Artigo Original

v. 6 n. 3 (2025)
ISSN: 2675-8008
Revista Multidisciplinar em Saúde

ACESSO ABERTO

Data de Recebimento:
12/09/2025

Data de Aceite:
18/09/2025

Data de Publicação:
25/09/2025

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Citação:
RUFINO, J.L.S, *et al*; chemical, clinical and environmental aspects of selenium present in brazil nuts: a literature review. **Revista Multidisciplinar em Saúde**, v. 6, n. 3, 2025. https://doi org/10.51161/integrar/rems/4523

DOI: 10.51161/integrar/rems/4523
Editora Integrar© 2025.

CHEMICAL, CLINICAL AND ENVIRONMENTAL ASPECTS OF SELENIUM PRESENT IN BRAZIL NUTS: A LITERATURE REVIEW

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ABSTRACT

Introduction: Selenium (Se) is an essential trace element for the human body and has been studied regarding its bioavailability and antioxidant action against diseases. **Objective:** In this review, we aim to present and update knowledge about the aspects that relate selenium from Brazil nuts, the advantages of its consumption for the prevention of oxidative damage and other relevant aspects to human health. **Methods:** This review brings together studies on the chemical composition, bioavailability, clinical effects and toxicological risks of Se present in Brazil nuts. **Results:** Among the nuts, the Brazil nut (Bertholletia excelsa H.B.K.) stands out for being one of the richest sources of Se, as well as for its different chemical forms, mainly linked to different proteins. Se is found in the active site of enzymes and catalyzes oxidation/reduction reactions, and is therefore essential for the synthesis of glutathione peroxidase, which prevents oxidative processes. **Conclusion:** Adequate intake of Se in the diet can improve immunity and fertility in humans and animals, as well as aid in resistance to oxidation, tumors and pathogenic microorganisms.

Keywords: Brazil nut; Bertholletia excelsa; Selenium; Antioxidant; Toxicity.

INTRODUCTION

The Amazon region has one of the richest biomes of the world, serving as a source of many natural ingredients used in food production. Among these, Brazil nuts stand out for their high economic relevance. It is an export commodity and known worldwide for having a high protein (15-20%) and lipids (60-70%) content as well as for having antioxidant properties; the latter being predominantly due to the presence of selenium (Se) and vitamin E (ALCANTARA *et al*., 2022).

Several dietary and health-promoting properties attributed to Brazil nuts are also linked to the presence of unsaturated fatty acids, sterols, tocopherols and tocotrienols, which makes Brazil nut oil valued by the food and cosmetic industry (MONIKA; ANNA, 2019) considering that oil compounds are attributed with anti-inflammatory and antioxidant activities. The figure 1 presents the relationship between Brazil nut composition and biological properties.

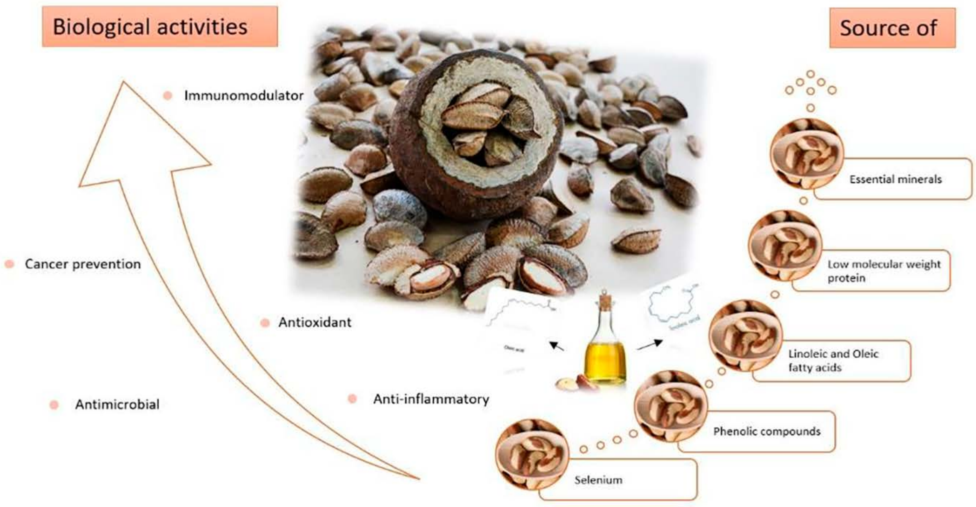

Figure 1: Relationship between biological activities and composition of Brazil nut.

Based on properties of Brazil nuts the objective of this review is to present knowledge about the relevant aspects to human health and advantages of its consumption through to the chemical composition, selenium presence, clinical aspects and their toxicity.

MATERIALS AND METHODS

This integrative literature review employed a qualitative approach to explore and synthesize scientific findings related to the nutritional profile and physiological implications of Brazil nut (Bertholletia excela). The review focused on compiling evidence from peer-reviewed articles that examine the biochemical constituents, micronutrient dynamics, and potential health impacts associated with its dietary.

The search was conducted across three major databases: PubMed, Scopus and Science Direct. The articles are in English from 2002 to 2025. The search strategy utilized controlled vocabulary and keyword combinations such as “Brazil nut; selenium; nutritional value; clinical outcomes; oxidative stress, and toxicity”, as can be seen in in the figure 2.

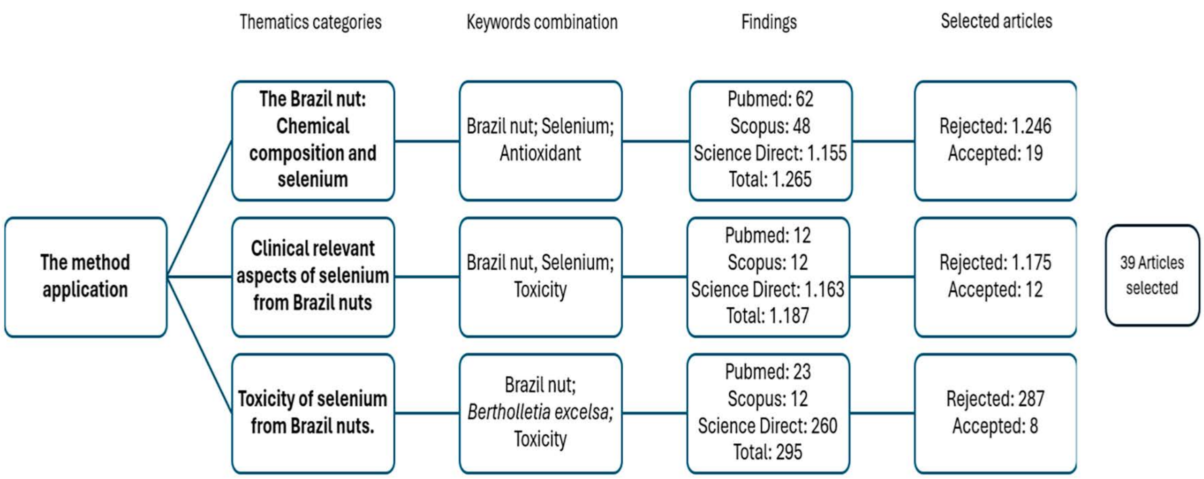

Figure 2: Flowchart depicting the methodological stages employed in the selection of relevant studies.

Articles published were screened and selected throught a stepwise process involving title assessment, removal of duplicate records and abstract review. Studies that did not investigate the Chemical, Clinical and envioromental aspects were excluded. The selected studies were full-text analyzed qualitatively, and their findings were systematically organized based on their capacity to investigate each respective thematics categories. 1º Thematic: “The Brazil nut: Chemical Composition and Selenium” 19 articles; 2º Thematic: “Clinically Relevant Aspects of Selenium from Brazil nuts” 12 articles; 3º Thematic: “Toxicity of Selenium from Brazil nuts” 8 articles. This thematic synthesis enabled the identification of coverging evidence, emerging insights, and knowledge gaps, contributing to a nuanced understanding of the subject matter.

RESULTS AND DISCUSSION

The search results were compiled and systematically organized into the following three thematic categories to enhance the analytical approach to the data.

The Brazil nut: Chemical composition and selenium

The antioxidant properties of Se can be explained by the fact that Se is a fundamental element in the constitution of the enzyme glutathione peroxidase (GPx), which is responsible for the sequestering of free radicals in the body, and this is one of the most important antioxidant defense mechanisms. Adequate intake of Se is essential for several enzymes involved in protecting the body against oxidative stress, the maintenance of the state redox, immune system and thyroid regulation. Regarding intake of Se via Brazil nuts, 100 µg of Se/day, equivalent to two units/day of Brazil nuts, for 3 months, were sufficient to elevate plasma levels of Se and glutathione peroxidase in healthy subjects (THOMSON *et al*., 2008). Another study reported that consumption of just one Brazil nut (5 g) daily for three months was effective for increasing concentrations of Se and glutathione peroxidase activity in patients with Se deficiency, thus improving their antioxidant capacity in the blood (STOCKLER-PINTO *et al*., 2010). The consumption of nuts with a significant Se content also demonstrated benefits in cases of dyslipidemia, in hypertensive patients and in patients during hemodialysis (TANGJADEE *et al*., 2023).

In this context, it is important to mention some points about the origin of Se in Brazil nuts and if, in fact, all nuts available for consumption have an adequate level of Se. Although the roots of the Brazil nuts tree absorb Se and other nutrients from the soil, these trees, because they are found in different geographical regions, may have a variation in the Se content in the soil in which they grow, which generates seeds with different Se contents depending on the area, and levels are sometimes so high that the nuts are toxic. In addition to total Se, soil acidity plays an important role in Se uptake by Brazil nut trees, which is possibly due to the importance of this soil property for Se retention in the soil (SILVA JUNIOR *et al*., 2017). As for the higher Se concentration in Brazil nuts, this has been correlated to the geographical origin of the trees in Brazil. In the state of Amazonas, the Se variation in seeds was correlated to the variation in the total Se concentration in the soil, which was higher in Amazonas than in the other states of the northern region of Brazil.

To understand the differences in selenium levels in Brazil nuts, it is important to take into account that there is substantial variation from seed to seed, and this is possibly caused by genetic variation between trees or by local variation in Se concentration in the soil or in selenium bioavailability due to soil acidity

(LIMA *et al*., 2019). Se variation in soil affects a variety of plant-based foods and this has been studied and reported in many countries and regions, including the United States, and compared to notably lower Se levels in many parts of Europe. There is a lower average Se intake in Eastern Europe than in Western Europe and Se deficiency has also been documented in countries such as China and New Zealand (SHREENATH; HASHMI; DOOLEY, 2023).

In foods such as Brazil nuts, Se is mainly associated with the protein fraction in the form of Se-methionine and/or Se-cystine. Among tree nuts, Brazil nuts are recognized as the best source of Se (MARTINS *et al*., 2012). Table 1 presents the Se content reported by different authors in previous studies.

Table 1 – Quantity of selenium in Brazil nuts in differents locations.

Location Sampled	Se mg/kg			Authors
	Average	Min	Max	
Macapá-AP	143.0	33.0	543.0	GOMES *et al*., (2024)
Itacoatiara-AM	20.5	11.1	34.7	
Autazes-AM	29.2	12.9	38.6	PACHECO & SCUSSEL, (2007)
Boca do Acre-AM	13.5	9.7	18.5	MARTINS *et al*., (2012)
Amaturá-AM	11.9	9.2	16.7	

RAMDONSKA *et al*. (2020) also cite that Se is a trace element that is characterized by having a narrow limit between adequate levels and deficiency/overdose. In dietary doses, it stimulates antioxidant activity after incorporation into selenoproteins, while in supra-nutritional doses it is a pro-oxidant and exhibits toxic effects.

Se is important for development and is an essential micronutrient in the diet, but attention to its toxicity tends to be neglected. The recommended daily intake (RDI) of selenium is 55 µg (IOM, 2002) and the range of safe doses of Se is considerably narrow. Therefore, a minimal increase of the required level will result in toxicity. The level of Se in the diet may affect microbial colonization of the gut, which may influence host Se level and selenoproteome expression. As a result, Se deficiency can bring about a phenotype of the gut microbiota that makes one more susceptible to cancer, thyroid dysfunctions, inflammatory bowel disease, and cardiovascular disorders. Gut bacteria can remove selenium from the host, resulting in two to three times lower levels of host selenoproteins under conditions of limited Se (FERREIRA *et al*., 2021).

Clinical relevant aspects of selenium from Brazil nuts

To understand the direct relationship between the concentrations of Se in the clinic aspects of patients, there may be health impairment due to the non-introduction of basic levels of Se in the body, and that deficiencies occur, especially when combined with other factors.

Among other observations regarding the action of Se, one can mention the synergy of the deficiency status associated with T-2 toxin that can exacerbate renal fibrosis (LIU *et al*., 2024); In their research, WANG *et al*. (2024) state that Se deficiency exacerbates oxidative stress-mediated pyroptosis. LEI *et al*. (2023) claim that Se deficiency is one of the causes of hypertension, as Se deficiency increases hydrogen peroxide production, decreases glutathione peroxidase synthesis, which culminates in a biochemical pathway that impairs sodium (Na) excretion and decreases the volume of urine production and increases blood pressure. Regarding the action of the substance in the body, it can be observed, in the reaction cascade of the stages of formation of thyroid hormones, such as thyroxine (T4) and triodonthyronine (T3), that Se causes the active formation of enzymes directly involved in the synthesis and metabolism of these hormones, so the relationship between the concentration of Se and hormones tends to be proportional.

According to FONTENELLE *et al*. (2021), the relationship between serum Se concentrations and thyroid hormone concentrations in obese patients indicated that the lower the Se concentration in the body, the lower the amount of synthesized thyroid hormones. They also compared their results to several other authors who reached similar conclusions. In addition to thyroid hormone production, the protective role of Se in the thyroid is reported in the literature. The thyroid gland has the highest amount of Se/g in tissue than any other organ and Se deficiency not only affects thyroid function but is also involved in pathogenesis and major thyroid diseases, including cancer (OGLIO *et al*., 2024).

Many diseases exacerbate harmful biological processes in the liver. When liver damage is caused by pathology and drug therapy, it can result in chronic liver disease that occurs at various stages of fibrosis processes. Liver fibrosis is the formation of an abnormally large amount of scar tissue in the liver and results from chronic liver injuries, including those caused by alcohol consumption, chronic viral hepatitis, autoimmune diseases, parasites, metabolic diseases, lipopolysaccharides (LPS) and other toxins or drugs; however, it is reversible in mild to moderate cases. When fibrosis is not controlled, it can develop into cirrhosis (ANDRADE *et al*., 2015).

In this scenario, the biological pathways responsible for liver damage are related to oxidative and inflammatory processes. It has been commonly observed that under normal physiological conditions of reactive oxygen species (ROS) and reactive nitrogen species (RNS), the balancing for homeostasis to occur is performed by the existing antioxidant mechanisms. During homeostasis, the liver maintains the balance between ROS and RNS via the antioxidant agents. Since this balance tends to increase the number of reactive species, some conditions end up being created that end up leading to deterioration of the liver. Therefore, ROS can cause nonspecific damage and participate in the degeneration of essential cellular components such as lipids, proteins, and DNA, potentially leading to senescence and cell death (SIMIC *et al*., 2022).

The relationship between oxidative stress and liver damage has been reported by several authors (LE DA-YOUNG *et al*., 2023). In this context of oxidative lesions promoted by various pathologies, the consumption of Brazil nuts, with high concentrations of Se, can be highlighted as beneficial because the Se from Brazil nuts can contribute to the maintenance of this intracellular defense system.

In the study conducted by LI *et al*. (2020), which aimed to investigate the effects of Brazil nuts on plasma levels of selenium, GPx (glucose peroxidase) and thyroid hormones, the authors obtained data that show sufficient evidence to support that the consumption of Brazil nuts, at an average dose of 9.42 mg/day for an average of 11 weeks, can cause significant improvements in plasma selenium and GPx, without also recording deleterious side effects during their consumption. In the study by DUARTE *et al*. (2019), although there were no changes in the levels of plasma inflammatory biomarkers, a significant increase in gene expression was an indication of a pro-inflammatory stimulus in obesity, induced by the consumption of Brazil nuts with high levels of Se.

There is also a correlation between the influences on the increase in concentrations of glutathione peroxidase percussors, due to the decrease in oxidative processes harmful to the liver, and the consumption of Brazil nuts, which influences the levels of Se in the body, this being the main precursor of glutathione formation (OJETOLA *et al*., 2021; HIRSCH *et al*., 2022). Several studies converge to the understanding that there is a possible influence on the increase of antioxidant substances through the consumption of Brazil nuts and that this increase can positively influence harmful processes of liver oxidative stress.

Toxicity of selenium from Brazil nuts

Due to the duality of the Se content, excessive intake can cause toxic effects in humans and results in death in cases of severe intoxication. Therefore, excessive supplementation of Se is harmful to the body and can cause selenosis or induce DNA mutations in severe cases (LV; LIANG; NONG, 2021). In humans, an increase in cases of selenosis has been observed, either due to long-term occupational exposure to excessive Se or due to abundance of Se in soils and food. With this, research into the toxicity of Se has gained attention around the world (KOHSHAHI *et al*., 2019).

Selenosis can be divided into acute, when it occurs in a short time, and chronic, when it is related to cumulative toxicity caused by taking low doses of Se in the long term, and manifests itself mainly as fatigue, depression, bad breath, anemia, lack of appetite, hair loss, growth retardation and liver cirrhosis (JU *et al*., 2018). Studies have shown that the toxicity of Se depends on certain factors and that the intensity of the toxic effects may vary with nutritional status and use of certain medications by the patient (CHANG *et al*., 2019).

When it comes to the chemical species of Se, in general, the inorganic Se compounds are more toxic than the organic Se compounds. Organic compounds of Se are generally more toxic than the nanoparticles of Se (Nano-Se) (LV; LIANG; NONG, 2021). The absorption of Se varies between species of animals and is affected by physiological characteristics, functional state, amount of intestinal Se content, chemical species of Se, and residence time of the substance in the intestine (WEI *et al*., 2019).

According to ALLARABI *et al*. (2019), under normal circumstances, Se enters the body mainly through the digestive tract, after which it is absorbed in the duodenum and cecum and enters the bloodstream, where it combines with plasma proteins to be transformed into biologically active selenoproteins, which are then transported to the tissues and organs of the body (Figure 1). Se is metabolized and excreted mainly through urine and feces, but in case of high intake, exhalation also serves as one of the important routes for excretion.

The main cause of the selenosis is that, after high concentrations of Se in the body, there is a competitive relationship between Se and sulfur due to similarity, since Se is prone to act as a substitute for sulfur in amino acids that contains sulfur in their composition, to become selenomethionine and selenocysteine, which disrupts protein expression and deactivates SH enzymes such as succinate dehydrogenase and δ-aminolevulinic acid to tissues and organs. As a result, individuals have abnormal physiological functions such as growth inhibition, mental disturbances, decline in fertility and immunosuppression.

Other studies have also shown that selenosis is mainly attributed to the fact that selenium methylation, the main Se detoxification pathway in the body, is inhibited. For example, HOSNEDLOVA *et al*. (2017) demonstrated that high doses of selenocysteine administered to mice can inhibit the methylation of Se by deactivating methionine adenosyltransferase (an enzyme responsible for the synthesis of S-adenosylmethionine), which leads to the accumulation of hepatotoxic selenides, especially large amounts of hydrogen selenide and, eventually, liver damage.

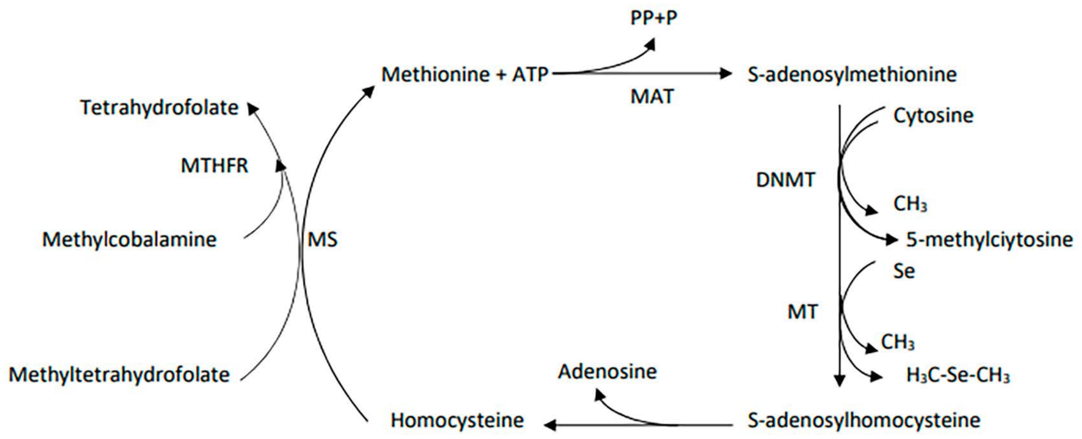

Figure 3. Selenium methylation process in biological systems (Adapted from GENCHI *et al*., 2023)

Microorganisms also play an important role in the geochemistry of Se. Studies have shown that microorganisms can metabolize Se through various transport, reduction, oxidation, assimilation and methylation pathways (Figure 3) to achieve transformation of Se species and self detoxification. There is growing evidence that in addition to toxic effects on growth and physiological functions related to humans, animals and plants, Se also has negative effects on microbial growth. Nano-Se has been reported to have a significant antibacterial effect on Staphylococcus aureus, and it is speculated that nano-Se may affect the growth of bacteria by inhibiting the formation of cell membranes (GUISBIERS *et al*., 2016).

Selenium and mycotoxins

With the growing concern about the quality of life of people, it has become common to investigate and find substances that are harmful to health in food products. Among these, the occurrence of mycotoxins deserves attention since they are highly toxic contaminants and can pose serious health risks to humans and animals. Among the mycotoxins, aflatoxins are the best known for being the most toxic (BAPTISTA *et al*., 2007).

In this context, the search for elements that can reduce the content of mycotoxins in food has become frequent. Biochemically, aflatoxins can interfere with the metabolism of energy, carbohydrates, lipids, nucleic acids and proteins. The biological effects resulting from this interference include the occurrence of carcinogenicity, mutagenicity, teratogenicity, hepatotoxicity and aflatoxicosis. It should be considered that any agent that can be considered an antioxidant is a viable option to try to inhibit the toxic effects of mycotoxins and Se is one of them. In addition to providing benefits to human health, this element, present in abundance in Brazil nuts, has been pointed out as a promising agent in reducing damage promoted by mycotoxins, especially by aflatoxins (BAPTISTA *et al*., 2007).

On the other hand, the aflatoxin content in Brazil nuts from different regions of the Amazon varies significantly. In general, the higher the Se content in the nut, the greater the chance of finding aflatoxin contamination (PACHECO & SCUSSEL, 2007). Unfortunately, contamination by aflatoxins has been associated with Brazil nuts in several studies, but the relationship between this contamination and the content of Se needs further investigation. At non-toxic levels, Se in both inorganic and organic forms has demonstrated efficacy in inhibiting aflatoxin B1-induced cytotoxicity. The organic form is less toxic than the inorganic form; however, the inorganic form is more effective at inhibiting aflatoxin-induced cell death.

To better understand how the Se can act by antagonizing the toxicity of mycotoxins, it is necessary to consider that, under regular physiological conditions, the organism constantly generates oxygen free radicals, while the antioxidants present in it continuously neutralize these free radicals, maintaining a dynamic balance. When the body produces an excessive amount of oxygen free radicals or when the body's antioxidant capacity is reduced, an imbalance occurs between the oxidation system and the antioxidant system, resulting in damage to the body (REN, HE, FAN, 2019).

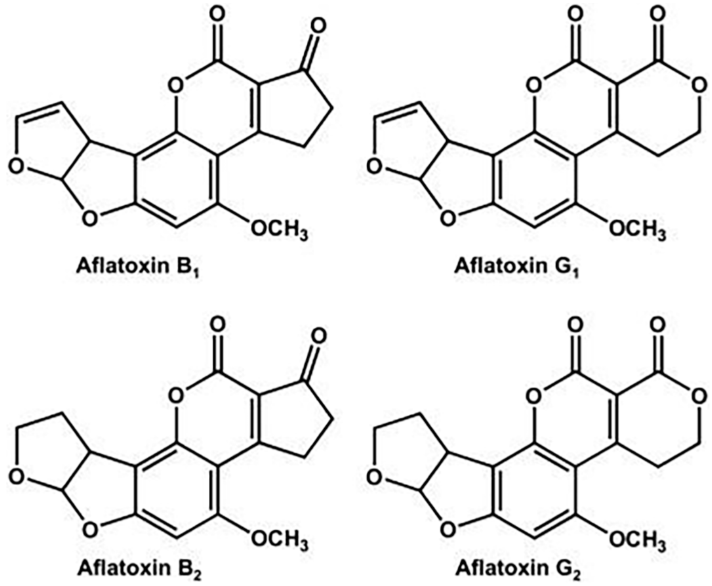

Figure 3: Chemical structures of aflatoxins B1, B2, G1 and G2 demonstrating the presence of oxygen in the molecule that can lead to the creation of reactive oxygen and cause damage to cells.

Recent studies have shown that one of the forms of mycotoxin toxicity may be the induction of lipid peroxidation in the body. The generation of active oxygen can cause damage to the genetic material, and such damage can indirectly result in the creation of ROS. These two elements are related and cause serious damage to cells. Aiming to insert a product into the diet that is proven to be an antioxidant and restore balance to the body, Se has been studied for this purpose. Se is an essential part of an antioxidant enzyme called GPx and, in its absence, the activity of this enzyme is reduced and lipid peroxidation rises, causing rapid apoptosis (YAO *et al*., 2013).

Supplementation with Se can lead to an increase in the activity of antioxidant enzymes such as GPx and superoxide dismutase (SOD) in animals, thus favoring their antioxidant capacity and neutralizing oxidative damage caused by mycotoxins. Se regulates Se1W transcription through the expression of mRNAs involved in Se protein synthesis and molecules involved in metabolism. It was also found that Se can regulate the expression of genes related to mitochondrial energy metabolism, mitochondrial apoptosis and kinetics. In addition, studies have investigated the mechanism by which the Se neutralizes the toxicity of mycotoxins in signaling pathways (RUAN & XU, 2010).

It has been shown that the consumption of Brazil nuts can improve the level of Se in the body and the lipid profile, which generates a positive effect on high-density lipoprotein cholesterol levels (COMINETTI *et al*., 2012), that can be a relevant factor for the reduction of mycotoxin levels in plasma or urine of these patients. In this context, the risks to public health offered by aflatoxins and the promising possibility of reducing toxin contamination with increased Se consumption via Brazil nuts from these areas make the development of further research relevant in this regard.

CONCLUSION

Brazil nuts are a rich source of bioavailable selenium, supporting antioxidant defenses, thryroid hormone metabolism, and immune function. However their narrow therapeutic window means that intakes above recommended levels can induce selenosis, manifesting as gastrointestinal disturbances, alopecia and neurotoxic effects, and therefore future research must standardize selenium quantification across Brazil nut batches, establish region-specific intake guidelines, and conduct long-term clinical trials to refine personalized dosing recommendations.

CONFLICTS OF INTEREST

There is no conflict of interest.

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