Acta Scientific Nutritional Health

Volume 2 Issue 5 May 2018

Mini Review

The Good and Bad of Peanuts

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Received: March 15, 2018; **Published:** April 19, 2018

Abstract

The peanut, also known as groundnut or legumes are taxonomically classified as Arachis hypogaea, It is widely grown, in the tropics and subtropics, and is an important commodity because of it many uses as food or food additives such as peanut butter, vegetable oils and complimentary for desserts. It is a nutritious food containing vitamins, essential amino acids as well as bioactive compounds that are beneficial for the human such as the phytosterol, alpha-tocopherol, and flavonoids. It is a good solution for malnutrition, and recommend for prevention of non-communicable diseases (NCDs) such as cardiovascular disease and type II diabetes. Despites its numerous good properties, peanut is also a source of potent and fatal food allergen. There are three major peanut allergens contributing to peanut allergy, a hypersensitivity reaction with symptoms varying from mild to severe anaphylaxis. Peanut allergy reduces the quality of life for the affected individuals, and has a substantial effect on social and economic burden of healthcare for allergic patients. To date, peanut allergy management is by avoidance or relieves symptoms via administration of epinephrine. Studies on oral immunotherapy using peanut has shown the ability to induce desensitization, shifting the allergen-specific cytokine production away from a TH2 response. Also effective are the use of lactic acid bacteria probiotics as food products capable of downregulating allergy due to its inherent immunomodulatory properties. This mini-review will give an insight into the good and bad of peanuts and current management towards peanut allergy.

Keywords: Peanut; Peanut Allergy; Oral Immunotherapy; Probiotic, Treatment

Abbreviations

APC: Antigen Presenting Cells; CVD: Cardiovascular Disease; OA: Oleic Acid; OIT: Oral Immunotherapy; RAST: Radioallergosorbent Test; SCIT: Subcutaneous Immunotherapy; SLIT: Sublingual Immunotherapy; SPT: Skin-Prick Testing; SREB : Sterol Regulatory Element Binding Protein; T-reg: T Regulatory Cells

Introduction

Peanut belongs to the family Leguminosae, which includes peas, beans and soy [1]. Peanut known scientifically as Arachis hypogea, is believed to have been cultivated since the prehistoric times where remnants of peanuts were discovered in tombs of Native Americans, and peanut kernels had also been found in Peruvian archeological sites for agriculture about 10,000 years ago [2]. It was originally cultivated from Northwestern Argentina to Southern Bolivia region of South America [3]. Ever since peanut has been distributed to other countries due to the European conquest. Peanut has been a legume food for centuries in native South American and is also an essential crop in Asia, Europe, Africa and North America. Peanut possess similar characteristic with tree nuts and seed, cashew, hazelnut and walnut.

Nutrition and uses of peanuts

Today, peanut is consumed and cultivated throughout the world, with China, India, and the USA being the main suppliers of peanut-based on economy value [4]. The highest use of peanut in the US is for peanut butter, while in India it is commonly used for oil production. Peanut is an increasingly important commodity in USA with around 6.8 billion pounds of peanut production, mainly to supplement the competitive peanut butter industry dominated by Jiff (J.M. Smucker), Skippy (Unilever) and Peter Pan (ConAgra).

As the market develops, the health benefits of peanuts became the main focus. It is a good nutritious food due to its protein, lipid and fatty acids composition which are essential for strenuous activity. Peanut kernels are made up of 50% oil, 25% of protein, 15% of carbohydrate and mixture of ash, moisture, and fiber. Therefore, peanut is a good source of food to prevent malnutrition in developing countries. Besides providing essential amino acids needed for normal body growth and metabolism, peanuts are rich in vitamin A and D [5], According to claims qualified by FDA on nuts and cardiovascular disease, peanut is useful for maintaining a healthy heart when consumed at 1.5 ounces (42g) per day. A total of 22% roasted dried peanut in 100 g serving size contained unsaturated fat (monounsaturated fat, polyunsaturated fat, omega 6, and omega 3 fatty acid), the largest contribution to the lipid content. Besides being a source of energy producing biomolecules, unsaturated fat has several human benefits associated with the prevention of cardiovascular disease (CVD) and reduced risk of developing type II diabetes [4]. From clinical and epidemiological studies, monounsaturated fat can reduce the risk of CVD by increasing the amount of HDL cholesterol and decreasing triglycerides and blood pressure [3]. Oleic Acid (OA), a monounsaturated fat derived from peanuts, has been reported to lower LDL cholesterol through the inactivation of the transcription factor sterol regulatory element binding protein (SREBP) which plays an important role in regulating cholesterol synthesis and LDL uptake [6].

Peanuts also contain biologically active compounds of alpha-tocopherols, flavonoids, phytosterols, resveratrol which contribute to the beneficial properties of peanuts [4]. Alpha-tocopherol is a vital source of vitamin E (the fat-soluble vitamin) important for maintaining essential physiological functions [5]. Vitamin E act as an anti-oxidative vitamin, able to eliminate free radicals by preventing the oxidation of unsaturated fatty acids present in consumed foods, respiratory membranes and mitochondrial matrix in the human body [5]. Resveratrol compound found in peanut has been reported to protect against cancers, heart disease, degenerative nerve disease, Alzheimer's disease, tumor, and inflammation [7]. On the other hand, phytosterols, a plant sterol, has been shown to lower total cholesterol up to 10% and LDL up to 14%, which explains for its benefit in preventing CVD [7]. Peanut also contains several minerals important for health, such as magnesium, calcium, iron, phosphorous, potassium, sodium, zinc, copper, manganese, and selenium [5].

Peanut is widely used in food products such as peanut butter or cream, roasted nuts and also a good source of vegetable oil [7]. It has also been used as topping for food and serves as complimentary in snacks and desserts. Besides its uses in food products, peanuts have extensive use in other applications such as adhesives, shampoo, and bleach [8].

Peanut allergen

As nutritious and healthy peanut is, the bad part of peanut is its allergens that may cause a fatal anaphylactic reaction when consumed by allergic individuals. It is considered as one of the deadliest food allergens to date. A total of 17 peanut allergens are characterized and reported by the Allergen Nomenclature Sub-Committee of the International Union of Immunological Societies [9]. Of the 17 allergens, the most prevalent is vicillin (Ara h 1), conglutin (Ara h 2) and glycinin (Ara h 3) [10]. The size of peanut allergens ranges from 5-17 kDa, except for the much larger Ara h 1 (64 kDa) and Ara h 3 (57 kDa) allergens.

The allergenicity of peanut allergens is due to its ability to maintain its function during ingestion in the stomach and to stimulate IgE production. Sufficient portion of the multiple IgE epitopes on the allergen can cross-link to the IgE-bound to FcεR1 receptors and cause degranulation of the mast cells to release inflammatory chemical mediators such as cytokines and chemokines. Biochemical and structural features of the allergens have a critical role in their immunogenicity. Ara h 1 is one of the most abundant peanut storage protein compromises of 12%-16% of the total protein content, which are used as a source of nitrogen and amino acid during plant development. On the other hand, Ara h 2 is a precursor protein in peanuts to aid protein transport from the cytoplasm to organelles. Both Ara h 1 and Ara h 2 are responsible for type 1 hypersensitivity where it is recognized by IgE-antibodies in more than 90% of patients with peanut allergy [11]. As such, among the allergens, the Ara h 1 and Ara h 2 were reported as the major peanut allergens due to high reactivity to IgE and are recognized by IgE in most peanut allergy individuals. Ara h 1 was found to be less allergenic compared to Ara h 2 [11]. Ara h 3 and 4 exhibit an IgE reactivity to 45% and 33% of peanut allergic patients respectively [12]. There are not much data available for the other types of peanut allergens. Ara h 5 exist in low levels in peanut extract and may recognize up to 13% of patients with peanut allergy. The Ara h 6, despite having 59% homology with Ara h 2, it is a heat and digestion stable protein [9,13]. The different types of peanut allergens are as shown in table 1.

Protein Superfamily	**Cupin**		**Prolamin**				**Bet v 1-like**	**Profilin**	**Glycosyltranferase GT-C**				**Scorpion toxin like knottin**		**Non-specific lipid transfer protein**	
Protein family	Vicillin or 7S globulin	Legumin or 11S globulin	2S albumin			nsLTP	Bet v 1 family	Profilin	Oleosin				Plant defensin		Transfer protein	
Allergen	Ara h1	Ara h3	Ara h2	Ara h6	Ara h7	Ara h 9	Ara h8	Ara h5	Ara h10	Ara h 11	Ara h 14	Ara h15	Ara h12	Ara h13	Ara h16	Ara h17
Size (kDa)	65.3	60.0	16.6/ 18.0	15.0	16.4/ 17.4	9.1	17.0	14.0	17.6	14.3	17.5	17.0	5.2	8.4	8.5	11.0
Prevalence of IgE binding (%)	30-80	16-57	42-100	86-92	43	8 - 60	22-66	3-24 birch or grass pollen allergy	Not known				Not known		Not known	

Table 1: Comparison of several peanut allergen families biological function and binding to IgE

Peanut Allergy

Peanut allergy is a type I hypersensitivity reaction. The immunologic mechanism of peanut allergy starts upon contact or consumption of peanuts. The peanut allergens penetrate the mucosal barrier for the first time and are taken up by the antigen presenting cells (APC) for presentation to TH2 lymphocytes. TH2 lymphocytes belong to a subset of T-cells that produce a special cytokine called interleukin-4 (IL-4). These TH2 cells will activate the other lymphocytes called B cells. B cells that can recognise the allergen will be activated to proliferate and differentiate into plasma cells that produce the allergen-specific IgE antibodies which can bind to the surface of basophils and mast cells. This event is known as the sensitisation phase. A group of memory B cells will be induced, and upon re-encounter with the same allergen, the allergen will cross-link with IgE bound to high-affinity IgE receptor (FcεRI) on the mast cells. This will eventually lead to basophils and mast cells to degranulate and release its contents comprising of a whole array of chemical mediators as histamines, leukotriene, numerous cytokine, and chemokines. Approximately 6 to 24 hours after the initial allergen encounter, an IgE mediated late-phase allergic response may occur, followed by edema and inflammatory cells influx [14]. At this stage, capillary permeability and smooth muscle

contraction in the airways and lungs will occur leading to increased mucus content. The inflammatory responses will cause difficulty in breathing due to the constricted airways (bronchoconstriction) and nasal congestion. In severe cases, the type I hypersensitivity results in anaphylactic shock in which shortness of breath is accompanied by shock due to vasodilation and fluid loss from blood [8].

Diagnosis and Therapy

Peanut allergy shows an acute symptom compare to the other type of allergies, because slight contact with the allergen, it will exhibit the allergic symptoms. The allergic reaction may occur within minutes upon exposure to hours after the ingestion of the allergen. Organ systems involved and resultant symptoms of peanut allergy are the skin (hives, reddening, tissue swelling), respiratory tract (wheezing, noisy breathing, cough, breathing difficulty, throat tightening, nasal congestion), gastrointestinal tract (vomiting, diarrhea, abdominal pain), and the cardiovascular system (drop in blood pressure, irregular heart rate, cardiac arrest) [15].

Anaphylaxis is a systemic allergic reaction caused by rapid release of potent mediators from mast cells and basophils which is IgE-mediated. It occurs suddenly after contact with an allergen and is potentially fatal [16]. Anaphylaxis may not necessarily be monophasic; it also can involve biphasic reaction in which the initial reaction is followed by a relative symptom-free period before symptoms recur, often in a severe form and less responsive to treatment. The severity of anaphylaxis may be affected by exercise, medication, anesthesia, and alcohol, and fatal anaphylaxis is more likely to occur in the individual with asthma. The frequent initial symptoms of anaphylaxis include the sense of threat and generalized warmth that is characterized by pruritus or tingling of the skin, palms of hands, soles of the feet, lips and on the genital area. Epinephrine can be prescribed for the treatment of anaphylaxis [16]. There is no specific symptom to differentiate peanut allergy from another type of allergies, because of the common symptoms observed [17]. Therefore, appropriate diagnostic test needs to be conducted to confirm the symptoms and the causative allergen.

The four major steps in diagnosis of peanut allergy, included (1) a medical history of allergy and appearance of symptoms after contact, (2) positive skin prick test (SPT), (3) presence of peanut allergen-specific IgE in sera measured using radioallergosorbent test (RAST) and (4) a positive food challenge test, where symptoms were observed upon exposure to peanuts [18].

Patient's medical history and physical examination are initial means of diagnosis for food allergy. The SPT fluoroenzyme immunoassay (Pharmacia Immuno CAP-FEIA) or oral food challenges are the further supplementary diagnostic test to confirm the presence of allergen-specific IgE. The type and quantity of food ingested, onset duration of symptoms, the severity of symptoms, and family history of allergy are essential information for diagnosis of food allergy which also applies to peanut allergy [18]

Food challenges are performed when there is a negative result for a diagnostic test despite patient having a medical history of a particular allergic reaction [18]. The most common method used is the double-blind placebo controlled food challenge. Sign and symptoms of allergenic reaction are recorded, and treatment given if allergic reaction occurs. The disadvantage of this test is time-consuming, risk of inducing severe allergic reaction in a patient, and it requires close supervision by medical expertise to conduct this test.

Immunotherapy is using the body's immune system for treatment and has been the recent strategy to treat food allergy, including peanut allergy. Food allergen immunotherapy aims to establish functional immune tolerance or state of unresponsiveness instead of sensitization leading to inappropriate inflammatory immune responses to the food allergen. Therefore, immunotherapy for peanut allergy attempts to desensitize the overactive immune response by repeated administration with increasing doses of the peanut or allergen in the absence of any danger signal, to achieve a state of sustained unresponsiveness where the probability of an allergic reaction decreases Despite the high risk of peanut allergens induced anaphylaxis, there exist several immunotherapy strategies such as oral immunotherapy (OIT), subcutaneous immunotherapy (SCIT) or sublingual immunotherapy (SLIT). Repeated administration of a specific peanut allergen with increasing dosage has been shown to reduce sensitivity towards the allergen [19].

Role of probiotics in peanut allergy

Probiotics are microorganism that when consumed (as food or a dietary supplement) maintains or restores beneficial bacteria to the digestive tract and are capable of conferring health benefits on the host when consumed in adequate amount ($> 1 \times 10^6$ cfu). Probiotics includes the *Lactobacillus* sp (*L. acidophilus, L. casei, L. plantarum*), *Bifidobacteria* sp (*B. bifidum B. bifidum, B. animalis*) and *Lactococcus* sp (*L. lactis, L. subtilis*). These bacteria contribute to the maintenance of intestinal microbial balance and modulate the host's immune system. They have been shown to promote hypoallergenic effect, protecting against atopic dermatitis in allergy. *Lactococcus* sp and *Lactobacillus* sp are food-grade lactic acid bacteria (LAB) and "generally recognised as safe" (GRAS) bacteria. A study on *L. plantarum* has shown its ability to elicit immunomodulatory effects on the T_H2 cells responses in allergic disorders [20]. We previously demonstrated that *L. casei* shirota strain has the ability to suppress T_H2 activation and proinflammatory cytokines production in a dustmite allergy mouse model [21]. More recently, the first randomized trial combining probiotic with peanut OIT was shown to be highly effective in modulating the peanut-specific immune response in 7 out of 9 children treated and showing sustained unresponsiveness [22]. Today, due to their contribution to human microbiome health, probiotics and prebiotics are found in many food products ranging from infant milk formula to health drinks (e.g. Vitagens, Yakults, yoghurts) and health supplement products for all ages.

Conclusion

Peanuts are as popular as they are healthy. They are considered as an excellent plant-based source of protein and are high in various vitamins, minerals and plant compounds which helped in the prevention of non-communicable diseases such as CVD and obesity. However, despite the good nutritional and beneficial properties of peanuts, the presence of peanut allergens confers serious health risk to peanut allergic individuals. Oral immunotherapy to desensitize or induce tolerance to these allergens and the use of probiotics are promising approaches for peanut allergy besides symptom control and avoidance.

Acknowledgements

This review article was funded by the Fundamental Research Grant Scheme from Ministry of Education (MoE) Malaysia (FRGS/2/2014/SG05/UCSI/02/1).

Conflict of Interest

The authors declared no competing interests.

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