Custard Apple Allergy with Glycosyltransferase as the Allergen Involved

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The Custard Apple, also known as Cherimoya, is a tropical fruit that belongs to the Annonaceae family. Although it originates from Central America, Spain is the leading producer in Europe. Its consumption is increasing in recent years due to the nutritional composition of this fruit, its content in specific phytochemical compounds and its impact on health benefits [1]. Nevertheless, hypersensitivity to cherimoya is infrequent [2]. To date, few allergy cases have been reported involving different allergens and most of them are related to cross-reaction with latex due the class I chitinases proteins [3]. The first report of custard apple allergy revealed the presence of a 20-25 kDa protein as the culprit [1], and the subsequent studies detected cross-reactivity between latex and cherimoya involving allergenic proteins around 40-45 kDa [2,4,5]. The most recent case report describes an IgE-binding band of 14 kDa that displays cross-reactivity with latex, papaya and avocado as a new allergen involved in cherimoya and latex cross-reaction [3].

We present a 11-year old child with the diagnosis of rhinoconjunctivitis due to Cupressus arizonica pollen, that during the previous years developed two episodes of oral allergy syndrome after custard apple ingestion. She presented no symptoms with latex and any other fruits, including peach, avocado, papaya and banana.

Skin prick test (SPT) with commercial extracts of latex, common inhalants, palm pollen profilin (Pho d 2), peach Lipid Transfer Protein (LTP) and prick-by-prick with fresh custard apple (peel and pulp) were performed. SPT were positive (mean wheal diameter
≥ 3 mm) only to *Cupressus arizonica* pollen and to custard apple (peel and pulp). Total and specific immunoglobulin (Ig) E were assessed using the CAP system (Phadia). Total IgE 859 kU/L. sIgE test against Pru p 3, profilin, latex and latex recombinants proteins (rHeb v 1, rHeb v 3, rHeb v 5, and rHeb v 6.01) were negative (<0.1 kU/L).

Protein extracts from cherimoya pulp and peel (CPE and CLE, respectively) were prepared by homogenization in phosphate-buffered saline, followed by centrifugation and dialyzation. Sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) IgE immunoblotting assays revealed IgE reactivity with a band of 50 kDa (Figure 1A) in the CLE. The protein/s from CLE were separated on a series of two-dimensional gel electrophoresis (2D) run with a pH gradient of 4 to 8 (Figure 1B) and, subsequently, transferred to a nitrocellulose membrane for incubation with a serum from allergic patient. A single protein from CLE with a molecular weight of approximately 50 kDa was recognized by IgE with a point isoelectric protein (pI) 5-5.8 (Figure 1C). The 50 kDa IgE binding spot was manually excised from the Coomasie blue-stained gel for tryptic digestion according to Shevchenko et al [6]. After digestion, peptide mass fingerprinting (PMF) was analyzed by MALDI-TOF MS for protein identification as previously described [6]. Additionally, when available and for confirmation of protein identify, peptide fragmentation was performed by MS in tandem MALDI LIFT TOT/TOF. Based on comparison with a database, the resulting peptides were analyzed using mass spectrometry and tandem mass spectrometry, which revealed a high homology with the glycosyltransferase of Capsicum baccatum in the CLE.

Glycosyltransferases comprise a large family of enzymes that catalyze glycosidic bond formation using sugar donors containing a nucleoside phosphate or a lipid phosphate leaving group to a variety of acceptor molecules, including proteins, lipids, polysaccharides, nucleic acids and small organic molecules [7]. As result, these
enzymes located in the Golgi apparatus generate a significant and diverse amount of glycoconjugates that are important for biological processes, such as cell signaling, cell-pathogen interactions, and the maintenance of the cellular architecture and metabolism [7]. Among glycosyltransferases, the enzyme beta1,2-xylosyltransferase adds xylose to glycoprotein, and may play a critical role in allergenicity by regulating the structure of the oligosaccharide chains and the targeting of these proteins to various organelles such as storage bodies [8]. In vitro reports have shown that IgE from sera of allergic individuals recognize core alpha1-3-fucosyltransferase in the prostate glands of snails, and it has been suggested that this protein could be allergenic [9]. Subsequent studies with demonstrated that complex plant N-glycans constitute a major class of the so-called carbohydrate cross-reactive determinants reactive with IgE antibodies in the sera of many allergic patients [10]. However, its real implication in clinical practice has not been demonstrated to date.

We report a case of IgE-mediated allergy to custard apple with a glycosyltransferase as the allergen involved. It is important to keep in mind that theoretically low-allergenic foods are always likely to cause problems. In addition, when facing an allergic patient, we must assess different allergenic sources other than those already known, in order to be able to make the appropriate avoidance recommendations.

Conflicts of interest

The authors have no conflict of interest to declare.

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References


**Figure Legend**

**Figure 1.** In vitro studies with custard apple extract

A) Immunoblot. IgE binding to custard apple extract in serum from allergic patient. B) 2D PAGE protein profile of CPE. C) 2D immunoblot analysis of custard apple with skin extract developed with serum of the patient. Protein spot was used for peptide mass print analysis and protein identification.

CLE: cherimoya peel extract, CPE: cherimoya pulp extract, kDa: kilodalton, M: molecular weight marker.