

Article type : Letter to Editor

Anaphylaxis to vanilla ice cream: a near fatal cross reactivity phenomenon

Uta Jappe^{1,2,3,4}, Skadi Kull^{1,4}, Annika Opitz^{1,4}, Peter Zabel^{2,4}

¹Division of Clinical and Molecular Allergology, Priority Research Area Asthma and Allergy, Research Center Borstel, Germany;

²Department of Pneumology, Medical Clinic, Research Center Borstel, Germany;

³Interdisciplinary Allergy Outpatient Clinic, Dept. of Pneumology, University of Luebeck, Germany;

⁴Airway Research Center North (ARCN); Member of the German Center for Lung Research (DZL)

Corresponding Author:

Prof. Dr. Uta Jappe, MD, MSc.

Division of Clinical & Molecular Allergology, Research Center Borstel,

Parkallee 35

23845 Borstel

Germany

E-mail: ujappe@fz-borstel.de

Phone : 0049 (0)4537188-7406

Fax: 0049 (0)4537188-6030

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/jdv.14445

This article is protected by copyright. All rights reserved.

Conflict of Interest

None declared.

Funding Sources

Part of the work is supported by the DFG JA 1007/2-1

Sir,

Although lupine is amongst the 17 foods that have to be declared it still has the features of a hidden allergen because those potentially allergic to lupine are not aware of the fact and, therefore, do not take adequate consequences, i.e. avoidance. Lupine occurs as additive in wheat flour, and is used as wheat and soy substitute. The significance of lupine is: a) its potential cross-reactivity with peanut and b) that the allergic reactions are mostly severe.¹ Lupine in contrast to soy is not genetically modified which makes it very attractive to health-conscious consumers, vegetarians and vegans. So far, only three lupine allergens (Lup an 1; Lup a 4; Lup a 5) and one isoform are documented by the WHO/IUIS Allergen Nomenclature Sub-Committee, (www.allergen.org) but are not yet available for routine allergy diagnostic tests.

The subject of this case report, a 29-year-old atopic man, had a severe peanut allergy since early childhood. In 2010, he had developed an anaphylactic reaction after accidental ingestion of peanut with angioedema, dyspnoea, gastrointestinal symptoms and loss of consciousness. Accidental consumption in general is common because open food preparations do not qualify for mandatory declaration so far. In 2015, he developed a similar allergic reaction after consumption of vanilla ice cream which proved to contain lupine. *In vitro* routine allergy diagnostic tests via CAP-FEIA (ImmunoCAP®, ThermoFisher Scientific, Freiburg, Germany) revealed IgE-reactivity to extracts of peanut (75.9 kU/L) and lupine seed (*Lupinus albus*) (5.55 kU/L). IgE to peanut storage proteins was positive: rAra h 1 (21.7

kU/L), rAra h 2 (51.0 kU/L), rAra h 3 (1.19 kU/L). Total serum IgE was 536 kU/L, serum tryptase was 14.9 µg/L; after control: 12.5 µg/L.

In order to identify potentially IgE reactive allergens in lupine extract, immunoblots were performed comparing acidic and basic extracts of lupine, peanut and the culprit ice cream. The patient's serum showed positive IgE binding against several proteins in immunoblots with lupine (Fig. 1A) and peanut (Fig. 1B) extracts, while in the immunoblots with lupine ice cream extracts the IgE-reactivity was almost exclusively directed against one main protein compound at ~32 kDa (Figures 1C and 2; reducing conditions) and 50 kDa (Fig. 2; non-reducing conditions). Using mass spectrometric analysis, this protein was identified as γ -conglutin. The ~32 kDa band corresponds to the larger subunit of the γ -conglutin and the ~50 kDa band to the monomeric whole protein; the smaller subunit does not seem to be IgE reactive.^{2,3}

It is reported that *L. albus* γ -conglutins consist of N-linked oligosaccharides with glyco-epitopes known as cross-reactive carbohydrate determinants (CCDs).^{3,4} Since the patient's serum has specific IgEs against CCD (MUXF: 4.25 kU/L), it cannot be ruled out completely that there is a cross-reaction to CCD on lupine compounds e.g. the γ -conglutin.

The severe similar clinical reactions of the patient to both legumes, peanut and lupine (in form of the lupine vanilla ice cream), suggests either the strong potency of lupine γ -conglutin as potential cross-reactive allergen or the presence of additional lupine allergens masked by the complex matrix of the ice cream.

This case report is an important example of the still low awareness regarding anaphylactic reactions to lupine in foods, although cross-reactivity between peanut and lupine is known since 1994⁵ and *de novo*-sensitization to lupine has been described in Germany in 2007^{6,7}. Cross-reactivity between legumes are not at all predictable, although it is anything but rare.⁸

In conclusion, lupine is no longer a hidden allergen according to mandatory labelling, however, it still is one when it comes to proper knowledge regarding cross-reactivity and awareness.

References

1. Jappe U, Vieths S. Lupine, a source of new as well as hidden food allergens. *Mol Nutr Food Res* 2010;**54**:113–26.
2. Duranti M, Consonni A, Magni C, Sessa F, Scarafoni A. The major proteins of lupin seed: Characterisation and molecular properties for use as functional and nutraceutical ingredients. *Trends Food Sci Technol* 2008;**19**:624–33.
3. Czubinski J, Barciszewski J, Gilski M, et al. Structure of γ -conglutin: insight into the quaternary structure of 7S basic globulins from legumes. *Acta Crystallogr D Biol Crystallogr* 2015;**71**:224–38.
4. Schiarea S, Arnoldi L, Fanelli R, De Combarieu E, Chiabrando C. In-Depth Glycoproteomic Characterization of γ -Conglutin by High-Resolution Accurate Mass Spectrometry. van Damme EJ, editor. PLoS ONE. 2013;**8**(9):e73906.
5. Hefle SL, Lemanske RF Jr, Bush RK. Adverse reaction to lupine-fortified pasta. *J Allergy Clin Immunol* 1994;**94**:167–72.
6. Brennecke S, Becker WM, Lepp U, Jappe U. Anaphylactic reaction to lupine flour. *JDDG* 2007;**5**:774–6.
7. Peeters KABM, Nordlee JA, Penninks AH, et al. Lupine allergy: Not simply cross-reactivity with peanut or soy. *J Allergy Clin Immunol* 2007;**120**:647–53.
8. Peeters KABM, Koppelman SJ, Penninks AH, et al. Clinical relevance of sensitization to lupine in peanut-sensitized adults. *Allergy* 2009;**64**:549–55.

