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Allergic primary sensitization to lupine seed

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Key words: cross-reactivity; food allergy; lupine allergy; lupine immunoblotting; oral allergic syndrome.

Dried and boiled lupine seed (*Lupinus albus*) is a traditional snack in some Mediterranean countries, namely in Portugal. The mixture of lupine with wheat flour was authorized in

Lupine is capable of inducing allergic sensitization out of the context of cross-reactivity with peanut.

Europe in the late 1990s in bread, pasta and bakery (1, 2).

Several allergic reactions to lupine ingestion have been reported since 1994, but they were generally considered as a result of cross-reaction to peanut and/or other legumes (1–5).

We have previously presented two atopic patients complaining of oral allergic syndrome following lupine ingestion, denying symptoms associated with peanut or other legumes (6). Patient 1 was a 50-year-old man, presenting allergic rhinitis and asthma, sensitized to house mites and patient 2, a 52-year-old woman, with allergic seasonal rhinitis and asthma, sensitized to house dust mite, grass, parietaria and mugwort pollens. They had negative skin prick tests to peanut, soy, beans and lentil and positive prick-to-prick tests to raw lupine seed. Specific IgE (ImmunoCAP, Pharmacia, Uppsala, Sweden) to lupine were 46.0 and 26.8 kUA/l and to peanut 0.39 and 0.84 kUA/l respectively. Sera from the

two patients were submitted to *L. albus* IgE inhibition by lupine and peanut extracts (Pharmacia UniCAP protocol). Inhibition values with lupine extract were 90%, while with peanut extract were 75% and 65%.

In this work, we tried to find lupine antigens responsible for a primary sensitization. Lupine and peanut protein extracts were obtained from smashed dry seeds. Protein separation was performed by isoelectrofocusing (IEF) and by SDS-PAGE, being blotted onto 0.2-µm-pore nitrocellulose membranes (Bio-Rad, Hercules, CA, USA) (7, 8), using a Nova Blot semi-dry system (Pharmacia Biotech, Uppsala, Sweden) for the latter (9). Each patient's serum was tested towards IEF and SDS-PAGE lupine separations by immunoblotting. Two controls were applied, one without serum and the other with neither serum nor secondary antibodies. Afterwards, immunoblotting inhibition with lupine and peanut extracts was performed, followed by antigen detection in blots

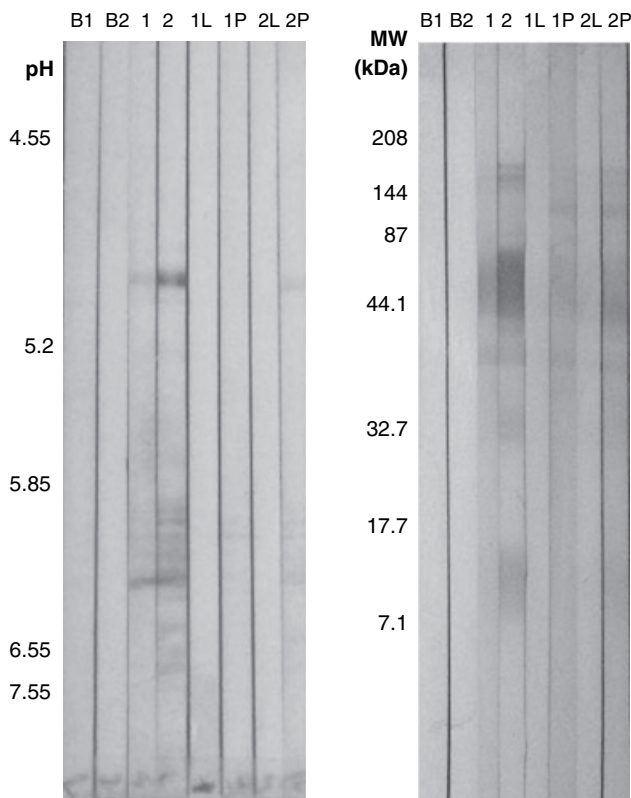


Figure 1. IgE immunoblots with *Lupinus albus* extract submitted to pH 3–10 IEF in polyacrylamide gel and blotted onto nitrocellulose membranes. B1, control without serum; B2, control without serum and secondary antibodies; 1 and 2, serum from patients 1 and 2, respectively. Serum inhibited by lupin extract (1L and 2L) and by peanut extract (1P and 2P).

from lupine IEF and SDS-PAGE separations (7).

IgE-binding proteins migrated to a pH ranging from 5 to 7. Those ones not inhibited by peanut extract migrated to pH 5 and to pH 6.05–6.3. Sera IgE from both patients recognized proteins of approximately 34 kDa and in the 40–65 kDa range. Patient 2 serum also recognized 7–15, 38, 77, 162 and 195 kDa proteins. Inhibition with lupine extract was complete for both sera. Serum preincubation with peanut extract did not inhibit patient 1 bands. On the other hand, it completely inhibited the 7–15 and 77 kDa bands and partially the 38, 40–65, 162 and 195 kDa components recognized by patient 2. Band of 34 kDa was never inhibited.

In this study, the clinical picture, skin prick tests and serum IgE to lupine and to peanut were suggestive of a sensitization to lupine not related to peanut allergy. The complete inhibition of lupine-specific IgE by lupine extract (90%) vs the only partial inhibition by peanut extract (65% and 75%) strongly supports this hypothesis. Immunoblotting studies performed by IEF as well as SDS-PAGE showed that some lupine IgE-binding proteins were inhibited by peanut extract, but they also evidenced bands only partially inhibited and others that suffered no inhibition at all, namely the 34 kDa protein and some of the proteins in the range of 40–65 kDa. These results clearly support that lupine is capable of inducing allergic sensitization out of the context of cross-reactivity with peanut. Taking them into account, we reinforce the need of including the lupine content in mandatory food labeling.

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Amoxicillin-induced exanthema in patients with infectious mononucleosis: allergy or transient immunostimulation?

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Key words: amoxicillin allergy; drug allergy; Epstein–Barr Virus infection; infectious mononucleosis; patch test.

Amino-penicillins are a major cause of delayed type reactions to penicillins. Furthermore, 70–100% of patients

receiving amino-penicillins during a florid Epstein–Barr virus (EBV)-infection develop a maculopapular rash

Delayed-type allergic reaction to amoxicillin triggered by EBV-infection can persist.

(1), the percentage being 14% for penicillin G, cloxacillin or tetracycline (2). This phenomenon may also occur with herpes simplex-, cytomegaly-, HI-virus- and, probably, many other viral infections. Hypotheses concerning the pathomechanism are (i) that the immune system of patients with infectious mononucleosis has decreased tolerance and/or (ii) enhancement of immune reaction to certain drugs or its metabolites (3). The general opinion documented even in high ranked review articles on drug eruptions (4) as well as allergy text books is that in most cases an EBV-associated amoxicillin rash is reversible and, as a consequence, a differentiated allergy diagnostic test is not considered or recommended (4).

To test the hypothesis that some EBV-infected patients in contrast might develop a 'true' allergic drug reaction to amino-penicillins, 41 Dermatology outpatients presenting with drug eruptions following the intake of amino-penicillins were consecutively investigated for additional acute infectious mononucleosis (fever, tonsillopharyngitis, lymphadenopathy). In case of suspicion, anti-EBV-IgM and -IgG antibodies were investigated. After complete resolution but not earlier than 3 months after the diagnosis of acute EBV-infection had first been confirmed, allergy diagnostic tests consisting of IgE-detection against amoxicillin, ampicillin, penicillin and cefaclor with CAP-FEIA (Phadia, Freiburg, Germany), skin prick tests and patch tests with amoxicillin trihydrate, cefotaxim sodium and benzyl penicillin 10 000 IE with readings after 48 and 72 h were performed. Eight out of 41 had a florid infectious mononucleosis at the time of the drug eruption, five of eight patients had positive patch tests to amoxicillin and two of five additionally to penicillin (Table 1). One patient out of five was challenged with verum and developed a rash after 48 h which resolved under systemic treatment with