the control group), a significant decrease in the circulatory levels of high-sensitivity C-reactive protein (hsCRP) was also evident. The intervention group showed an average decrease of 28.2% in the serum levels of hsCRP. High-sensitivity C-reactive protein is considered as a prognostic marker of several carcinomas, including gastrointestinal malignancies (Shrotriya, Walsh, Bennani-Baiti, Thomas, & Lorton, 2015; Yuan, 2013).

An examination of the role of oleic acid in cultured cardiomyocytes, vascular smooth muscle cells, and endothelial cells has suggested that oleic acid can attenuate the activation of NF-κB and JNK1/2, which are activated by pro-inflammatory stimuli such as TNF-α and palmitate (Perdomo et al., 2015). This study demonstrates that oleic acid exerts direct anti-inflammatory cellular effect that can be considered as anti-atherogenic.

In a recent study, the effects of oleic acid on overall metabolism and liver health were reported. In this study, mice were injected with palmitate (PA) or oleate (OL) to ascertain their effects on liver and heart metabolism (Enot et al., 2015). Palmitate and oleate are known to promote autophagy in mammalian cells via distinct mechanisms. Palmitate-induced autophagy is related to the activation of phosphatidylinositol 3-kinase, catalytic subunit type 3 (PIK3C3, also known as VPS34) and involves beclin-1 (BECN1), whereas oleate-induced autophagy is independent of these effectors. Enot et al. (2015) observed that palmitate treatment results in the depletion of amino acids that inhibit autophagy from the liver. Depletion of the anti-aging metabolites spermine and spermidine from the liver was also noted when mice were injected with palmitate. In heart tissue, the levels of acyl-carnitines (considered as cardiotoxic) were elevated when mice were injected with palmitate, but not with oleate. Exposure to oleate also resulted in an increase in the levels of nicotinamide adenine dinucleotide (NAD) in the liver (Enot et al., 2015). NAD is a co-factor for the sirtuin family of autophagy-promoting enzymes. These results overall indicate that oleic acid can stimulate metabolic pathways that potentially exhibit anti-aging and lifespan-increasing effects.

An inverse association between the prevalence of arachidonic acid (C20:4n6) and oleic acid (C18:1n9) in blood phospholipids has been reported. Hostmark and Haug examined the relative abundance of these two fatty acids in blood from 11 men and 35 women (mean age: 23.8 $\pm$ 2.5 (SD) years; body mass index: 23.5 $\pm$ 3.2 (SD) kg/m^2) (Høstmark & Haug, 2013), and found an inverse relationship ($r = -0.563$, $p < 0.001$; $n = 46$) in the amounts of arachidonic and oleic acid. The inverse relationship between oleic and arachidonic acid persisted even when other factors such as age and gender were included in the analysis. Furthermore, the study's preliminary estimate of the activity of the delta 5/6-desaturase and elongase-5 enzymes hinted at the non-involvement of these enzymes in the observed inverse relationship (Høstmark & Haug, 2013). Arachidonic acid is a precursor of pro-inflammatory eicosanoids, such as leukotrienes and prostaglandins markedly influencing the immune response and regulating homeostatic processes. The majority of eicosanoids derives from the oxidation of arachidonic acid, which belongs to omega-6 PUFAs. However, other PUFAs (e.g., omega-3 fatty acids) have opposite action to arachidonic acid and in turn inhibit formation of arachidonic acid derived pro-inflammatory eicosanoids (Dennis & Norris, 2015). Low level of cellular content of arachidonic acid is crucial for suppression of pro-inflammatory eicosanoids production. Therefore, overall the maintenance of a low ratio of arachidonic to oleic acid is likely to suppress inflammatory processes that lead to atherogenesis.

The physiological importance of a high prevalence of oleic acid in the serum fatty acid pool is also illustrated in a recent study using a mouse model of experimental sepsis (Gonçalves-de-Albuquerque et al., 2016). In this work, mice were provided oral doses of oleic acid for 14 days prior to induction of sepsis on the 15th day by cecal ligation and puncture. The clinical sepsis scores of the mice provided with oral oleic acid was lower than those of the control mice. The degree of renal and hepatic dysfunction was lower upon oleic acid supplementation, and there was an overall increase in the survival rate. The production of reactive oxygen species was also reduced in animals treated with oleic acid (Gonçalves-de-Albuquerque et al., 2016).

8. Tocopherols and their bioeffects

As already mentioned above, pecan nuts are a rich dietary source of tocopherols (Fig. 2) (Ryan et al., 2006). Four different forms of each tocopherols and tocotrienols are available with the diet and together referred as Vitamin E (Mène-Saffrané & Pellaud, 2017). While alpha-tocopherol is the most potent vitamin E form, the main dietary form is gamma-tocopherol. This general notion is also exemplified from pecan nuts which contain much more gamma-tocopherol (168.5 ± 15.9 mg/g) than alpha-tocopherol (12.2 ± 3.2 mg/g) (Ryan et al., 2006). While tocopherols are found in diverse plant-derived dietary sources, they are especially abundant in vegetable oils and nuts. Vitamin E was originally identified as a nutritional factor important for reproduction (Evans & Bishop, 1922), and consequently it was established that it represents a powerful lipid-soluble antioxidant which protects cell membrane lipids from oxidation (Yokota et al., 2001). Aside from the antioxidant effects, recent research also points to a variety of additional functions of the vitamin E forms, including regulation of cell signalling and gene expression (Brigelius-Flohé, 2006). Whereby alpha-Tocopherol appears to be most potent modulator of gene expression, gamma-tocopherol appears to be highly effective in preventing cancer-related processes (Brigelius-Flohé, 2006). Effectiveness of vitamin E supplementation for disease prevention or treatments has been explored with clinical trials in conditions associated with oxidative stress, such as cardiovascular disease, cancer and neurodegenerative disease. However, these trials were mainly designed based on the misconception of tocopherols and tocotrienols simply acting as antioxidants, usually applying supranutritional amounts, with little attention being paid to the used form of vitamin E and respective gene-regulating potential. Consequently, little or no benefit of direct vitamin E supplementation could be convincingly demonstrated in the majority of the studied conditions, and potential benefits of vitamin E supplementation via dietary modifications remain debatable (Brigelius-Flohé, 2006; Mène-Saffrané & Pellaud, 2017; Traber, 2014).

9. Discussion and conclusions

The inclusion of a variety of unprocessed natural foods is a viable option for management of obesity and its incumbent health problems. Tree nuts, can be incorporated into food regimens as snacks and be used as thickeners for soups and gravies. Consumption of tree nuts can allow for the isocaloric replacement of carbohydrate-generated calories with calories from health-promoting fat species. Although the strategy seems counterintuitive at first, owing to the greater calorific value of fats, unsaturated fatty acids were shown to display a range of health benefits. Nuts also contain other constituents (e.g., EGCG) with beneficial effects on human metabolism. Consumption of tree nuts has been shown to be correlated with improvements in blood lipid parameters as well as reduction in waist circumference. Dietary intake of unsaturated fatty acids has also been linked with a lower hazard ratio for all-cause mortality (Wang et al., 2016).

In this work, we have comprehensively reviewed the composition and potential health benefits of pecan nuts. Pecans are a dietary source of PUFAs like linoleic acid, MUFAs like oleic acid, and polyphenolic compounds such as EGCG. All these constituents have demonstrated effects on health parameters and might work together towards controlling changes that lead to atherosclerosis, obesity and metabolic syndrome (Legeay et al., 2015; Piroddi et al., 2017; Wu et al., 2014).

Polyphenolic compounds from pecans are easily bioavailable and clearly associated with a range of beneficial bioactivities. EGCG, in particular, has been extensively studied, and its beneficial effects on managing obesity have been documented (Legeay et al., 2015; Wang et al., 2014). While the amounts of EGCG from pecan nuts are not comparable to that obtained from green tea, the availability of another food source of EGCG is of interest as an alternative. Pecan nuts can be consumed as a stand-alone snack as well as an ingredient of other food preparations. Being a solid food source, pecans provide an attractive option to drinking several cups of green tea to supply physiologically significant quantities of EGCG.

Over the last few decades, the search for nutritional solutions to the obesity problem has led to the vilification of fats and by extension, foods rich in fats. It is worth noting, however, that layman awareness about the types of fats and their effects on human physiology is limited. Pecan nuts, in particular, are high in fats such as linoleic acid and oleic acid, both of which display potential in preventing obesity and reducing atherosclerotic risk. Foods promoted as being low-fat alternatives are likely to contain high sodium and high sugar content to replace the fats; this combination is more conducive towards increasing of adiposity, rather that acting as a promoter of weight loss. Natural unprocessed fats, such as linoleic acid and oleic acid within nuts, are anti-obesogenic. Supplementation with oils rich in linoleic acid increases lean mass and decreases trunk adipose mass. A study with 139 participants found that higher erythrocyte linoleic acid is associated with improved insulin resistance, body composition, and inflammation markers (Belury et al., 2016). Findings of this and other studies support the potential benefit of the inclusion of natural sources of linoleic acid and other unsaturated fatty acids, like pecans and walnuts, in regular diets.

Pecans represent a good combination of healthy fats and polyphenolic compounds. These constituents are capable of contributing to human health in ways that lead to favorable blood lipid profiles and management of blood glucose. Pecans are similar to walnuts in chemical composition, albeit with some differences. Between these two kinds of nuts, the nutritional value of walnuts has been studied more extensively and their benefit for the management of obesity is more evident (Fink et al., 2014; Haddad, Gaban-Chong, Oda, & Sabaté, 2014; Katz et al., 2012). Consumption of tree nuts, including walnuts has been associated with beneficial effects on a variety of parameters related to cardiovascular and metabolic diseases (O'Neil & Nicklas, 2015; O'Neil et al., 2015).

Healthy MUFAs, PUFAs, polyphenolic compounds, and other constituents from pecans offer significant health benefits in the context of adiposity management and cardiovascular disease prevention. Therefore, similarly to walnuts, pecans may be included as a beneficial supplement in nutrition strategies that are intended to reduce adiposity and improve physiological parameters of cardiovascular health.

Acknowledgements

The authors acknowledge the support by the Austrian Science Fund (FWF) project P25971-B23, and by the Polish KNOW (Leading National Research Centre) Scientific Consortium “Healthy Animal—Safe Food”, decision of Ministry of Science and Higher Education No. 05-1/KNOW2/2015. The authors also thank the ReadyToPub team (readytopub.com) for the assistance in the improvement of the manuscript.

References

Abe, L. T., Lajolo, F. M., & Genovese, M. I. (2010). Comparison of phenol content and antioxidant capacity of nuts. *Food Science and Technology (Campinas), 30*, 254–259.

Adamo, K. B., Ferraro, Z. M., & Brett, K. E. (2012). Can we modify the intrauterine environment to halt the intergenerational cycle of obesity? *International Journal of Environmental Research and Public Health, 9*, 1263–1307.

Asghari, G., Ghorbani, Z., Mirmiran, P., & Azizi, F. (2017). Nut consumption is associated with lower incidence of type 2 diabetes: The Tehran lipid and glucose study. *Diabetes & Metabolism, 43*, 18–24.

Atanasov, A. G., Waltenberger, B., Pferschy-Wenzig, E.-M., Linder, T., Wawrosch, C., Uhrin, P., et al. (2015). Discovery and resupply of pharmacologically active plant-derived natural products: A review. *Biotechnology Advances, 33*, 1582–1614.

Belury, M. A., Cole, R. M., Bailey, B. E., Ke, J. Y., Andridge, R. R., & Kiecolt-Glaser, J. K. (2016). Erythrocyte linoleic acid, but not oleic acid, is associated with improvements in body composition in men and women. *Molecular Nutrition & Food Research, 60*, 1206–1212.

Brigelius-Flohé, R. (2006). Bioactivity of vitamin E. *Nutrition Research Reviews, 19*, 174–186.

Cai, S., Yang, H., Zeng, K., Zhang, J., Zhong, N., Wang, Y., et al. (2016). EGCG inhibited lipofuscin formation based on intercepting amyloidogenic β-sheet-rich structure

conversion. *PloS One, 11*, e0152064.
Ceriello, A., & Motz, E. (2004). Is oxidative stress the pathogenic mechanism underlying insulin resistance, diabetes, and cardiovascular disease? The common soil hypothesis revisited. *Arteriosclerosis, Thrombosis, and Vascular Biology, 24*, 816–823.
Chen, C. O., & Blumberg, J. B. (2008). Phytochemical composition of nuts. *Asia Pacific Journal of Clinical Nutrition, 17*, 329–332.
Choo, J., Ueshima, H., Curb, J. D., Shin, C., Evans, R. W., El-Saed, A., et al. (2010). Serum n− 6 fatty acids and lipoprotein subclasses in middle-aged men: The population-based cross-sectional ERA-JUMP study. *The American Journal of Clinical Nutrition, 91*, 1195–1203.
Damasceno, N. R., Sala-Vila, A., Cofán, M., Pérez-Heras, A. M., Fitó, M., Ruiz-Gutiérrez, V., et al. (2013). Mediterranean diet supplemented with nuts reduces waist circumference and shifts lipoprotein subfractions to a less atherogenic pattern in subjects at high cardiovascular risk. *Atherosclerosis, 230*, 347–353.
Del Gobbo, L. C., Falk, M. C., Feldman, R., Lewis, K., & Mozaffarian, D. (2015). Effects of tree nuts on blood lipids, apolipoproteins, and blood pressure: Systematic review, meta-analysis, and dose-response of 61 controlled intervention trials. *The American Journal of Clinical Nutrition, 102*, 1347–1356.
Dennis, E. A., & Norris, P. C. (2015). Eicosanoid storm in infection and inflammation. *Nature Reviews Immunology, 15*, 511–523.
Domínguez-Avila, J. A., Alvarez-Parrilla, E., López-Díaz, J. A., Maldonado-Mendoza, I. E., del Consuelo Gómez-García, M., & Laura, A. (2015). The pecan nut (*Carya illinoinensis*) and its oil and polyphenolic fractions differentially modulate lipid metabolism and the antioxidant enzyme activities in rats fed high-fat diets. *Food Chemistry, 168*, 529–537.
El-Badry, A. M., Graf, R., & Clavien, P.-A. (2007). Omega 3–Omega 6: What is right for the liver? *Journal of Hepatology, 47*, 718–725.
Engler Ribeiro, P. C., de Britto Policarpi, P., Dal Bo, A., Barbetta, P. A., & Block, J. M. (2017). Impact of pecan nut shell aqueous extract on the oxidative properties of margarines during storage. *Journal of the Science of Food and Agriculture, 97*, 3005–3012.
Enot, D. P., Niso-Santano, M., Durand, S., Chery, A., Pietrocola, F., Vacchelli, E., et al. (2015). Metabolomic analyses reveal that anti-aging metabolites are depleted by palmitate but increased by oleate in vivo. *Cell Cycle, 14*, 2399–2407.
Eskelinen, M. H., Ngandu, T., Helkala, E. L., Tuomilehto, J., Nissinen, A., Soininen, H., et al. (2008). Fat intake at midlife and cognitive impairment later in life: A population-based CAIDE study. *International Journal of Geriatric Psychiatry, 23*, 741.
Evans, H. M., & Bishop, K. S. (1922). On the existence of a hitherto unrecognized dietary factor essential for reproduction. *Science, 56*, 650–651.
Favero, G., Paganelli, C., Buffoli, B., Rodella, L. F., & Rezzani, R. (2014). Endothelium and its alterations in cardiovascular diseases: Life style intervention. *BioMed Research International, 2014*, 801896. http://dx.doi.org/10.1155/2014/801896.
Fink, A., Rüfer, C. E., Le Grandois, J., Roth, A., Aoude-Werner, D., Marchioni, E., et al. (2014). Dietary walnut oil modulates liver steatosis in the obese Zucker rat. *European Journal of Nutrition, 53*, 645–660.
Fonolla-Joya, J., Reyes-García, R., García-Martín, A., López-Huertas, E., & Muñoz-Torres, M. (2016). Daily intake of milk enriched with n-3 fatty acids, oleic acid, and calcium improves metabolic and bone biomarkers in postmenopausal women. *Journal of the American College of Nutrition, 35*, 529–536.
Fraser, G. E., Sabate, J., Beeson, W. L., & Strahan, T. M. (1992). A possible protective effect of nut consumption on risk of coronary heart disease: The adventist health study. *Archives of Internal Medicine, 152*, 1416–1424.
Georgakopoulou, E., Tsimaratou, K., Evangelou, K., Fernandez, M.-P., Zoumpourlis, V., Trougakos, I., et al. (2013). Specific lipofuscin staining as a novel biomarker to detect replicative and stress-induced senescence. A method applicable in cryo-preserved and archival tissues. *Aging (Albany NY), 5*, 37–50.
González-Muniesa, P., Mártinez-González, M.-A., Hu, F. B., Després, J.-P., Matsuzawa, Y., Loos, R. J. F., et al. (2017). Obesity. *Nature Reviews Disease Primers, 3*, 17034.
Gonçalves-de-Albuquerque, C. F., Medeiros-de-Moraes, I. M., de Jesus Oliveira, F. M., Burth, P., Bozza, P. T., Faria, M. V. C., et al. (2016). Omega-9 oleic acid induces fatty acid oxidation and decreases organ dysfunction and mortality in experimental sepsis. *PloS One, 11*, e0153607.
Haddad, E. H. (2011). *Health effects of a pecan [Carya illinoinensis (Wangenh.) K. Koch] nut-rich diet-chapter, Vol 105*.
Haddad, E. H., Gaban-Chong, N., Oda, K., & Sabaté, J. (2014). Effect of a walnut meal on postprandial oxidative stress and antioxidants in healthy individuals. *Nutrition Journal, 13*, 4.
Han, J. C., Lawlor, D. A., & Kimm, S. Y. S. (2010). Childhood obesity. *The Lancet, 375*, 1737–1748.
Hilbig, J., Policarpi, P. B., Grinevicius, V. M. A. S., Mota, N. S. R. S., Toaldo, I. M., Luiz, M. T. B., et al. (2017 Aug 12). Aqueous extract from Pecan nut [*Carya illinoinensis* (Wangenh) C. Koch] shell show activity against breast cancer cell line MCF-7 and Ehrlich ascites tumor in Balb-C mice. *Journal of Ethnopharmacology, 211*, 256–266. http://dx.doi.org/10.1016/j.jep.2017.08.012 [Epub ahead of print].
Høstmark, A. T., & Haug, A. (2013). Percentages of oleic acid and arachidonic acid are inversely related in phospholipids of human sera. *Lipids in Health and Disease, 12*, 106.
Hudthagosol, C., Haddad, E. H., McCarthy, K., Wang, P., Oda, K., & Sabaté, J. (2011). Pecans acutely increase plasma postprandial antioxidant capacity and catechins and decrease LDL oxidation in humans. *The Journal of Nutrition, 141*, 56–62.
Kanoski, S. E., & Davidson, T. L. (2011). Western diet consumption and cognitive impairment: Links to hippocampal dysfunction and obesity. *Physiology & Behavior, 103*, 59–68.
Katz, D. L., Davidhi, A., Ma, Y., Kavak, Y., Bifulco, L., & Njike, V. Y. (2012). Effects of walnuts on endothelial function in overweight adults with visceral obesity: A randomized, controlled, crossover trial. *Journal of the American College of Nutrition, 31*, 415–423.
Keske, M. A., Ng, H. L., Premilovac, D., Rattigan, S., Kim, J., Munir, K., et al. (2015). Vascular and metabolic actions of the green tea polyphenol epigallocatechin gallate. *Current Medicinal Chemistry, 22*(1), 59–69.
Kim, Y., Keogh, J. B., & Clifton, P. M. (2016). Polyphenols and glycemic control. *Nutrients, 8*, 17.
Lai, M.-C., Teng, T.-H., & Yang, C. (2013). The natural PPAR agonist linoleic acid stimulated insulin release in the rat pancreas. *Journal of Veterinary Medical Science, 75*, 1449–1454.
Legeay, S., Rodier, M., Fillon, L., Faure, S., & Clere, N. (2015). Epigallocatechin gallate: A review of its beneficial properties to prevent metabolic syndrome. *Nutrients, 7*, 5443–5468.
Loos, R. J., & Yeo, G. S. (2014). The bigger picture of FTO [mdash] the first GWAS-identified obesity gene. *Nature Reviews Endocrinology, 10*, 51–61.
Lozano, A., Perez-Martinez, P., Marin, C., Tinahones, F. J., Delgado-Lista, J., Cruz-Teno, C., et al. (2013). An acute intake of a walnut-enriched meal improves postprandial adiponectin response in healthy young adults. *Nutrition Research, 33*, 1012–1018.
Luo, S., Romero, A., Adam, T. C., Hu, H. H., Monterosso, J., & Page, K. A. (2013). Abdominal fat is associated with a greater brain reward response to high-calorie food cues in hispanic women. *Obesity, 21*, 2029–2036.
Ma, Y., He, F., & MacGregor, G. (2015). High salt intake: Independent risk factor for obesity. *Hypertension, 66*, 843–849.
Matsuzawa, Y., Guddeti, R. R., Kwon, T.-G., Lerman, L. O., & Lerman, A. (2015). Treating coronary disease and the impact of endothelial dysfunction. *Progress in Cardiovascular Diseases, 57*, 431–442.
McDermott, M., Eustace, A. J., Busschots, S., Breen, L., Crown, J., Clynes, M., et al. (2015). In vitro development of chemotherapy and targeted therapy drug-resistant cancer cell lines: A practical guide with case studies. *Multidrug Resistance in Cancer: Pharmacological Strategies from Basic Research to Clinical Issues, 32*.
Mène-Saffrané, L., & Pellaud, S. (2017). Current strategies for vitamin E biofortification of crops. *Current Opinion in Biotechnology, 44*, 189–197.
Molteni, R., Barnard, R., Ying, Z., Roberts, C., & Gomez-Pinilla, F. (2002). A high-fat, refined sugar diet reduces hippocampal brain-derived neurotrophic factor, neuronal plasticity, and learning. *Neuroscience, 112*, 803–814.
Morgan, W. A., & Clayshulte, B. J. (2000). Pecans lower low density lipoprotein cholesterol in people with normal lipid levels. *Journal of the American Dietetic Association, 100*, 312–318.
Nigro, E., Scudiero, O., Monaco, M. L., Palmieri, A., Mazzarella, G., Costagliola, C., et al. (2014). New insight into adiponectin role in obesity and obesity-related diseases. *BioMed Research International, 2014*, 658913. http://dx.doi.org/10.1155/2014/658913.
Niu, L., Li, J., Chen, M.-S., & Xu, Z.-F. (2014). Determination of oil contents in Sacha inchi (Plukenetia volubilis) seeds at different developmental stages by two methods: Soxhlet extraction and time-domain nuclear magnetic resonance. *Industrial Crops and Products, 56*, 187–190.
O'Neil, C. E., & Nicklas, T. A. (2015). Tree nut consumption is associated with better nutrient adequacy and diet quality in adults: National Health and Nutrition Examination Survey 2005–2010. *Nutrients, 7*, 595–607.
Oginsky, M. F., Goforth, P. B., Nobile, C. W., Lopez-Santiago, L. F., & Ferrario, C. R. (2016). Eating 'junk-food'produces rapid and long-lasting increases in NAc CP-AMPA receptors: Implications for enhanced cue-induced motivation and food addiction. *Neuropsychopharmacology, 41*, 2977–2986.
Ortiz-López, L., Márquez-Valadez, B., Gómez-Sánchez, A., Silva-Lucero, M., Torres-Pérez, M., Téllez-Ballesteros, R., et al. (2016). Green tea compound epigallo-catechin-3-gallate (EGCG) increases neuronal survival in adult hippocampal neurogenesis in vivo and in vitro. *Neuroscience, 322*, 208–220.
O'Neil, C. E., Fulgoni, V. L., & Nicklas, T. A. (2015). Tree nut consumption is associated with better adiposity measures and cardiovascular and metabolic syndrome health risk factors in US adults: NHANES 2005–2010. *Nutrition Journal, 14*, 64.
Park, H. R., Park, M., Choi, J., Park, K.-Y., Chung, H. Y., & Lee, J. (2010). A high-fat diet impairs neurogenesis: Involvement of lipid peroxidation and brain-derived neurotrophic factor. *Neuroscience Letters, 482*, 235–239.
Perdomo, L., Beneit, N., Otero, Y. F., Escribano, Ó., Díaz-Castroverde, S., Gómez-Hernández, A., et al. (2015). Protective role of oleic acid against cardiovascular insulin resistance and in the early and late cellular atherosclerotic process. *Cardiovascular Diabetology, 14*, 75.
Phillips, K. M., Ruggio, D. M., & Ashraf-Khorassani, M. (2005). Phytosterol composition of nuts and seeds commonly consumed in the United States. *Journal of Agricultural and Food Chemistry, 53*, 9436–9445.
Pilkington, T., Stafford, J., Hankin, V., Simmonds, F., & Koerselman, H. (1960). Practical diets for lowering serum lipids. *British Medical Journal, 1*, 23.
Piroddi, M., Albini, A., Fabiani, R., Giovannelli, L., Luceri, C., Natella, F., et al. (2017). Nutrigenomics of extra-virgin olive oil: A review. *Biofactors, 43*, 17–41.
Pistell, P. J., Morrison, C. D., Gupta, S., Knight, A. G., Keller, J. N., Ingram, D. K., et al. (2010). Cognitive impairment following high fat diet consumption is associated with brain inflammation. *Journal of Neuroimmunology, 219*, 25–32.
Rajaram, S., Burke, K., Connell, B., Myint, T., & Sabaté, J. (2001). A monounsaturated fatty acid–rich pecan-enriched diet favorably alters the serum lipid profile of healthy men and women. *The Journal of Nutrition, 131*, 2275–2279.
Ros, E. (2009). Nuts and novel biomarkers of cardiovascular disease. *The American Journal of Clinical Nutrition, 89*, 1649S–1656S.
Ryan, E., Galvin, K., O'connor, T., Maguire, A., & O'brien, N. (2006). Fatty acid profile, tocopherol, squalene and phytosterol content of Brazil, pecan, pine, pistachio and cashew nuts. *International Journal of Food Sciences and Nutrition, 57*, 219–228.
Sabaté, J., Oda, K., & Ros, E. (2010). Nut consumption and blood lipid levels: A pooled analysis of 25 intervention trials. *Archives of Internal Medicine, 170*, 821–827.
Sabate, J., & Wien, M. (2010). Nuts, blood lipids and cardiovascular disease. *Asia Pacific*

Journal of Clinical Nutrition, 19, 131–136.
Salas-Salvadó, J., Guasch-Ferré, M., Bulló, M., & Sabaté, J. (2014). Nuts in the prevention and treatment of metabolic syndrome. *The American Journal of Clinical Nutrition, 100*, 399S–407S.
Schachter, D. (1984). Fluidity and function of hepatocyte plasma membranes. *Hepatology, 4*, 140–151.
Shrotriya, S., Walsh, D., Bennani-Baiti, N., Thomas, S., & Lorton, C. (2015). C-reactive protein is an important biomarker for prognosis tumor recurrence and treatment response in adult solid tumors: A systematic review. *PloS One, 10*, e0143080.
Silva, A. S., & Gatenby, R. A. (2010). A theoretical quantitative model for evolution of cancer chemotherapy resistance. *Biology Direct, 5*, 25.
Steinmann, D., Baumgartner, R. R., Heiss, E. H., Bartenstein, S., Atanasov, A. G., Dirsch, V. M., et al. (2012). Bioguided isolation of (9Z)-Octadec-9-enoic acid from Phellodendron amurense Rupr. and identification of fatty acids as PTP1B inhibitors. *Planta Medica, 78*, 219–224.
Tachibana, H. (2011). Green tea polyphenol sensing. *Proceedings of the Japan Academy, Series B, 87*, 66–80.
Thomas, F., Sibui, P., & Debabrata, M. (2016). Antioxidants in the practice of medicine; what should the clinician know? *Cardiovascular & Haematological Disorders-drug Targets, 16*, 13–20 Formerly Current Drug Targets-Cardiovascular & Hematological Disorders.
Tian, C., Huang, Q., Yang, L., Légaré, S., Angileri, F., Yang, H., et al. (2016). Green tea consumption is associated with reduced incident CHD and improved CHD-related biomarkers in the Dongfeng-Tongji cohort. *Scientific Reports, 6*.
Toden, S., Tran, H.-M., Tovar-Camargo, O. A., Okugawa, Y., & Goel, A. (2016). Epigallocatechin-3-gallate targets cancer stem-like cells and enhances 5-fluorouracil chemosensitivity in colorectal cancer. *Oncotarget, 7*, 16158.
Traber, M. G. (2014). Vitamin E inadequacy in humans: Causes and consequences. *Advances in Nutrition: An International Review Journal, 5*, 503–514.
Venkatachalam, M., Kshirsagar, H. H., Seeram, N. P., Heber, D., Thompson, T. E., Roux, K. H., et al. (2007). Biochemical composition and immunological comparison of select pecan [Carya illinoinensis (Wangenh.) K. Koch] cultivars. *Journal of Agricultural and Food Chemistry, 55*, 9899–9907.
Venkatachalam, M., & Sathe, S. K. (2006). Chemical composition of selected edible nut seeds. *Journal of Agricultural and Food Chemistry, 54*, 4705–4714.
Viguiliouk, E., Kendall, C. W., Mejia, S. B., Cozma, A. I., Ha, V., Mirrahimi, A., et al. (2014). Effect of tree nuts on glycemic control in diabetes: A systematic review and meta-analysis of randomized controlled dietary trials. *PloS One, 9*, e103376.
Waltenberger, B., Mocan, A., Šmejkal, K., Heiss, E. H., & Atanasov, A. G. (2016). Natural products to counteract the epidemic of cardiovascular and metabolic disorders. *Molecules, 21*, 807.
Wang, X., Jiang, P., Wang, P., Yang, C. S., Wang, X., & Feng, Q. (2015). EGCG enhances cisplatin sensitivity by regulating expression of the copper and cisplatin influx transporter CTR1 in ovary cancer. *PloS One, 10*, e0125402.
Wang, D. D., Li, Y., Chiuve, S. E., Stampfer, M. J., Manson, J. E., Rimm, E. B., et al. (2016). Association of specific dietary fats with total and cause-specific mortality. *JAMA Internal Medicine, 176*, 1134–1145.
Wang, L., Waltenberger, B., Pferschy-Wenzig, E.-M., Blunder, M., Liu, X., Malainer, C., et al. (2014). Natural product agonists of peroxisome proliferator-activated receptor gamma (PPARγ): A review. *Biochemical Pharmacology, 92*, 73–89.
Wei, J. C.-C., Huang, H.-C., Chen, W.-J., Huang, C.-N., Peng, C.-H., & Lin, C.-L. (2016). Epigallocatechin gallate attenuates amyloid β-induced inflammation and neurotoxicity in EOC 13.31 microglia. *European Journal of Pharmacology, 770*, 16–24.
Wu, X., Beecher, G. R., Holden, J. M., Haytowitz, D. B., Gebhardt, S. E., & Prior, R. L. (2004). Lipophilic and hydrophilic antioxidant capacities of common foods in the United States. *Journal of Agricultural and Food Chemistry, 52*, 4026–4037.
Wu, J. H., Lemaitre, R. N., King, I. B., Song, X., Psaty, B. M., Siscovick, D. S., et al. (2014 Oct 7). Circulating omega-6 polyunsaturated fatty acids and total and cause-specific mortality: The cardiovascular health study. *Circulation, 130*(15), 1245–1253. http://dx.doi.org/10.1161/CIRCULATIONAHA.114.011590.
Yokota, T., Igarashi, K., Uchihara, T., Jishage, K.-i., Tomita, H., Inaba, A., et al. (2001). Delayed-onset ataxia in mice lacking α-tocopherol transfer protein: Model for neuronal degeneration caused by chronic oxidative stress. *Proceedings of the National Academy of Sciences, 98*, 15185–15190.
Yuan, J. M. (2011). Green tea and prevention of esophageal and lung cancers. *Molecular Nutrition & Food Research, 55*, 886–904.
Yuan, J.-M. (2013). Cancer prevention by green tea: Evidence from epidemiologic studies. *The American Journal of Clinical Nutrition, 98*, 1676S–1681S.
Zhang, B., Wang, B., Cao, S., & Wang, Y. (2015). Epigallocatechin-3-Gallate (EGCG) attenuates traumatic brain injury by inhibition of edema formation and oxidative stress. *The Korean Journal of Physiology & Pharmacology, 19*, 491–497.
Zhao, Y., Wang, L., Qiu, J., Zha, D., Sun, Q., & Chen, C. (2013). Linoleic acid stimulates [Ca 2+] i increase in rat pancreatic beta-cells through both membrane receptor-and intracellular metabolite-mediated pathways. *PloS One, 8*, e60255.