

## **NMR structural and immunological investigation of hazelnut allergens**

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Allergies represent a serious and potentially life-threatening health problem, with symptoms ranging from scratching and itching of the throat to severe symptoms like rhino conjunctivitis and anaphylaxis. In industrialized countries, many people are suffering from allergies after consumption of certain fruits or vegetables. For hazelnuts, apples, plums, and kiwi, these allergic reactions result from initial sensitization to the birch pollen allergen Bet v 1 and subsequent development of so-called cross-allergic reactions. Cross-reactive fruits contain proteins with a three-dimensional structure similar to the sensitizing protein Bet v 1 in birch pollen. To understand the cross-reactivity on a molecular basis, it is necessary and critical to determine the three-dimensional structure of these proteins at high resolution and to determine their allergenic potential.

Apart from apples (80%) and kiwi (48%), hazelnuts (60%) are the most frequent cross-reactive plant food source. We were able to determine NMR solution structures of the hazelnut isoforms Cor a 1.0401, Cor a 1.0402, and Cor a 1.0403 and a CS-Rosetta structural model of the isoform Cor a 1.0404, which all show the highly conserved PR-10 fold. Furthermore, we were able to extract the isoforms from hazelnuts under mild conditions and analyzed the extracts in terms of natural modifications of these allergens.

Using ELISA tests with serum from allergic patients we were able to determine the allergenic potential of the four isoforms. We could show, that Cor a 1.0401 has the highest allergenic potential followed by Cor a 1.0402 and Cor a 1.0403. The isoform Cor a 1.0404 has the lowest allergenic potential, which very likely arises from partly unfolding over time.