Lupin Allergy – a scientific review

Food allergy is an uncommon immune response to naturally occurring food proteins or peptides that elicit a reaction via immunoglobulin E (IgE). A person must first be sensitised by previous exposure to the protein to develop IgE antibodies which react to subsequent exposure.

Food allergies are not the same as food intolerances, which are generally caused by chemical agents (eg. sulphites), or certain digestive deficiencies (such as lactose intolerance or favism).

The most common food allergy triggers are hen's egg, cow's milk, peanut, tree nuts, shellfish, sesame, soybean, and wheat. Peanut, tree nuts and seafood are less likely to be outgrown and tend to be lifelong allergies.

Some food allergies can result in potentially serious anaphylactic reactions.

The prevalence of food allergies varies across geographic regions. Peanut allergy is higher in Europe and USA, whilst soybean allergy is more common in Japan. In India chickpea allergy is more prevalent, whereas in Spain, lentil allergy more common (1).

Prevalence and legume co-reactivity

Over the past 20 years an increasing number of European, Australian, and North American populations have been exposed to a wider range of processed food products containing lupin ingredients. It is likely that the incidence of lupin allergy in these populations will be similar to the incidence of other legume allergies once this population has been well exposed to lupin foods.

It has been claimed that fewer than 1% of the population that have eaten lupin-based foods have been reported to show an immediate allergic reaction (2).

Lupin allergy has also been reported in people who co-react to peanuts, as well as those who are not allergic to peanuts or other legumes.

In a French study, primary sensitisation to lupin was observed in 3.7% of the 1,422 patients with current atopic disease and 1.8% of the 226 patients with latent atopy. An investigation carried out in France and Belgium by the Allergy Vigilance Networks found that 14.5% of adults and 17% of children with peanut allergy had cross-sensitisation with lupin (3).

It is important to note that these, and several other published studies, which screened large numbers of people for sensitisation, did so by skin prick test or by radio-allergosorbent (RAST) antibody detection. Serological cross-reactivity between members of the legume family is observed frequently. However, sensitisation does not necessarily mean an individual will experience a clinically symptomatic allergic reaction (1). In a 2014 published study, Bansal et al. report that in their practice they observed lupin sensitisation in approximately one-fifth of patients with peanut allergy. However, only a few presented with clinically symptomatic allergies, which were mostly mild and localised in nature (4).

Allergenic lupin proteins

The lupin protein α-conglutin is a 11S legumin-like globulin that has sequence alignment to the peanut allergen Ara h3/4. It is believed to be the allergen that triggers a reaction in most people that react to lupin and to peanut (5).

The lupin protein β-conglutin is a 7S vicilin-like globulin that, whilst having sequence alignment to the peanut allergen Ara h1, is likely the allergen that triggers a reaction in most people that react to lupin but not to peanut (6). The *L. angustifolius* β-conglutin has been designated Lup an 1 by the International Union of Immunological Societies (IUIS) allergen nomenclature subcommittee.

There is a recent report suggests that a third lupin protein (γ-conglutin), a 7S basic globulin may also be allergenic (7).

These conglutin proteins are present in all lupin species (land races and domesticated varieties) that are utilised as a traditional or novel foods. Those species include the Australian Sweet Lupin (*L. angustifolius*), also known as the blue lupin; the European White Lupin (L. albus) also known as lupini, tremocos, altramuces, termes; the yellow lupin (L. luteus), and the Andean lupin (L. mutabilis) also known as chocho or tarwi. Thus, food from all lupin varieties is potentially allergenic.

Allergenic proteins may have a number of specific epitopes that bind IgE. The epitope being the portion of the protein that binds to an IgE to initiate the allergic reaction. Different people may have IgE that recognises different epitopes on the same protein or IgE that binds to multiple epitopes on an allergen.

People allergic to lupin and peanut may be reacting to cross-reactive allergens - where they have IgE that binds to a common, or very similar, epitope on proteins in the two seeds; or have multiple sensitisation - where they have been sensitised to lupin and peanut separately. In this case the IgE that binds to an epitope in a lupin protein would not bind to the peanut proteins and vice versa.

There are as many as nine postulated allergenic peanut proteins. Each of these peanut proteins has multiple IgE specific binding epitopes some of which have been characterised. Much less is known about the specific epitopes of the lupin conglutins.

It has been reasonably postulated that a gene editing approach could be utilised to breed a lupin variety that is non-allergenic. The lack of current knowledge of the epitopes for each lupin conglutin makes this a complex task.

Symptoms

Symptoms of lupin allergy are similar to those observed with other food or inhalant allergens (4).

Most individuals only experience a mild reaction; however, some patients will present more severe symptoms. Symptoms that have been reported vary from urticaria, atopic dermatitis, facial oedema, rhinoconjunctivitis, oral allergy syndrome, mucosal erythema, angioedema, asthma, throat tingling, cough, abdominal pain, to some rare cases of anaphylaxis (8).

There is no evidence that lupin is quantitatively more potent an allergen than other foods. The range of severity of reaction to lupin is similar to that seen with other food allergens (2).

Allergy triggering dose

Limited studies have reported the allergy-eliciting dose of lupin and there is a significant difference among those doses and lupin material concerned.

The lowest eliciting dose described by Moneret-Vautrin *et al*. was 265 mg of lupin flour which induced abdominal pain and asthma in patients who were allergic to peanuts (9). In a study by Fiocchi et al., positive clinical reactions were observed in two peanut-allergic children, on consumption of 50 mg and 1.6 g of lupin protein, respectively (10).

Subjective symptoms have been reported to 0.5 mg of lupin flour. Allergic reactions were reported in 5 out of 6 children allergic to peanut at doses of lupin flour from 265 to 1000mg (2).

According to the recently published VITAL (Voluntary Incidental Trace Allergen Labelling) program of The Allergen Bureau of Australia and New Zealand (ABA), the reference allergenic dose of lupin protein is 4 mg, while that for peanut was much lower (0.2 mg of peanut protein) (11).

There are records of an allergic response to lupin by inhalation of lupin pollen or flour (often occupational) (12).

Some food products contain only the lupin hull (testa) as a source of cellulosic fibre, or a soluble fibre by-product of lupin protein isolate manufacture. Whilst the lupin conglutin proteins reside in the kernel (cotyledons), commercial scale de-hulling of the whole seed and extraction of the fibre fractions is unlikely to be sufficiently free of kernel protein to make these foods allergy free.

Heat and processing stability

Normal cooking and food preparation processes do not disrupt lupin proteins sufficiently to reduce the risk of an allergic response. Microwave cooking, boiling and extrusion cooking produce minimal changes on IgE binding to lupin proteins (13).

There is a report that suggests that instantaneous controlled dropped high pressure treatment of lupin flour in which steam pressure (up to 8 bar) with heat (up to 170°C) are combined for a short time of up to 3 minutes may reduce allergenicity (14).

Conclusions

Much of the concern around lupin allergy stems from lupin being a relatively new food ingredient, and being incorporated (often unlabelled) in a wide range of baked goods and dairy analogues (15). These food products have relatively recently been exposed to consumers beyond the traditional lupin consuming communities in the Mediterranean, Middle East and South America.

Medical scientists suggest a positive skin prick test to one legume should not warrant dietary elimination of all legumes from the diet without confirmation via a positive oral food challenge (16).

People with confirmed lupin allergy should be advised to avoid lupin containing foods. Also, people with a known allergy to peanuts should be advised to avoid products containing lupin until they can be specifically tested.

In 2006, the European Union included lupin among allergenic foods for which labelling is mandatory (17). Similarly, given the increasing consumption of lupin products in Australia, Food Standards Australia and New Zealand (FSANZ) added lupin to the mandatory food labelling list in 2018.

The peak professional body the Australian Society of Clinical Immunology and Allergy (ASCIA) provides key messages on its website for health professionals, food manufacturers, retailers, the food service sector, and consumers (www.allergy.org.au).

Disclaimer

Information contained in this document is not intended to replace medical advice. Any questions regarding a medical diagnosis or treatment should be directed to an appropriately qualified medical practitioner.

References

1. Ramanujami, R, Fiocchi, A, and Smith, W. (2016). Lupin allergy: Is it really a cause for concern? Agro FOOD Industry Hi Tech 27(1): 16-21.

2. ASCIA (2015). Lupin allergy. The Australasian Society of Clinical Immunology and Allergy -: www.allergy.org.au

3. Gayraud, J., Mairesse M., Fontaine JF., et al. (2009). The prevalence of sensitization to lupin flour in France and Belgium: a prospective study in 5,366 patients, by the Allergy Vigilance Network. Eur Ann Allergy Clin Immunol 41, 17-229.

4. Bansal, AS, Sanghvi, MM, Bansal, RA, et al. (2014). Variably severe systemic allergic reactions after consuming foods with unlabelled lupin flour: a case series.
J Med Case Rep, 8, 55.

5. Smith, PMC, Goggin, DE, Mir, GA, et al. (2008). Characterisation of allergenic proteins in lupin seeds and the relationship between peanut and lupin allergens. In J.A. Palta and J.B. Berger (eds). 'Lupins for Health and Wealth' Proceedings of the 12th International Lupin Conference, 14-18 Sept. 2008, Fremantle, Western Australia. International Lupin Association, Canterbury, New Zealand; pp.459-462.

6. Goggin DE, Mir G, Smith WB, Stuckey MS and Smith PMC (2008) Proteomic analysis of lupin seed proteins to identify conglutin β as an allergen, Lup an 1. Journal of Agricultural and Food Chemistry 56: 6370-7.

7. Aguilera-Insunza,R., et al. (2023). High prevalence of lupin allergy among patients with peanut allergy. Identification of g-conglutin as major allergen. Annals of Allergy, Asthma & Immunology 130: 225-232.

8. Fæste, CK (2010). "Lupin Allergen Detection". Chapter 22. In: Molecular Biological and Immunological Techniques and Applications for Food Chemists. Edited by Popping B, DiazAmigo C, Hoenicke K. Ed. Wiley.

9. Moneret-Vautrin, DA, Kanny, G., Morisset, M., et al. (2004). Severe food anaphylaxis: 107 cases registered in 2002 by the Allergy Vigilance Network. Allerg Immunol (Paris), 36: 46–51.

10. Fiocchi, A., Sarratud, P., Terracciano, L., et al. (2012). Assessment of the tolerance to lupine-enriched pasta in peanut-allergic children" Clin Exp Allergy 39: 1045-51.

11. Taylor, L, Baumert, JL, Kruizinga, AG, et al. (2014). Establishment of Reference Doses for residues of allergenic foods: report of the VITAL Expert Panel. Food Chem Toxicol, 63: 9-17.

12. Campbell, C., Jackson, AS, Johnson, .R., et al. (2007). Occupational sensitization to lupin in the workplace: occupational asthma, rhinitis, and work-aggravated asthma", J Allergy Clin Immunol. 119, 1133-9.

13. Alvarez-Alvarez J, Guillamon E, and Crespo JF (2005). Effects of extrusion, boiling, autoclaving, and microwave heating on lupine allergenicity. J Agric Food Chem. 53: 1294–1298.

14. Guillamon E, Burbano C, Cuadrado C, Muzquiz M, M Pedrosa AM, Sanchez M, Canbanillas B., Crespo JF, Rodriguez J, Haddad J, and Allaf K. (2008). Effect of an instantaneous controlled pressure drop on in vitro allergenicity to lupins (Lupinus albus var Multolupa). Int Arch Allergy Immunol 145: 9–14.

15. Bansal AS, Sanghvi MM, Bansal RA, and Hayman GR. (2014). Variably severe systemic allergic reactions after consuming foods with unlabelled lupin flour: A case series. J Med Case Rep.8: 55.

16. Ibáñez, MD, Martínez, M., Sánchez, JJ, *et al*. (2003). Legume cross-reactivity. Allergol. Immunopathol. (Madrid) 31: 151-61

17. European Commission. Directive 2006/142/EC of 22 December 2006, amending Annex IIIa of Directive 2000/13/Ec of the European Parliament and of the Council listing the ingredients which must under all circumstances appear on the labelling of foodstuffs. Off J Eur Union L368: 110–111. (2006).

Further Reading

ASCIA (2014) Australasian Society for Clinical Immunology and Allergy SCIA Information for patients, consumers and carers (Accessed January 9 2015) http://www.allergy.org.au/images/pcc/ASCIA_PCC_Food_Allergy_2014.pdf

de Jong, NW, van Maaren, MS, Vlieg-Boersta, BJ, Dubois, AEJ, de Groot H, and van Wijk RG. (2010). Sensitization to lupine flour: is it clinically relevant? Clin. Exp. Allergy 40: 1571–1577.

Foley RC, Jimenez-Lopez JC, Kamphuis LG, Hane JK, Melser S, Singh KB. (2015). Analysis of conglutin seed storage proteins across lupin species using transcriptomic, protein and comparative genomic approaches. BMC Plant Biol. 15: 106.