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Tree nuts and allergy: a review

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Abstract

In recent years, research has emphasized the health benefits of tree nuts, particularly in cardiovascular disease prevention, metabolic health, and neurological function. However, they are also among the most common food allergens, capable of triggering severe reactions, including anaphylaxis. Food allergies result from immune responses to food proteins, involving rapid mediator release, such as histamine.

Proteins are the primary allergens in tree nuts, with key families including seed storage proteins, lipid transfer proteins (LTPs), and pathogenesis-related proteins (PR-10). These proteins differ in stability during heat processing and digestion, affecting allergic reaction severity.

Almonds contain allergens Pru du 6 and Pru du 4, while Brazil nuts have Ber e 1, a seed storage protein. Walnuts' major allergens, Jug r 1 (2S albumin) and Jug r 3 (LTP), contribute to cross-reactivity with hazelnuts and pecans. Hazelnuts contain Cor a 1 and Cor a 9, whereas cashews and pistachios, with Pis v 1 and Pis v 3, exhibit strong cross-reactivity with other tree nuts and seeds. Macadamia nuts, though allergenic, cause fewer reactions.

Despite their nutritional benefits, tree nuts present significant allergenic risks, varying across nut types. This review underscores the importance of balancing their health advantages with their potential to cause severe allergic responses.

Keywords: *allergenic proteins, anaphylaxis, tree nut allergy, vegetal protein.*

INTRODUCTION

Tree nuts, such as walnuts, almonds, cashews, pistachios, and hazelnuts, are widely recognized for their rich nutritional profile, including healthy fats, proteins, vitamins, and minerals. Recent studies have demonstrated that regular consumption of these nuts is associated with a reduced risk of cardiovascular diseases, improved lipid profile, and better blood sugar regulation, in addition to potential neuroprotective effects. However, despite their health benefits, tree nuts are among the most common food allergens worldwide, capable of triggering severe allergic reactions, including anaphylaxis.

Food allergy is an immune response triggered by specific food proteins that act as allergens. Allergic reactions to tree nuts involve immune mechanisms that may or may not be mediated by immunoglobulin E (IgE) and are characterized by the rapid release of inflammatory mediators such as histamine. Different protein families found in these nuts, such as seed storage proteins, lipid transfer proteins (LTPs), and pathogenesis-related proteins (PR-10), are linked to distinct allergic responses. Their stability during heat processing and digestion varies, influencing the severity of allergic reactions.

Given the high prevalence of tree nut allergies and the potential severity of these reactions, understanding their immunological mechanisms, specific allergens, and factors contributing to cross-reactivity among different nuts and other protein sources is essential. Therefore, this review aims to explore the nutritional and immunological aspects of tree nuts, addressing their beneficial properties, key allergens involved, and emerging strategies for managing tree nut allergies.

MATERIALS AND METHODS

For the development of this review, a systematic search of the scientific literature was conducted using recognized databases such as PubMed, Scopus, and Google Scholar. Articles and scientific papers published from 2015 onwards were selected to ensure the inclusion of updated and relevant studies on the topic.

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The inclusion criteria considered peer-reviewed articles that directly addressed the proposed topic, prioritizing experimental studies, systematic reviews, and meta-analyses. Studies with poorly detailed methodologies, isolated case reports, or publications not indexed in scientific databases were excluded.

The search was conducted using combinations of specific keywords and descriptors, adjusted as needed to encompass a broad spectrum of relevant publications. The main keywords used were tree nut, allergy, protein and allergenicity, anaphylaxis, and tree nut. After the initial screening, the selected articles were critically analyzed regarding their methodology, results, and contributions to the field, allowing for the construction of a coherent and well-founded synthesis of the existing literature.

DISCUSSION

Tree nuts: benefits and composition

Tree nuts, such as walnuts, almonds, cashews, pistachios, and hazelnuts, have long been recognized for their rich nutritional profile, including healthy fats, proteins, vitamins, and minerals. In recent years, research has increasingly highlighted the role of tree nuts in promoting health, particularly in the context of cardiovascular disease prevention, metabolic health, and neurological function. As part of a healthy diet, tree nuts have been shown to contribute to improved cholesterol levels, reduced inflammation, and better blood sugar regulation (Micha et al., 2019; Ros et al., 2020).

Several studies have demonstrated that the regular consumption of tree nuts is associated with a lower risk of heart disease, particularly in individuals with high cardiovascular risk (Banel & Hu, 2021). A large body of evidence points to the beneficial effects of tree nuts on lipid profiles, particularly the reduction of low-density lipoprotein (LDL) cholesterol and the enhancement of high-density lipoprotein (HDL) cholesterol (Flores et al., 2020). Additionally, the antioxidant properties of tree nuts, particularly walnuts and almonds, have been attributed to polyphenolic compounds that help combat oxidative stress (Hidalgo et al., 2020).

In addition to cardiovascular benefits, the potential neuroprotective effects of tree nuts have garnered significant attention. Walnuts, in particular, are rich in omega-3 fatty acids and polyphenols, which have been linked to improved cognitive function and a reduced risk of neurodegenerative diseases such as Alzheimer's disease (Pires et al., 2021). Furthermore, recent studies suggest that nuts may play a role in managing weight by providing a satisfying, nutrient-dense snack option that promotes satiety (Zhao et al., 2021).

This growing body of evidence underscores the significance of including tree nuts in the diet as part of an overall strategy to promote long-term health and prevent chronic diseases, because they have significative amount of proteins and lipids according Table 1.

Nutrient (g%)	Brazil Nut[1]	Pistachio[2]	Hazelnut[2]	Walnut[1]	Almond[1]
Proteins	14.3	7.9	20.6	15.0	15.2
Lipids	66.4	75.8	44.4	61.4	65.2
Carbohydrates	11.7	13.8	28.3	16.7	13.7
Fiber	7.5	8.0	10.6	9.7	6.7

Table 1. Nutrients of tree nuts
[1]Taco, 2011; [2]Gonçalves et al., 2023.

Allergy and tree nuts

Adverse reactions caused by the consumption of some foods have been widely studied and reported since ancient times. They can occur by several mechanisms.

However, the food allergies are caused by specific immune responses (immune mediated). Food allergy is defined as an immune response to food proteins disease (Sicherer and Sampson, 2018). For example, in the urticaria (commonly referred to as hives) the symptoms and the anaphylaxis are triggered by the immunoglobulin E (IgE), which is antibody-mediated immune responses. On the other hand, the cell-mediated diseases (eosinophilic esophagitis and enterocolitis), which are also induced by food proteins. The allergic reactions involve immunologic mechanisms that may or may not be mediated by the IgE. They are usually associated to food allergies and hypersensitivity reactions characterized by a rapid release of mediators such as histamine (Figure 1).

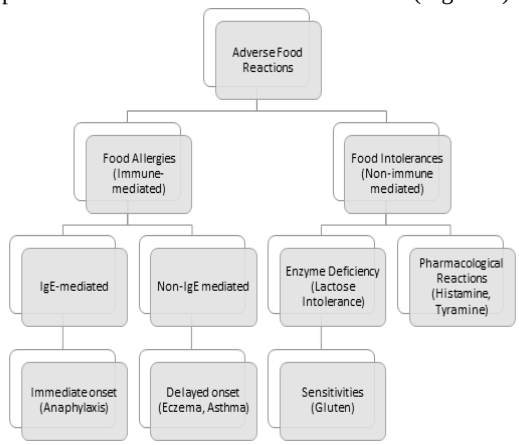

Figure 1. Types of adverse reactions developed through foods ingestion (a) Immune mediated and (b) Non-immune mediated (adapted from Taylor and Baumert, 2020).

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On the other hand, the term food intolerance (non-immune mediated) refers to any abnormal response to (one or more than one) specific food, food substance (lactose/caffeine/fish proteins) or additive (sulfites) without the involvement of immunologic mechanisms.

Allergies are characterized by the IgE synthesis against antigens that enter the body through ingestion, the inhalation (particles) or dermis contact (skin). Food allergy is an increasingly common problem in Western countries, and an effective therapeutic treatment is needed, however, it has not been On the other hand, the term food intolerance refers to any abnormal response to one or more specific foods, food substances, or additives without the involvement of immune mechanisms. Allergies are characterized by the synthesis of IgE against antigens that enter the body through ingestion, inhalation, or skin contact (Fernandez et al., 2024).

Immune Mechanisms

Adverse reactions caused by the consumption of certain foods have been studied extensively. These reactions can occur through various mechanisms. Food allergy is defined as an immune response to food proteins. For example, in urticaria (commonly known as hives), symptoms and anaphylaxis are triggered by immunoglobulin E (IgE), which mediates antibody-based immune responses. On the other hand, cell-mediated diseases (eosinophilic esophagitis and enterocolitis), which are also induced by food proteins, are classified as mixed IgE-mediated and non-IgE-mediated mechanisms (YANG et al., 2023).

Allergic reactions involve immune mechanisms that may or may not be mediated by IgE. These reactions are often associated with food allergies and hypersensitivity responses, characterized by the rapid degranulation and release of mediators such as histamine (Figure 2).

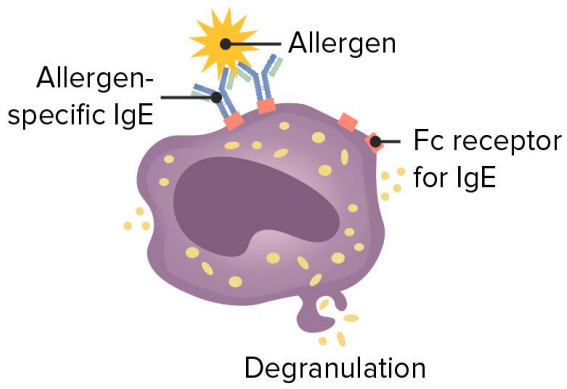

Figure 2. Histamine Degranulation in Allergic Reactions (Adapt from Schatz, 2020).

Proteins and Allergy

Proteins play a central role in food allergies, as they are the primary allergens triggering immune responses in sensitive individuals.

Table 2. Components, protein families and cross-reactivity of tree nuts.

Protein	Protein Family	Tree Nut	Characteristics	References
Cor a 9	Legumin	Hazelnut	Associated with systemic reactions	Geiselhart et al., 2018
Ana o 3	2S Albumin	Cashew	High cross-reactivity with pistachio	Willison et al., 2017
Jug r 4	Legumin	Walnut	Strong cross-reactivity with pecan	Andorf et al., 2017
Ber e 1	2S Albumin	Brazil nut	Heat and digestive stability, triggers systemic reactions	Geiselhart et al., 2018
Ber e 2	Legumin		Associated with IgE reactivity	

Tree nuts contain diverse protein families such as seed storage proteins, lipid transfer proteins (LTPs), and pathogenesis-related proteins (PR-10), each linked to specific allergic reactions. These proteins vary in their stability during heat processing and digestion, influencing the severity of allergic responses.

Cross-reactivity between proteins of different nuts or between nuts and pollens is another crucial factor. Allergens like Ara h 2 in peanuts or Cor a 14 in hazelnuts (table 2) demonstrate significant immunogenicity, often leading to systemic reactions. This highlights the importance of advanced diagnostic tools, such as component-resolved diagnostics (CRD), in distinguishing between primary and cross-reactive allergies.

Management strategies for nut allergies often focus on avoidance, as exposure can result in severe anaphylaxis. However, oral immunotherapy is emerging as a potential approach for desensitization. This treatment aims to increase the threshold of reactivity to allergens, though its safety and long-term effectiveness require further investigation.

Advancements in allergen identification and treatment approaches are paving the way for better management of food allergies, improving quality of life for affected individuals while reducing the risk of severe allergic reactions.

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Tree nuts and allergic reactions

Tree nuts are among the most common food allergens worldwide, and allergies to them can cause severe reactions, including anaphylaxis. These reactions are typically mediated by immunoglobulin E (IgE), though there are also non-IgE-mediated allergic conditions. The most common tree nuts responsible for allergies include Brazil nuts, walnuts, hazelnuts, almonds, pistachios, and macadamias. Each of these nuts has specific allergenic properties that may lead to varying allergic reactions depending on the individual's sensitivity (Sicherer and Sampson, 2018).

Brazil nuts

Brazil nuts (*Bertholletia excelsa*) are native to the Amazon region and contain high levels of protein, fats, and essential micronutrients. However, they are also potent allergens. The primary allergen in Brazil nuts is a protein known as Ber e 1, which is classified as a seed storage protein (Geiselhart et al., 2018).

Allergic reactions to Brazil nuts are often severe and can include symptoms such as urticaria, angioedema, gastrointestinal distress, and anaphylaxis. Studies have shown that the protein Ber e 1 has a high degree of stability, which makes it resistant to heat and processing, further contributing to the risk of allergic reactions (Weinberger & Sicherer, 2018). A notable characteristic of Brazil nut allergy is the cross-reactivity with other tree nuts, particularly those in the same family, which can exacerbate symptoms in individuals already sensitized to one type of nut.

Walnuts

Walnuts (*Juglans regia*) are among the most frequently reported tree nuts causing allergic reactions. The main allergens in walnuts are Jug r 1, a 2S albumin, and Jug r 3, a lipid transfer protein (LTP). Walnuts are associated with a high risk of cross-reactivity with other tree nuts, especially hazelnuts and pecans. Individuals allergic to walnuts may also experience reactions to other members of the Juglandaceae family (Ballmer-Weber et al., 2019).

Allergic reactions to walnuts can range from mild symptoms such as oral itching to more severe manifestations like respiratory distress and anaphylaxis. One of the distinguishing features of walnut allergies is the presence of LTPs, which are resistant to heat and digestion, making walnut allergies particularly persistent and difficult to manage (Mendes et al., 2019).

Hazelnuts

Hazelnuts (*Corylus avellana*) are widely consumed worldwide, particularly in confections and processed foods. The main allergens in hazelnuts are Cor a 1 (a 12S globulin) and Cor a 9 (a lipid transfer protein). The presence of LTPs in hazelnuts increases the likelihood of oral allergy syndrome (OAS), which includes symptoms like itching, swelling of the lips, and mouth irritation (Giannetti et al., 2023).

Hazelnut allergies often lead to systemic reactions, including anaphylaxis, especially in individuals who also have pollen allergies, particularly to birch pollen, as pollen-food syndrome is common in this context (Calamalli et al., 2021). This cross-reactivity between birch pollen and hazelnuts is well-documented and suggests a common sensitization pathway involving IgE-mediated responses.

Almonds

Almonds (*Prunus dulcis*) are one of the most widely consumed tree nuts, found in a variety of products such as snacks, milk substitutes, and baked goods. The primary allergens in almonds include Pru du 6 (a vicilin-like storage protein) and Pru du 4 (a 2S albumin) (Zhang et al., 2019). Almond allergies are often associated with oral allergic reactions such as itching and swelling of the mouth and throat.

Severe reactions to almonds can lead to anaphylaxis, particularly in individuals who have existing allergies to other tree nuts or seeds. Due to their widespread use in food processing, cross-contamination is a common concern, and individuals with almond allergies are typically advised to avoid any food products containing traces of almonds or processed almond derivatives (Sullivan et al., 2020).

Pistachios

Pistachios (*Pistacia vera*) belong to the Anacardiaceae family, making them closely related to cashews and poison ivy. The major allergens in pistachios include Pis v 1 (a 7S globulin) and Pis v 3 (a lipid transfer protein) (Cox et al., 2018). Similar to cashews, pistachios are associated with cross-reactivity with other tree nuts and seeds, which can increase the risk of allergic reactions in sensitive individuals.

Pistachio allergies are generally characterized by symptoms like urticaria, gastrointestinal discomfort, and anaphylaxis. A unique feature of pistachio allergies is their high rate of co-sensitization with allergies to cashews and mangoes, making this group of allergens particularly challenging to diagnose and manage (Cox et al., 2021).

Macadamia

Macadamia nuts (*Macadamia integrifolia*) are another tree nut with significant allergenic potential, though they tend to cause fewer allergic reactions compared to the others mentioned above. The main allergen in macadamias is Mac i 1 (a storage protein) (Mendes et al., 2019). Reactions to macadamia nuts can range from mild symptoms to severe reactions, including anaphylaxis.

While macadamia allergies are less common, they have been reported in individuals with existing tree nut allergies, and cross-reactivity with other nuts like cashews and pistachios may occur. The nuts' high-fat content and delicate flavor make them a popular ingredient in various food products, which raises concerns about cross-contamination for individuals with allergies (Gutiérrez-Díaz et al., 2024).

Table 3 highlights the prevalence of tree nut allergies in patients from various countries. In Brazil, information on the prevalence and incidence of food allergies remains scarce. The Brazil nut (*Bertholletia excelsa* HBK), a seed native to the Amazon region, is known for its exceptional nutritional value, particularly its high protein and sulfur amino acid content. Despite these benefits, the nutrient composition of

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tree nuts is linked to allergic reactions. Nut allergies can pose serious health risks, especially in individuals with a strong family history of atopy and heightened allergic tendencies, regardless of age (Kluczkovski-Scussel, 2015). To fully understand the risks and benefits, it is essential to assess both the nutritional and therapeutic potential of tree nuts, as well as the immune and pathological reactions they may provoke

Table 3. Prevalence of Tree Nut and Pulse Allergy in Populations from Different Countries

Reference	Prevalence (%)	Allergen Type	Population Characteristics	Origen
Maloney et al. (2015)	0.5–3.0 (peanut)	Tree Nuts and Peanut	General population	United States
Ball et al. (2019)	0.6–2.1 (tree nuts)	Tree Nuts	Children[3]	United Kingdom
McWilliam et al. (2019)	3.1 (peanut), 1.9 (tree nuts)	Tree Nuts & Peanut	Infants[4] (HealthNuts study)	Australia
Cousin et al. (2017)	2.0–5.6 (tree nuts)	Tree Nuts	Adults	France
Vereda et al. (2011)	4.0 (peanut, Ara h 9)	Peanut (LTP sensitization[1])	[2]	Spain
Asero et al. (2018)	2.5 (tree nuts)	Tree Nuts	General population	Italy
Elizur et al. (2019)	3.2 (tree nuts and peanut)	Tree Nuts & Peanut	Chindren[3]	Israel
Sicherer et al. (2018)	2.1–3.5 (peanut and tree nuts)	Tree Nuts & Peanut	General population	Canada

[1] lipid transfer protein; [2] not informed; [3] not specify children's age; [4] 12 months old.

CONCLUSIONS

Tree nuts are highly nutritious foods with a well-documented role in promoting cardiovascular, metabolic, and neurological health. Despite these benefits, they are among the most prevalent food allergens, with significant variability in allergenic potential across different nut types. The immune mechanisms underlying nut allergies, including IgE-mediated and non-IgE-mediated reactions, highlight the complexity of these conditions, which can range from mild symptoms to severe anaphylaxis. The identification of specific allergenic proteins, such as Ber e 1 in Brazil nuts and Jug r 1 in walnuts, underscores the importance of advanced diagnostic methods to improve allergy management. Cross-reactivity among different nuts and related allergens further complicates clinical diagnosis and treatment. While avoidance remains the primary strategy for managing tree nut allergies, emerging approaches like oral immunotherapy offer promise for desensitization and improving quality of life for affected individuals.

This review emphasizes the need for a balanced perspective on tree nuts, considering both their nutritional and health-promoting attributes and their potential to provoke severe allergic reactions. Future research should focus on improving diagnostic accuracy, exploring novel therapeutic strategies, and enhancing public awareness to optimize the safe consumption of tree nuts.

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