

Medicinal Chemistry of Brazil Nuts: An Overview

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Abstract: Brazil nuts are very consumed in the North of Brazil as well in other regions. Those nuts are rich in mono and polyunsaturated fatty acids, as well as essential and non-essential aminoacid residues, selenium, tocopherols and phytosterols. Although some studies pointed out some protective effect of Brazil nuts against cancer, in fact the best evidence supports cardiometabolic protection by regular ingestion of 1 nut *per day*.

Keywords: Cardiovascular, selenium, vitamin E, phytosterols, arginine.

INTRODUCTION

Brazil nut (*Bertholletia excelsa*) is a seed from a taller tree native from South America, especially at the border of the Amazon and Nigro rivers, which grows in Brazil, Colombia, Ecuador, Peru, and Venezuela [1].

Brazil nut is an adequate source of protein (17%), oil (60-70%), fiber, selenium, vitamin E, phosphorus, potassium, thiamin, magnesium, niacin, piridoxin, iron, zinc, calcium and copper [1].

Brazil nut is considered the richest food source of selenium in nature, although the content of this element is dependent on selenium concentration in the soil that is lower in acidic soil conditions [2].

The objective of this article is to bring an overview of the health benefits of bioactive compounds present in Brazil nuts.

EPIDEMIOLOGICAL ASPECTS

One of the oldest studies regarding nut comprises an article of composition of Cashew nut published in 1930 [3].

Just 59 years later a position statement on fiber and health, endorsed by the American Medical Association, stated that many fiber-rich foods, including nuts, should be regularly eaten by the population in order to achieve better health [4].

The classical Adventist Health Study was the first to support the idea that regular dietary nut consumption (5 times *per week*) decreased by 48% the risk of deaths by coronary heart [5].

Similar interesting results were found some years later in the Nurses' Health Study. In that study, Hu *et al.* [6] reported that daily dietary intake of nuts significantly reduced the risk of non-fatal myocardial infarction and coronary heart disease.

Recent meta-analyses studies that have been evaluated the relationship between nut consumption and health outcomes reported that regular intake of those seeds can materially decrease the risk of both cardiovascular and cerebrovascular diseases [7,8].

It has been estimated that about 13% of the population from the Central-Western region of Brazil consume Brazil nuts and other nuts at least three days per week [9].

BRAZIL NUTS: A COMPOSITION WITH SPECIAL BENEFITS?

Brazil nuts are considered very nutritious, since they contain considerable amounts of selenium, tocopherols, phytosterols, fiber, aminoacids and protein, oils, potassium, magnesium, calcium, zinc, manganese and copper [10].

ARGININE AND AMINOACIDS IN BRAZIL NUTS

Brazil nut is a good source of protein and aminoacids. It is rich in essential aminoacids like leucine, valine, lysine, methionine, cysteine, phenylalanine and tyrosine, but it also contains a considerable amount of non-essential aminoacids such as glycine, proline, serine, alanine. It contains also the highest arginine amounts amongst the oilseeds, and has a higher content of aspartic and glutamic acids [11].

The arginine has many biological activities such as [12-14]:

- Stimulation of prolactin, glucagon, and insulin secretions;

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- Precursor of nitric oxide biosynthesis, a potent vasodilator agent;
- Increasing collagen synthesis and wound healing;
- Stimulation of cellular immunity (increases both NK cells populations, delayed-type hypersensitivity responses, and T-cell mitogenic responses; enhance cytokines' releasing).

BRAZIL NUT: FROM FATTY ACIDS TO PHYTOSTEROLS

Bertholletia excelsa nuts are rich food sources of both monounsaturated (omega-9= oleic acid) and polyunsaturated (n-6 or omega-6, the *cis*-linoleic acid) fatty acids as well as tocopherols (α and γ), and phytosterols such as β -sitosterol and estigmasterol, with considerable amounts of campesterol, another important phytosterol [15,16].

It should be emphasized that phytosterols can reduce both blood cholesterol and inflammatory biomarkers decreasing the risk of atherosclerosis and thrombosis [17-19].

The composition of monounsaturated, polyunsaturated fatty acids and fiber of those nuts are responsible for the protective effect against cardiovascular diseases [20].

Monounsaturated and polyunsaturated fatty acids have antioxidant activity and their regular intake protects brain, heart and other tissues, organs and cells against cell degeneration, cell death and aging [21]. Furthermore, both mono- and polyunsaturated fats have anti-inflammatory properties and also acts as lipid-layers that can stabilize mitochondrial membranes, improving cell respiratory function which is associated with increased lifespan and decreased risk of cardiometabolic and neurodegenerative diseases [22,23].

POLYPHENOLS OF BRAZIL NUTS

Brazil nuts are also rich in phenolic compounds [1,15,24].

Polyphenols also display antioxidant, anti-inflammatory and anti-apoptotic activities which can rescue cell life, decreasing cell degeneration and death. Their ingestion displays positive impacts on reduction of both morbidity and mortality as well as improvement on life span [22,23].

COENZYME Q10: IT PROTECTS BRAIN, SPERM AND THE WHOLE BODY!

Coenzyme Q10 (ubiquinone), an electron acceptor of the complex I and II of the respiratory chain, is present in peanuts and nuts [25-27]. The real content of ubiquinone in Brazil nuts must be determined.

Ubiquinone restores mitochondrial respiration in many diseases. When administered to a mice model of amyotrophic lateral sclerosis, coenzyme Q10 reversed mitochondrial decay and decreased brain striatal damage induced by 3-nitropropionic acid, increasing animal life span [28]. Stimulation of mitochondrial ubiquinone inhibit hydrogen peroxide-induced cell death (by apoptosis), but had no effect on tumor necrosis factor- α induced cell death [29]. Soy oil (92mg/100g), colza seed oil (73mg/100g), sesame seed oil (32mg/100g), meat (32mg/100g), peanut (27mg/100g), nuts (19mg/100g) and other foods are plenty of coenzyme Q10 [25].

It should be noted that coenzyme Q10 is important to prevent mitochondrial dysfunction in cardiovascular diseases, sperm function, neurological diseases and pancreatic cells, among other cell and tissue types [26,27].

VITAMIN E AND TOCOPHEROLS IN BRAZIL NUTS

Vitamin E should also be considered a mitochondrial stabilizer agent. It has been observed that vitamin E deficiency was associated with increased lipid peroxidation and partially impaired mitochondrial respiration, since NADH-CoQ10 reductase and cytochrome oxidase activities were diminished in skeletal muscle cells [30]. However, the same authors reported increased mitochondrial activities and lipid peroxidation in the liver. Other authors have found mitochondrial failure during liver aging in vitamin E-deficient rats [30]. Far beyond its general protective effect on biological membranes [31], tocopherol blocks the oxidative decay of respiratory complex III [32].

SELENIUM: THE DARLING ELEMENT

Selenium is found in higher amounts in Brazil nuts. In fact, it has been suggested that Brazil nuts are the richest food source of Selenium. Selenium has important antioxidant activities and comprises the active center of four isoforms of Glutathione Peroxidase (GPX) enzyme as a form of selenocysteine, as well the thyroid hormone deiodinases, thioredoxin-reductases, and 25 types of selenoproteins (I, K, M, N, O, P, S, T, U, X, W, among others) [33-38].

Selenium deficiency impairs antioxidant defenses by decreasing glutathione peroxidase synthesis, increasing the risk of viral infections (influenza and coxsackievirus) and cardiac disease as described in the classical Keshan's disease [39]. Dietary selenium supplementation has been found to recover cardiac, mitochondrial and cytosolic GPx values in aged rats previously submitted to ischemic-reperfusion injury [40]. Selenium is also associated with decreased risk of cancers [41].

HEALTH BENEFITS OF BRAZIL NUTS: FROM ANTIOXIDANT ACTIVITY TO ANTI-INFLAMMATORY ACTIONS

Since 2002, Brazil nuts have been considered a rich source of bioactive compounds with antioxidant activity whose intake brings benefits to our health [42].

Evaluating twenty foods, some of them regularly eaten by the Brazilian population, it was reported that

Brazil nuts had the highest total antioxidant capacity *in vitro* [43].

In this sense, dietary intake of Brazil nuts is an effective strategy to improve selenium status, increasing GPx levels.

Pre-school children who received 30g of Brazil nuts 3 days per week had increased selenium status according to a study conducted in Amapá, Brazil [44].

Dietary Intake of Brazil nuts improved both selenium and GPx levels and decreased also DNA damage in obese women [45].

Brazil nut intake by elderly subjects improved both selenium status and GPx, and increased cognitive performance of people with mild cognitive status [46].

Other benefits of regular intake of Brazil nuts are related to improvement on blood lipids and lipid peroxidation.



Figure 1: Cardiovascular benefits of dietary intake of Brazil nuts.

Lipid peroxidation and an inflammatory micro-environment on subendothelial space is responsible for atherosclerosis pathogenesis and progression of both atherosclerosis and thrombosis [47].

Regular dietary intake of flour made by partially defatted Brazil nuts had diminished total cholesterol and apolipoprotein-A1 in dyslipidemic hypertensive patients [48].

Brazil nut supplementation of rats submitted to high-fat diets decreased total cholesterol and triglycerides, as well as lipid peroxidation but have no effect on HDL cholesterol levels [49].

A single intake of a Brazil nut portion decreased four inflammatory parameters (IL-1, IL-6, INF- γ , TNF- α) and did no adverse effects on kidney or liver in healthy human subjects [50].

Another study also reported that ingestion of Brazil nuts decreased inflammatory biomarkers, oxidative DNA biomarkers and LDL-cholesterol levels, whereas intake of those nuts increased both GPx and HDL cholesterol levels in patients undertaken hemodialysis treatment [51].

The major cardiovascular benefits linked to the dietary intake of Brazil nuts are represented in Figure 1.

ADVERSE HEALTH CONCERNS REGARDING BRAZIL NUT INTAKE

Beyond the possible contamination by fungi, aflatoxins and bacteria, Brazil nuts can induce allergy and possible selenium-induced toxic effects [52,53].

CONCLUSIONS

Newer studies are necessary in order to better characterize the content of coenzyme Q10 and specific polyphenols in Brazil nuts.

However, dietary intake of Brazil nuts presents many health benefits contributing to substantial decrement of disease risk.

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