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Review

Brazil nuts and associated health benefits: A review

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ABSTRACT

Epidemiological studies have shown an inverse relationship between nut intakes and chronic diseases such as cardiovascular diseases and cancers. The composition of lipids, minerals, and phytochemicals, and their associated health functions in Brazil nuts are critically reviewed. The nuts have high nutritive food value containing 60–70% oil and 17% protein. Brazil nuts contain abundant dietary antioxidants, especially selenium (Se). One single Brazil nut provides 160% of the US Recommended Daily Allowance (RDA) of selenium - perhaps the best source of Se from plant-based foods. Brazil nuts possess phenolics and flavonoids in both free and bound forms and are rich in tocopherol, phytosterols, and squalene. These compounds' possible beneficial effects are due to their antioxidant and antiproliferative activities, which are linked to a reduced risk for developing atherosclerosis and cancer.

1. Introduction

Brazil nuts are the largest of the commonly consumed nuts from the giant Brazil nut tree (*Bertholletia excelsa*), which is a native of South America. The Brazil nut tree is originally discovered growing in hard, well-drained soil along the Amazon River in countries such as Brazil, Peru, Colombia, Venezuela, and Ecuador. The tree belongs to the lecythis family (*Lecythidaceae*), and is a tropical evergreen tree which can reach a height of over 150 feet. It can in fact tower over the dense forest canopy along the Amazon and Rio Nigro Rivers. Morphologically, the tree has large leathery leaves up to 2 feet long and 6 in wide. The Brazil nuts are round, about 6 in in diameter, with a hard shell nearly 0.5 in thick. They produce a large round or pear-shaped fruit further protected by an outer skin that is thick and woody in character. Each fruit contains anywhere from 12 to 24 three-sided angular nuts. The individual nut is of triangular shape and the nut itself is of stretched shape, irregularly cylindrical and of light cream color. The woody and thick-walled seed capsules are about the size of a large grapefruit and weigh up to 2 kg (wikipedia.org, 2009).

Brazil nuts are not grown commercially in the U.S., but are imported in large quantities. A significant portion of the crop for international trade is sourced from the wild rather than from plantations. Therefore, the collection and export of Brazil nuts is a major industry for countries in the Amazon region. Its importance to the economy of Amazonia has warranted extensive study regarding the ecology and socioeconomics of the Brazil nut harvest (Escobal & Aldana, 2003; Peres et al., 2003; Silvertown, 2004; Zuidema & Boot, 2002). A mature Brazil nut tree can produce between 250 and 500 pounds of unshelled nuts a year. The amount of Brazil alone exports 45,000 tons of nuts annually worth an anticipated $33 million.

Nutritionally, Brazil nuts are a good source of nutrients, including protein, fiber, selenium (Se), magnesium, phosphorus and thiamin. They also contain niacin, vitamin E, vitamin B_6, calcium, iron, potassium, zinc and copper. The nuts have high nutritive food value containing 60–70% oil and 17% protein. Moreover, the oily endosperm contains about 70% unsaturated fats but can also lead to rancidity issues. Brazil nuts are unique in that they are the highest known food source of selenium (Se). They are perhaps the best source of Se from plant-based foods and are a mineral needed for proper thyroid and immune function. Se may also protect against cancers of the prostate, liver and lungs. Due to high levels of phytonutrients, Brazil nuts have been associated with many health benefits, mainly including cholesterol-lowering effects, antioxidant activity, and antiproliferative effects. In this review, Brazil nuts and their associated health effects will be elucidated.

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2. Composition

Despite their similarities in fat and protein, nuts have wide range of chemical compositions. Fig. 1 shows the macronutrient distribution of different nuts whose data can be found in the USDA National Nutrient Database for Standard Reference (USDA Nutrient Database 2009: USNDB). The water, carbohydrate, protein, and total lipid contents of Brazil nuts are 3.5%, 12.3%, 14.3%, and 66.4%, respectively. Coconuts contain the highest water content among the eleven nuts. Peanuts have the highest protein level. Cashews possess the maximum carbohydrate content. Macadamias exhibit the highest total lipid content followed by pecans, pine nuts, Brazil nuts, hazelnuts, walnuts, almonds, peanuts, pistachios, cashews, and coconuts.

2.1. Lipids

Nuts are good sources of unsaturated fatty acids including monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA), and their levels can be found in Fig. 2 as sourced from the USDA Nutrient Database (2009). Brazil nuts contain approximately 15% of saturated fatty acids (SFA), 25% of MUFAs, and 21% of PUFAs. Except coconuts, the saturated fat content of Brazil nuts is among the highest of all the nuts, surpassing even macadamia nuts. Brazil nuts are also important for containing omega-3 fatty acid (α-linolenic acid) near almost about 7% of the total fats. Of the remaining fats, over half is monounsaturated fat (mainly oleic), followed by 25% of polyunsaturated fat (linoleic, omega-6), and around 19% of saturated fat (palmitic and stearic).

An evaluation of the fatty acid profile of ten nuts shows that broad variation exists. These differences or similarities can be found in Table 1, described by the O'Brien group (Maguire, O'sullivan, Galvin, O'Connor, & O'Brien, 2004; Ryan, Galvin, O'Connor, Maguire, & O'Brien, 2006). The profiles were determined via a basic extraction procedure using hexane/isopropanol (3:2, v/v) at ambient temperature under vigorous stirring for 1 h. The primary SFAs detected in all ten nuts were palmitic acid (C16:0) and stearic acid (C18:0), with the Brazil nut containing an especially high concentration of 13.50% and 11.77%, respectively. Oleic acid (C18:1) was the major MUFA present in all ten nuts, which is particularly high in the hazelnut and the almond. The most abundant PUFA present in the ten nuts was linoleic acid (C18:2), which is rich in the walnut and the pecan.

2.2. Minerals

Nuts are also high in trace elements which are essential in the diet. These elements including Cr, Cu, Fe, etc act as cofactors for many physiological and metabolic functions. Typically, the order of element levels in nuts including Brazil nuts follows the pattern Mg > Ca > Fe > Cu > Cr > As > Se. Brazil nuts are rich in Se, although the amount of Se varies greatly (Moodley, Kindness, & Jonnalagadda, 2007). The elemental composition of Brazil nuts can be found in Table 2. In fact, it is the very few consumable products with exceptionally high levels of Se. In contrast, most common foods contain Se in the 0.01–1 μg/g range. Moreover, it is important to note that Brazil nuts are also abundant in magnesium and calcium.

In comparison with other tree nuts, Se is found particularly in Brazil nuts, in greater concentrations in those with Brazil nut shells. The work of Kannamkumarath, Wrobel, Vonderheide, and Caruso (2002) further verified the high values of Se in Brazil nuts and showed it considerably greater than that found in walnuts, cashew nuts and pecans. The Se content in Brazil nuts is primarily dependent on the soil Se concentration. Nuts originating from the central part of Brazil have as over ten times the Se as the nuts harvested in the western part of Brazil. The Se content even varies among nuts from the same tree (Chang, Gutenmann, Reid, & Lisk, 1995; Dumont, Vanhaecke, & Cornelis, 2006). One single Brazil nut provides 160% of the US RDA for Se. The proteins present in Brazil nuts are very high in S-containing amino acids (Ampe et al., 1986; Sun, Altenbach, & Leung, 1987). The presence of these amino acids (mainly Met) boosts the absorption of Se and other minerals in the amino acids. Factors affecting Se level in Brazil nuts are soil type, pH, moisture content, maturity of the tree, and the root system, as well as the position of the nut (Secor & Lisk, 1989).

3. Phytochemicals

Phytochemicals are an array of bioactive non-nutrient compounds which have been related to reductions in the risk of major chronic diseases. They can be found in fruits, vegetables, nuts, whole grains, wine, tea, chocolate and other cocoa products as well as other plant-based foods. An estimated 8000 phytochemicals have been identified from various sources (Shahidi & Naczk, 2003). Nonetheless a large proportion has not yet been

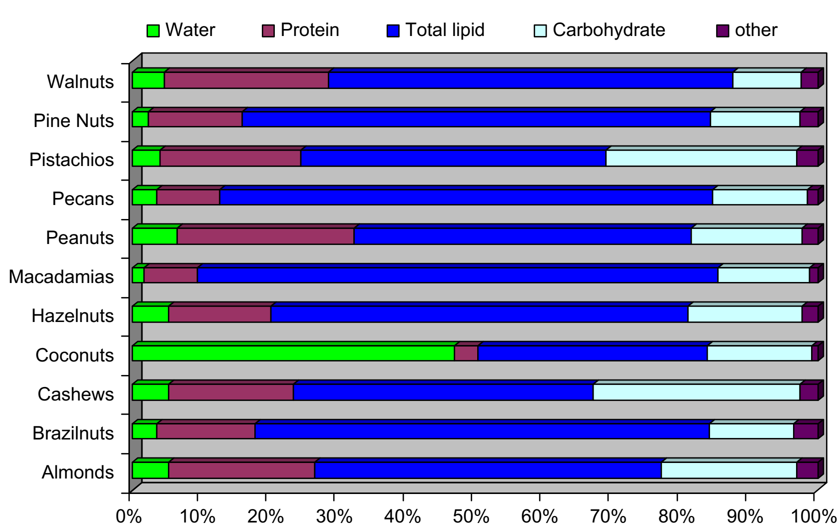


Fig. 1. Macronutrient composition of nuts (Based on data from U.S. National Nutrient Database (USNDB)).

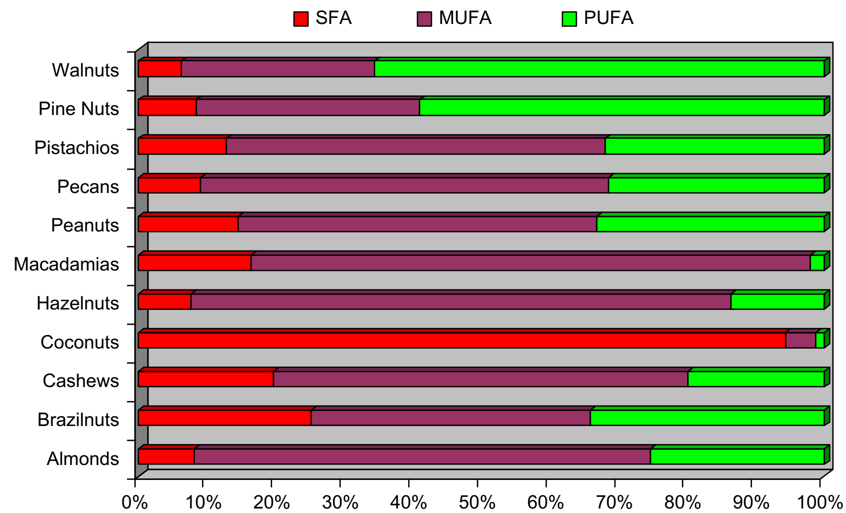


Fig. 2. Fatty acid composition of nuts (Based on data from USNDB).

characterized and therefore their health benefits remain unknown. Quantitative data on phytochemicals in Brazil nuts are limited, diffuse, or dated.

3.1. Phenolics

Phytochemicals can be classified as either alkaloids, carotenoids, phenolics, nitrogen-containing compounds, or organosulfur compounds. Phenolics constitute one of the largest and most ubiquitous groups of phytochemicals. They can be divided into more than ten types based on their chemical structure (Liu, 2004; Strack, 1997). Phenolics share a common chemical structure and differ in their linkages to other compounds. All phenolics possess an aromatic ring bearing one or more hydroxyl groups. The majority of phenolics have a sugar residue, such as a monosaccharide, disaccharide, or oligosaccharide, linked to the carbon skeleton. Other residues include amines, organic acids, carboxylic acids, and lipids. The thousands of identified phenolic structures vary from simple compounds such as phenolic acids with a C6 ring structure to highly polymerized molecules such as tannins.

There is a paucity of information regarding the phenolics in Brazil nuts. Furthermore, the phenolic content in nuts was underestimated in the literature because bound phenolics were not included. The free and bound phenolics in Brazil nuts and other nuts have been subsequently quantified by Yang, Liu, and Halim (2009). In this study, soluble free phenolics of samples were extracted using chilled 80% acetone (1:2, w/v), and 50% methanol/water (1:1, v/v). The methanol/water mixture was washed using hexane by centrifugation. For the bound phenolic extraction, 10 grams of the solid residue from the soluble free extraction were collected, flushed with nitrogen gas, sealed, and hydrolyzed directly with 40 mL of 4 mole/L NaOH at room temperature by shaking for 1 h. The mixture was then neutralized with concentrated hydrochloric acid to pH 7.0. Then 10 mL of solution was applied to a column packed with 20 g of muffled Celite (ratio 1:2, v/w). Approximately 200 mL of 20% methanol/ethyl acetate was used as the mobile phase to wash the phytochemicals out of the column. The washout was evaporated at 45°C to dryness. Bound phenolics were reconstituted in 10 mL of MilliQ water, aliquoted into 2 mL per tube, and saved. The extracts were stored at −40°C until use. The study showed that, among nine tree nuts and peanuts commonly available in the United States, walnuts contained the highest soluble free phenolic content ($p < 0.05$) followed by pecans, peanuts, pistachios, cashews, almonds, Brazil nuts, pine nuts, and macadamia nuts (Table 3). Macadamia nuts had the highest level of bound phenolics ($p < 0.05$) followed by peanuts, hazelnuts, walnuts, pecans, pistachios, cashews, almonds, Brazil nuts, and pine nuts.

Flavonoids, widely distributed in plant-based foods, consist of two aromatic rings (A and B rings) linked by 3 carbons typically in an oxygenated heterocycle C ring (Fig. 3). Based on differences in the heterocycle C ring, flavonoids are categorized as flavonols (quercetin, kaempferol, and myricetin), flavones (luteolin and apigenin), flavanols (catechins, epicatechin, epigallocatechin, epicatechin gallate, and epigallocatechin gallate), flavanones (naringenin), anthocyanidins, and isoflavonoids (genistein, daidzein, dihydrodaidzein, and equol). Naturally occurring flavonoids

Table 1
Fatty acid composition (% of total) of oil extracted from ten edible nuts.

Oil sample	Fatty acid													
	14:0	16:0	16:1	17:0	18:0	18:1	18:2	18:3	20:0	20:1	20:3	20:5	22:0	22:1	22:6
Almond	0.06	6.85	0.63	ND	1.29	69.24	21.52	0.16	0.16	ND	ND	ND	0.05	ND	ND
Brazil Nut	0.06	13.50	0.33	0.22	11.77	29.09	42.80	0.20	0.54	0.21	ND	ND	0.12	0.34	ND
Cashew	0.07	9.93	0.36	0.14	8.70	57.24	20.80	0.23	0.97	0.25	ND	ND	0.39	0.28	ND
Hazelnut	0.13	5.82	0.29	ND	2.74	79.30	10.39	0.46	0.16	ND	ND	ND	ND	ND	ND
Macadamia	0.95	8.37	17.28	ND	3.17	65.15	2.31	0.06	2.28	ND	0.01	ND	0.2	ND	0.27
Peanut	0.03	11.08	0.15	ND	2.66	38.41	44.6	0.58	1.57	ND	0.02	0.02	0.1	ND	0.75
Pecan	ND	4.28	0.09	0.10	1.80	40.63	50.31	0.65	Tr	1.21	ND	ND	0.16	0.25	ND
Pine nut	ND	6.87	0.14	0.10	4.48	39.55	45.41	0.63	1.04	1.06	ND	ND	0.33	0.40	ND
Pistachio	0.09	7.42	0.70	ND	0.86	58.19	30.27	0.44	0.59	0.60	ND	ND	0.34	0.57	ND
Walnut	0.13	6.70	0.23	ND	2.27	21.00	57.46	11.58	0.08	ND	ND	0.06	0.07	ND	ND

Results are the mean value from three independent experiments. ND: not detected. Tr: trace amounts (<0.05).

Table 2
Total element concentrations in Brazil nut expressed as μg g^{-1} of sample.

Element	As	Ca	Cr	Cu	Fe	Mg	Mn	Se	Zn
Amount	0.017 ± 0.002	7432.8 ± 10.2	1.34 ± 0.19	59.44 ± 0.51	74.26 ± 0.46	9678.5 ± 68.5	3.40 ± 0.21	36.1 ± 0.4	110.31 ± 1.25

Table 3
Total phenolic and flavonoid contents of nine tree nuts and peanuts (mean ± SD, $n = 3$).

Edible nut seeds	Phenolics (mg/100 g)			Flavonoids (mg/100 g)		
	Free Form	Bound Form	Total	Free Form	Bound Form	Total
Almonds	83.0 ± 1.3	129.9 ± 13	212.9 ± 12.3	39.8 ± 2.0	53.7 ± 11.9	93.5 ± 10.8
Brazil Nuts	46.2 ± 5.7	123.1 ± 18.4	169.2 ± 14.6	29.2 ± 7.2	78.6 ± 9.2	107.8 ± 6.0
Cashews	86.7 ± 8.1	229.7 ± 15.1	316.4 ± 7.0	42.1 ± 3.8	21.6 ± 5.2	63.7 ± 2.1
Hazelnuts	22.5 ± 1.1	292.2 ± 48.4	314.8 ± 47.3	13.9 ± 2.3	99.8 ± 28.5	113.7 ± 30.2
Macadamia Nuts	36.2 ± 2.6	461.7 ± 51.2	497.8 ± 52.6	9.4 ± 0.7	128.5 ± 9.3	137.9 ± 9.9
Peanuts	352.8 ± 22.2	293.1 ± 25.0	645.9 ± 47.0	145.5 ± 10.0	44.2 ± 5.2	189.8 ± 13.1
Pecans	1227.3 ± 8.4	236.6 ± 28.1	1463.9 ± 32.3	639.3 ± 17.0	65.4 ± 12.7	704.7 ± 29.5
Pine Nuts	39.1 ± 0.6	113.8 ± 14.3	152.9 ± 14.1	13.0 ± 1.5	32.0 ± 6.8	45.0 ± 5.4
Pistachios	339.6 ± 15.1	232.2 ± 13.3	571.8 ± 12.5	87.4 ± 14.0	55.9 ± 13.6	143.3 ± 18.7
Walnuts	1325.1 ± 37.4	255.4 ± 25.0	1580.5 ± 58.0	535.4 ± 71.5	209.4 ± 22.1	744.8 ± 93.3

are mostly conjugated in glycosylated or esterified forms but can occur as aglycones, especially as a result of the effects of food processing (Hollman & Arts, 2000). It is estimated that flavonoids account for nearly 60% of the phenolics in our diet, and the remaining 30% are from phenolic acids.

Among the nine tree nuts and peanuts tested (Table 3), pecans contained the highest soluble free flavonoid content ($p < 0.05$), followed by walnuts, peanuts, pistachios, cashews, almonds, Brazil nuts, hazelnuts, pine nuts, and macadamia nuts. Walnuts had the highest bound flavonoid content ($p < 0.05$) followed by macadamia nuts, hazelnuts, Brazil nuts, pecans, pistachios, almonds, peanuts, pine nuts, and cashews (Yang et al., 2009).

3.2. Tocopherol

Tocopherols (Fig. 4) are powerful antioxidants and have been shown to lower the risk of coronary heart disease (CHD) by inhibiting LDL cholesterol oxidation (Meydani, 2004). In 100 grams of Brazil nuts (NDB No: 12078), there are 5.73 ± 1.54 mg of α-tocopherol, 7.87 ± 2.15 mg of γ-tocopherol, and 0.77 ± 0.66 mg of δ-tocopherol. No β-tocopherol was found in Brazil nuts. Theα, γ-Tocopherol contents of oil extracted from the ten nuts were quantified (Maguire et al., 2004; Ryan et al., 2006). The contents of total tocopherols are dramatically different, ranging from 452.0 to 60.8 μg/g oil. The decreasing order of total tocopherol level was almond > hazelnut > walnut > pistachio > pine nut > Brazil nut > pecan > peanut > macadamia > cashew. α-Tocopherol was detected in contents ranging from 3.6 ± 1.4 in the cashews to 439.5 ± 4.8 μg/g oil in the almonds. γ-Tocopherol concentration ranged from 12.5 ± 2.1 in the almond to 300.5 ± 31.0 μg/g oil in the walnuts (Table 4).

3.3. Phytosterols

Phytosterols, found in plant foods, are structurally and functionally analogous to cholesterol in vertebrate animals. These phytochemicals possess the same basic cyclopentano-perhydrophenanthrene ring as cholesterol, but differ in the presence of a C24 side chain, the position and configuration of unsaturated double bonds and the optical rotation at the chiral carbons (Fig. 5) (Goad, 1991; Grunwald, 1975). Phytosterols are categorized by the number of methyl groups at the C4 position. In foods, phytosterols are the 28- and 29-carbon 4-desmethyl sterols including β-Sitosterol, campesterol, and stigmasterol. In fact 95% of the total phytosterols in the diet are made up by β-Sitosterol, campesterol, and stigmasterol. Biologically, phytosterols reduce blood cholesterol, lower the risk of certain types of cancer, and enhance immune

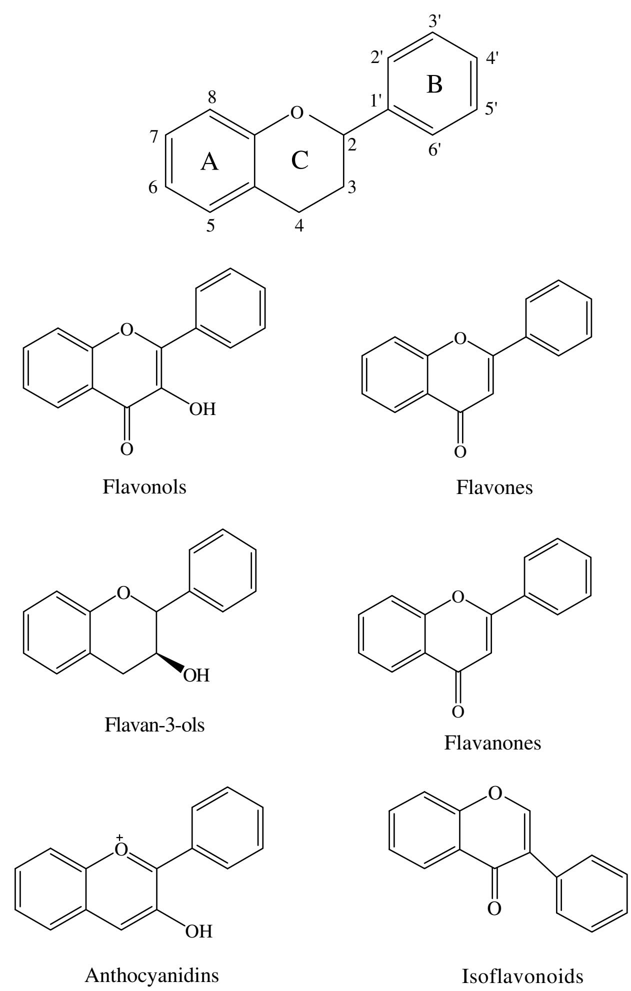


Fig. 3. Structure of main classes of dietary flavonoids.

Tocopherol Homologues	Substitutions		
	R_1	R_2	R_3
α- tocopherol	CH_3	CH_3	CH_3
β- tocopherol	CH_3	H	CH_3
γ- tocopherol	H	CH_3	CH_3
δ- tocopherol	H	H	CH_3

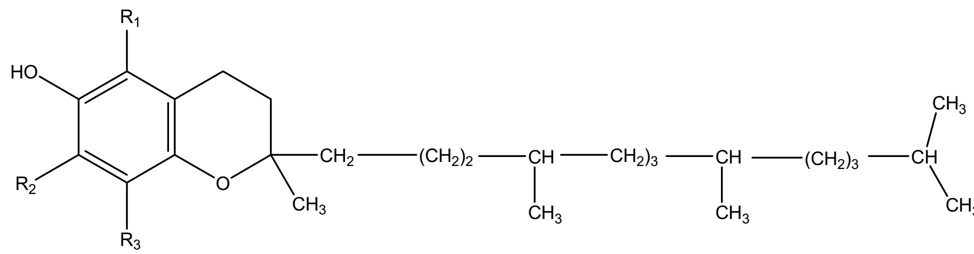


Fig. 4. Chemical structure of tocopherol.

function (Awad & Fink, 2000; Bouic, 2001; Ling & Jones, 1995; Moreau, Whitaker, & Hicks, 2002).

The total phytosterols of the ten nuts are shown in Table 4. The pistachio had the highest phytosterol content, averaging 5586 μg/g oil, while the lowest content was measured in hazelnut, averaging 1096 μg/g oil. There is approximately a 5-fold difference in phytosterol content between the highest and the lowest ranked nuts. The decreasing order of total phytosterol content was pistachio > pine nut > almond > cashew > pecan > Brazil nut > peanut > macadamia > walnut > hazelnut. β-Sitosterol was the most abundant sterol, ranging from 991.2 ± 73.2 in the hazelnut to 4685.9 ± 154.1 μg/g oil in the pistachio. There was approximately a 4.8-fold difference in β-Sitosterol content between the highest and the lowest ranked nuts. In addition, β-Sitosterol was found in much higher concentrations than campesterol and stigmasterol in all ten nuts. The β-Sitosterol, campesterol, and stigmasterol contents present in Brazil nut were 1325.4 ± 68.1, 26.9 ± 4.4, and 577.5 ± 34.3 μg/g oil, respectively.

3.4. Squalene

Squalene (Fig. 6) is a hydrocarbon steroid precursor with a linear configuration and 30 carbons in length. It can be found in both plant and animal cells. Goodwin (1996) reported that squalene is converted to phytosterols in plant cells. Squalene is a powerful antioxidant to inhibit lipid oxidation, be an effective quencher of singlet oxygen, suppress sodium arsenite-induced sister chromatid exchanges in Chinese ovary-K1 cells, and protect against H_2O_2-induced SCE in Chinese hamster V79 cells (Fan, Ho, Yeoh, Lin, & Lee, 1996; Kohno et al., 1995; O'Sullivan, Woods, & O'Brien, 2002).

From Table 4, the Brazil nut (1377.8 ± 8.4) contained the highest squalene content. The lowest squalene level occurred in the walnut (9.4 ± 1.8), with around a 147-fold difference in squalene between the highest and the lowest ranked nuts.

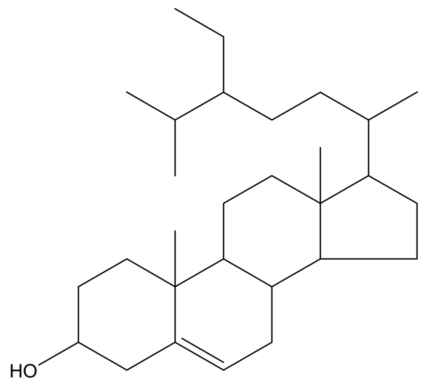
4. Health benefits

Brazil nuts are a good source of micronutrients, particularly selenium, phytosterols, tocopherol, squalene, and phenolics all attributed to various potential health benefits. Moreover, the FDA approved the following health claim for Brazil Nuts: "Scientific evidence suggests, but does not prove, that eating 1.5 ounces per day of most nuts, such as Brazil nuts, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease (FDA, 2008)". The rich micronutrient composition allows for numerous pathways in which Brazil nuts can help to prevent heart disease and cancer. Although not all mechanisms have been elucidated, one proposed suggests that the reduced risk of chronic disease with consuming Brazil nuts is from their antioxidant activity and ability to regulate hormone levels in the body (González & Salas-Salvadó, 2006). Moreover, extensive scientific evidence in cell cultures, experimental studies performed in animals, and observational epidemiological studies indicates that antioxidants can prevent the development of cancer and cardiovascular diseases (Kris-Etherton, Zhao, Binkoski, Coval, & Etherton, 2001). Of the antioxidant

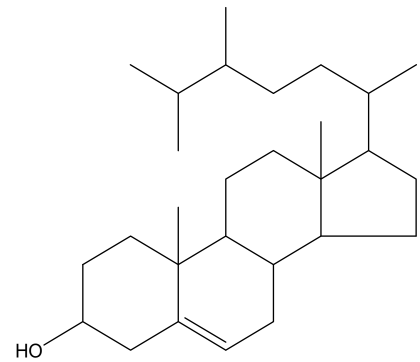
Table 4
Tocopherol, squalene, and phytosterol content of oil extracted from ten edible nuts.

Oil Sample	Tocoperol (μg/g oil)		Squalene (μg/g oil)	Phytosterol (μg/g oil)		
	α-Tocopherol	γ-Tocopherol		β-Sitosterol	Campesterol	Stigmasterol
Almond	439.5 ± 4.8	12.5 ± 2.1	95.0 ± 8.5	2071.7 ± 25.9	55.0 ± 10.8	51.7 ± 3.6
Brazil Nut	82.9 ± 9.5	116.2 ± 5.1	1377.8 ± 8.4	1325.4 ± 68.1	26.9 ± 4.4	577.5 ± 34.3
Cashew	3.6 ± 1.4	57.2 ± 6.2	89.4 ± 9.7	1768.0 ± 210.6	105.3 ± 16.0	116.7 ± 12.6
Hazelnut	310.1 ± 31.1	61.2 ± 29.8	186.4 ± 11.6	991.2 ± 73.2	66.7 ± 6.7	38.1 ± 4.0
Macadamia	122.3 ± 24.5	Tr	185.0 ± 27.2	1506.7 ± 140.5	73.3 ± 8.9	38.3 ± 2.7
Peanut	87.9 ± 6.7	60.3 ± 6.7	98.3 ± 13.4	1363.3 ± 103.9	198.3 ± 21.4	163.3 ± 23.8
Pecan	12.2 ± 3.2	168.5 ± 15.9	151.7 ± 10.8	1572.4 ± 41.0	52.2 ± 7.1	340.4 ± 29.5
Pine nut	124.3 ± 9.4	105.2 ± 7.2	39.5 ± 7.7	1841.7 ± 125.2	214.9 ± 13.7	680.5 ± 45.7
Pistachio	15.6 ± 1.2	275.4 ± 19.8	91.4 ± 18.9	4685.9 ± 154.1	236.8 ± 24.8	663.3 ± 61.0
Walnut	20.6 ± 8.2	300.5 ± 31.0	9.4 ± 1.8	1129.5 ± 124.6	51.0 ± 2.9	55.5 ± 11.0

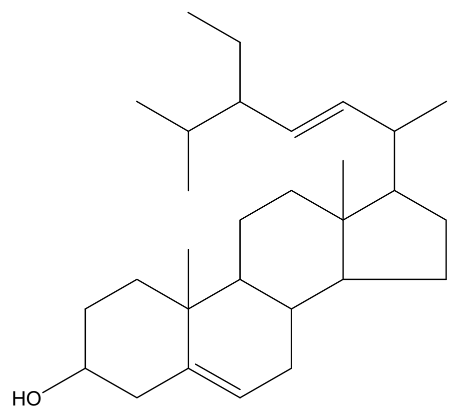
Results are the mean ± standard error of the mean for at least three independent experiments. Tr: trace amounts.



β-Sitosterol



campesterol



stigmasterol

Fig. 5. Chemical structure of β-Sitosterol, campesterol, and stigmasterol.

compounds contained in Brazil nuts, one of the most important is Se, another is vitamin E.

Se is an essential trace mineral. Adequate Se is necessary for the normal functioning of the immune system and thyroid gland. Se is not directly an antioxidant but an important component of antioxidant enzymes. It is receiving considerable attention for its possible role as an effective naturally occurring anti-carcinogenic agent. Animal studies have shown a beneficial effect of high-Se levels in the prevention of cancer (Patrick, 2004). The anti-carcinogenic activity of Se, partially in combination with vitamin E or other antioxidants, was found in non-prostate cancer animal models (Combs & Scott, 1977; Horvath & Ip, 1983; Lippman et al., 2005). The chemopreventive mechanisms of Se may be attributed to its ability to act as an antioxidant (Zhong & Oberley, 2001), function in cell cycle arrest (Dong, Zhang, Hawthorn, Ganther, & Ip, 2003), inhibit proliferation (Venkateswaran, Fleshner, & Klotz, 2004), induce apoptosis (Jiang, Wang, Ganther, & Lu, 2001), facilitate DNA repair by activation of p53 (Seo, Kelley, & Smith, 2002), be a key component of selenozymes (Driscoll & Copeland, 2003; Menter, Sabichi, & Lippman, 2000), and disrupt androgen receptor signaling (Dong et al., 2004). Se may also boost mood and mental performance in patients with early Alzheimers disease (Benton, 2002).

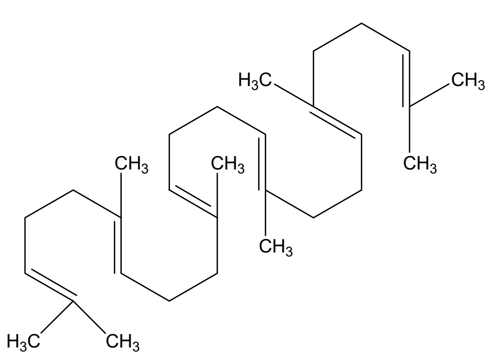


Fig. 6. Chemical structure of squalene.

Although some studies have shown that the effects of Se on prostate cancer are inconclusive, epidemiological evidence and randomized intervention trials suggest that the risk of prostate cancer may be lowered by increased Se intake (Dunn, Ryan, & Ford, 2009; Lippman et al., 2009). The redox characteristics of selenocysteine impart antioxidant properties to selenoenzymes, such as glutathione peroxidases, selenoprotein P, and thioredoxin reductase, which are all expressed in the prostate (Brooks et al., 2001; Calvo et al., 2002; Gladyshev & Hatfield, 1999). In the mid-1990s, the Nutritional Prevention of Cancer Trial study found that men who received 200 μg Se/day exhibited a significantly reduced risk of prostate cancer (Clark et al., 1996; Duffield-Lillico et al., 2002). This study highlighted the ability of Se to have potential preventive effects against prostate cancer. Similarly, in the Baltimore Longitudinal Study of Aging (BLSA), researchers at Stanford University delivered a case control study of 52 men with known prostate cancer and compared them to 96 men with no detectable prostatic disease. It was found that high blood levels of the mineral Se were associated with a four- to five-fold decrease in the risk of prostate cancer. Since plasma Se decreases with patient age, particularly older men, the evidence indicated that supplementing the diet with Se may reduce the risk of prostate cancer (Brooks et al., 2001). In a Harvard Physicians' Health Study (Li et al., 2004), 586 men who developed prostate cancer during a 13-year follow-up were compared with 577 control subjects. Those with the highest baseline plasma Se levels also had a 48% reduced risk of prostate cancer than those with the lowest levels. Men with prostate-specific antigen (PSA) scores of less than 4 and high plasma Se levels exhibited a far lower risk of prostate cancer compared with others. Therefore, the higher levels of Se may also slow prostate cancer tumor progression. Moreover, the Selenium and Vitamin E Cancer Prevention Trial (SELECT), a randomized prospective double-blind study, will determine whether Se and vitamin E lower the risk of prostate cancer in 32,400 healthy men. Enrollment began in 2001 and final results are anticipated by 2013. The preclinical, epidemiological, and phase III data suggests that Se and vitamin E indeed have potential efficacy for preventing prostate cancer (Klein et al., 2003).

A relationship between the intake of Brazil nuts and the prevention of mammary cancer was also reported by Ip and Lisk (1994a). Their study evaluated the preventive nature of Se naturally present in food on cancer. A dose-dependent inhibitory response was observed in two separate experiments at dietary Se concentrations of 1–3 μg/g in dimethylbenz[α] anthracene-treated rat model. The natural source of Se utilized in these studies was Brazil nuts. Moreover, these studies concluded that Brazil nuts were at least as effective as sodium selenite when similar levels of Se were administered to rats. A subsequent study by the authors went on to evaluate the nutritional biopotency of Se from Brazil nuts in two selenoenzymes - glutathione peroxidase and type I 5'-deiodinase, of Se-deficient rats. Their result suggested that 0.05–0.2 μg/g of dietary Se from Brazil nuts produced an increase in enzyme restoration. During Brazil nuts feeding trials of mammary cancer patients a direct correlation between the quantities of Brazil nuts consumed and increased Se retention in the liver, kidney, mammary gland, and plasma has been observed. The magnitude of tissue Se accumulation was proportional to the amount of Brazil nuts added to the diet. Natural and food-derived forms of Se may have beneficial effects not shared by human-synthesized Se compounds (Schrauzer, 2000). In order to compare the physiological response of high-Se natural products with that elicited by selenite or selenomethionine, three Se-rich natural products (high-Se garlic, high-Se onion and Brazil nuts) were fed to rats (Ip & Lisk, 1994b). Endpoints typical of mammary cancer studies including tissue Se profiles, liver glutathione level, and mammary cancer inhibition in the dimethylbenz[α] anthracene model were evaluated. The result showed that the ingestion of high-Se garlic and onion did not lead to an exaggerated accumulation of tissue Se; however, the feeding of Brazil nuts exhibited an accumulation of tissue selenium.

Epidemiological studies in humans have shown that a high consumption of vitamin E can protect against tumors in different locations (WCRF & AICR, 1997). Numerous experimental studies in different cell lines and animals have shown that α-tocopherol can inhibit cell proliferation (Greenwald, Clifford, & Milner, 2001) and, therefore, lower the risk of carcinogenesis. As previously mentioned, synergistic effects of Se and Vitamin E as well as other antioxidants play an important role in the prevention of prostate cancer cells (Blot et al., 1993; Peters et al., 2007; Richards, Benghuzzi, Tucci, & Hughes, 2003; Venkateswaran, Klotz, & Fleshner, 2002; Zu & Ip, 2003). Epidemiologic study, conducted in malnourished populations in Linxian, China, also showed that the combined intervention of Se, vitamin E, and β-carotene has been associated with the reduced incidence and mortality of gastric cancer and total cancer. Lastly, the high Se consumption may protect humans from lung cancer (Reid et al., 2002). A study of antiproliferative activity in cell cultures for different nuts was performed by Yang et al (2009). The inhibition of $HepG_2$ human liver and Caco-2 human colon cancer cell proliferation was observed in a dose-dependent manner after exposure to free soluble nut extracts. The antiproliferative activities of ten nuts differed in the $HepG_2$ and Caco-2 cell lines. Nuts showed a greater ability to inhibit Caco-2 cell proliferation than $HepG_2$ cell proliferation. The inhibition of cancer cell proliferation by nut extracts can be partially explained by the total phenolic contents in the nuts tested, suggesting that a specific phenolic compound or a class of phenolics in nuts was responsible for their antiproliferative activities. Alternatively, particular phenolic compounds may act additively, synergistically, and/or antagonistically with other compounds to play a role in antiproliferative activity.

5. Conclusion

Brazil nuts have been found to be rich sources of unsaturated fatty acids, protein, fiber, micronutrients, vitamins, and phytochemicals. Brazil nuts with high Se levels discourage the aging process and stimulate the immune system. They may slow the aging process, stimulate the immune system, and protect against heart disease and certain forms of cancer. There are numerous mechanisms by which the components present in Brazil nuts can intervene in the prevention of cancer, although they have not been fully elucidated. Phytochemical extracts from Brazil nuts exhibit antioxidant and antiproliferative activities, and the majority of total antioxidant and antiproliferative activities are from the combination of phytochemicals and Se. It is proposed that the nutrients in Brazil nuts work independently and/or synergistically with one other to achieve its health benefits. Practically a diet modified to consume a wide variety of plant-based foods including Brazil nuts is scientifically supported to optimize the general health and lower the risk of chronic diseases. The present review article summarizes the evidence for minerals, phytochemicals, their mechanisms, and their associated health benefits in Brazil nuts. Nonetheless, there is still an absence of information on the phytochemicals present in Brazil nuts. Although several of the bioactive constituents in Brazil nuts have been identified, many more remain unidentified and uncharacterized. Further research of regarding these phytochemicals for biological relevance of the Brazil nuts such as antioxidant and anti-cancer activities, the effect on functional enzymes and signal transducers is worthy of investigation.

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