

Review

Not peer-reviewed version

Cross-Reactions at the Table: Pollen Food Allergy Syndrome in Southern Europe's Adults

[Christina Rousou](#) , [Egor Kostin](#) , [Eleni Christodoulou](#) , Theodoros Theodorou , [Zenon Pavlou](#) , [Constantinos Pitsios](#) *

Posted Date: 27 January 2025

doi: 10.20944/preprints202501.2002.v1

Keywords: pollen-food allergy syndrome; oral allergy syndrome; pollen; South Europe; food allergy; allergic rhinitis



Preprints.org is a free multidisciplinary platform providing preprint service that is dedicated to making early versions of research outputs permanently available and citable. Preprints posted at Preprints.org appear in Web of Science, Crossref, Google Scholar, Scilit, Europe PMC.

Copyright: This open access article is published under a Creative Commons CC BY 4.0 license, which permit the free download, distribution, and reuse, provided that the author and preprint are cited in any reuse.

Review

Cross-Reactions at the Table: Pollen Food Allergy Syndrome in Southern Europe's Adults

Christina Rousou, Egor Kostin, Eleni Christodoulou, Theodoros Theodorou, Zenon Pavlou and Constantinos Pitsios *

Medical School, University of Cyprus, Nicosia 2109, Cyprus

* Correspondence: pitsios.constantinos@ucy.ac.cy

Abstract: Oral Allergy Syndrome (OAS) and Pollen Food Allergy Syndrome (PFAS) represent significant challenges in allergy research. This review examines the epidemiology, pathogenesis, and diagnostic approaches of OAS and PFAS, with a focus on their prevalence and impact in the adult population in Southern Europe. Key panallergens such as profilins, PR-10 proteins, and lipid transfer proteins (LTPs) are highlighted for their role in mediating PFAS, and their regional variation. The review explores the differential prevalence of PFAS across Southern Europe countries, where multisensitization to pollen like Olive, Cypress, Parietaria, Mugwort, and Grass is common, and underscores unique environmental and ecological factors contributing to this phenomenon. Cross-reactivity, a hallmark of PFAS, is explored with emphasis on the interactions between common Southern European pollens and foods, such as fruits, nuts, and vegetables. Diagnostic challenges, including symptom variability, underreporting, and the need for region-specific diagnostic algorithms, are discussed. This comprehensive review aims to deepen understanding of OAS and PFAS among adults in the Mediterranean region of Southern Europe, offering insights that can improve the diagnosis, management, and overall care for this population.

Keywords: pollen-food allergy syndrome; oral allergy syndrome; pollen; South Europe; food allergy

1. Introduction

IgE-mediated food allergy remains a significant clinical problem in Europe, with a pooled point prevalence of 2.7% (95% CI: 1.7–3.7), defined as the presence of symptoms combined with a positive IgE response to at least one food [1]. The ability of linear or conformational epitopes of food allergens to elicit, and bind to elicited IgE immunoglobulins, is the cornerstone of IgE-mediated food allergies. Linear epitopes, typically associated with the life-threatening reactions of food allergies, are continuous stretches of amino acids. In contrast, conformational epitopes, which are implicated in the development of oral allergy syndrome (OAS), are formed by protein folding that brings distally located amino acids or peptides into spatial proximity.

The term OAS was initially used in the 1980s to describe the oral mucosal symptoms caused by cross-reactivity of airborne allergens and food allergens [2,3]. Pollen Food Allergy Syndrome (PFAS) is nowadays used to better describe the fact that primary sensitization to cross-reacting allergens is occurring in the respiratory system by pollen, and that the elicitation of symptoms after ingestion of homologous food proteins (called also pan-allergens) may involve the oral cavity but also the skin, gastrointestinal tract, and the respiratory system. Symptoms appear immediately or within 5-10 minutes after ingestion of the implicated food and usually gradually subside within 30 minutes [4,5]. Notably, in rare cases, PFAS may progress to anaphylactic reactions [4,5].

A wide variation in the incidence of PFAS is noticed around the globe, attributed to factors such as differences in climate and vegetation, dietary habits, the prevalence of atopy in each country, and syndrome's registration by healthcare professionals [6]. The aim of the present review is to comprehensively examine the existing literature on the epidemiology, clinical background and pathogenesis of PFAS. Pollinosis is widespread in Southern European countries, with the majority of

allergic rhinitis patients being polysensitized. Sensitization to pollen is strongly associated with a high incidence of PFAS. This review will explore the panallergens responsible for PFAS, with a specific focus on Southern Europe.

2. Materials and Methods

The Materials and Methods should be described with sufficient details to allow others to replicate and build on the published results. Please note that the publication of your manuscript implicates that you must make all materials, data, computer code, and protocols associated with the publication available to readers. Please disclose at the submission stage any restrictions on the availability of materials or information. New methods and protocols should be described in detail while well-established methods can be briefly described and appropriately cited.

Research manuscripts reporting large datasets that are deposited in a publicly available database should specify where the data have been deposited and provide the relevant accession numbers. If the accession numbers have not yet been obtained at the time of submission, please state that they will be provided during review. They must be provided prior to publication.

Interventionary studies involving animals or humans, and other studies that require ethical approval, must list the authority that provided approval and the corresponding ethical approval code.

3. Results

3.1. Pathogenesis of PFAS

PFAS occurs in individuals previously sensitized to pollen allergens through the respiratory tract, leading to the development of allergic rhinitis [7]. PFAS typically involves “Class 2” food allergens, which are conformational epitopes sensitive to heat, gastric acid, and digestive enzymes [8,9]. Primary sensitization occurs via pollen (which contains these allergens), leading to the development of allergic rhinitis [10]. Upon exposure to raw plant foods like fruits and vegetables containing cross-reactive allergens, specific IgE antibodies (sIgE) generated against pollen allergens bind to these food proteins, triggering PFAS symptoms [7,11]. In contrast, linear epitopes of plant-origin food allergens (“Class 1” food allergens) are typically sensitizing directly via ingestion [12]. These allergens are resistant to heat and gastrointestinal pH fluctuations, properties that enable them to cause systemic allergic reactions [9,12].

3.2. Epidemiology of PFAS/OAS

There is a wide variety of PFAS' prevalence in different geographical regions. Rates between 4.7% and more than 20% have been reported in children, and 13% to 53.8% in adults [13]. Studies aiming to determine the prevalence of PFAS often begin with populations that include individuals with allergic rhinitis or sensitivities to aeroallergens associated with PFAS. This selection bias may lead to artificially elevated prevalence rates [13]. Additionally, epidemiological studies face limitations such as varying definitions of PFAS and OAS, underreporting of symptoms that do not significantly affect daily quality of life, and underdiagnosis in individuals often labeled as 'picky eaters'.

In Asia, South Korea is the country with apparently the highest prevalence of PFAS (42.7%) [14], followed by Japan (34.6%) [15]. In a study performed in Armenia, its prevalence in young adults was 13% [16]. PFAS appears to be less widespread in USA; an old study performed with mailed questionnaire reported median estimates of the prevalence of OAS among the patients with pollen allergy were 5% among children and 8% among adults [17]. In Australia, the outcomes of a study performed in children and adolescents resulted that the prevalence of OAS was 14.7% and PFAS was 4.9% [18].

In Europe, particularly in central and northern areas, sensitization to Bet v1 allergen contained in birch pollen is the main cause of seasonal allergic rhinitis, as well as of PFAS, elicited by the ingestion of plant foods containing Bet v1-homologous PR10 proteins, such as Mal d1 in apple and Cor a1 in hazelnut [13,19]. In Europe, PFAS also occurs in allergic rhinitis patients, who have been

sensitized to panallergens present in the pollen of Grass or Ragweed [5]. The rise of temperatures due to the climate change is leading to a lengthening of the pollen season, increasing prevalence of allergic rhinitis and therefore growing prevalence of PFAS [5].

There is a higher incidence of PFAS in countries of northern Europe, compared to the south ones. The influence of birch and ragweed on the prevalence of PFAS in Europe is evident, with reports indicating a prevalence of 40%–50% among patients with pollen allergies [2,20]. In contrast, the prevalence is approximately 20% in the Mediterranean region, which is free of this pollen [21]. In pediatric studies performed in Sweden and United Kingdom the prevalence of PFAS was estimated to be 25% and 48%, respectively [22,23]. As far as the pediatric population in the Mediterranean area of South Europe is regarded the prevalence of PFAS is estimated; 35.9% in Italy, or in 27% of the ones with seasonal allergic rhinitis [6,24], 29.7% in Croatia [25], 16% in French children with asthma [26] and 3.3% in Turkish children with respiratory allergies [27].

3.3. PFAS in Adults of Southern Europe

Several studies show that the prevalence of PFAS varies significantly across Mediterranean countries, ranging from approximately 7.5% to 41.4% of the general population [6]. Variability is observed in the age of symptom onset, seasonality and frequency of symptoms, severity, and the occurrence of comorbidities [6]. Additionally, multisensitization to various pollen associated with PFAS distinguishes Mediterranean countries from those in Central and Northern Europe.

An effort to describe the occurrence of PFAS in the adult population of Southern Europe is outlined next. The @IT.2020 was a multicenter study conducted in the region, and has provided valuable insights on this topic [6].

3.3.1. Portugal

A study conducted in Portugal using telephone interviews reported a self-reported prevalence of OAS in adults, at 16.6% [28]. However, after medical assessment and IgE testing, food allergies (including OAS) were confirmed in fewer than 0.71% of the cases [28]. In data referring to the Portuguese population in the Porto area, it was observed that allergic symptoms typically begin at a very young age (around 7 years) and PFAS occurred in 23.5% [6]. Atopic dermatitis was found to be a common concomitant atopic disease, affecting 11 out of 24 patients.

More than half of the surveyed patients with PFAS (13 out of 24) reported experiencing at least one systemic symptom, with profilin identified as the predominant panallergen associated with PFAS symptoms [6]. Grass, Olive, Parietaria and Mugwort were identified as the predominant sensitizing pollen in Portugal [6]. Most of these pollen (Graminaceae, Artemisia, Olea europea) may act as primary sensitizers for profilin [29,30]. The foods most commonly causing PFAS in Portugal are kiwi, melon, peach, apricot, apple, banana and watermelon [6].

3.3.2. Spain

In an older study conducted in Spain, 6.51% of adolescent and adult patients referred to an Allergy Unit were diagnosed with OAS, representing 46.5% of those with a food allergy [31]. In a cross-sectional study, including a mix (children and adult) population OAS was estimated to be present in 33.6% of who visited an Allergist [32]. PFAS was observed in 14.1% of a Spanish cohort from the Valencia area, with atopic dermatitis reported as a common concomitant atopic disease among them [6].

Data from the @IT.2020 [6] study reported sensitivity to (the irrelevant to PFAS allergens) nsLTP in 4 out of 10 patients studied [6]. Sensitization to Pru p3, a nsLTP protein, is notable in many areas of Spain [33]. In contrast to PFAS, primary food sensitization to an nsLTP epitope, such as Pru p3 found in peaches, can result in a cross-reaction with Mal d3, found in apples, leading to systemic anaphylaxis after their ingestion [34].

Significant variability in sensitizations of adult patients is observed in Spain, influenced by geographic region, which affects the occurrence of PFAS. For instance, there is a higher frequency of sensitizations to Grass in the south-western region near Portugal, to Olive in the southern region, to Salsola kali in central-eastern region, and to Plantago lanceolata in the center-western region [21,33]. Notably, central Spain is home to the largest Quercus ilex (oak) forest area in the world, which may cause sensitization to Que i1, a PR10 allergen responsible for PFAS [32].

The foods most commonly causing PFAS in Spain are peach, almond, kiwi, pear, cherry, melon [6,35].

3.3.3. France

Few data on PFAS in French adults exist. In the @IT.2020 [6] study, patients from Marseille, France, presented the lowest incidence of PFAS (7.5%) within the studied cohort [6]. All French PFAS patients had moderate/severe allergic rhinitis [6]. PR10 was the prevalent panallergen in this patient cohort, and PFAS-associated foods were mainly kiwi, almond, sesame, watermelon, apple, banana and peach [6].

In a study conducted in France, patients who tested SPT-positive for Birch, and had Birch pollinosis reacted to rBet v1 (a PR-10 allergen), while sensitization to rBet v2 (a Birch-pollen profilin) may have also resulted from cross-sensitization to other pollen, such as Grass [36]. Allergies to apples, cherries, and hazelnuts were observed in these Birch-sensitized patients [36]. In Southern France, allergy to Cypress pollen has been connected to PFAS after peach and citrus ingestion, through sensitization to a Snakin/gibberellin-regulated protein sensitization [37].

3.3.4. Italy

In a large multicenter study performed in Italy, it was calculated that 57% of adults visiting an Allergy Clinics presented with "Type-2 food allergy", a term used to describe PFAS (97% of Type-2 food allergy patients), latex-fruit allergy syndrome (3%), and mugwort-celery-spice syndrome (<1%) [38]. PFAS patients had only mild symptoms; however, 5% of them reported systemic symptoms [38]. Regarding the geographical distribution of PFAS, a progressive decrease was registered southbound. The same southbound decrease was noticed for birch pollen sensitization [38,39].

A paradox that has been observed in the adult population of Genoa, located in Northern Italy, is that although there is a high percentage of Bet v1-positive patients, they have a low occurrence of OAS. This is explained by the fact that they live in a birch-free area, and positive Bet v1 sensitization is due to cross-reaction with Ost c1, the homologous allergen identified in hop-hornbeam (Ostrya carpinifolia), which has a wide distribution in the area [39].

Regarding allergenic foods in Italy, fruits and vegetables were the most commonly reported ones. Although this can be explained by the high occurrence of PFAS, no parallel increase in sensitization to them was noticed northbound [38]. Epidemiological registration of foods connected to PFAS in Italian adults remains an unmet need. Data from pediatric populations indicate that kiwi and peach are the main fruits causing PFAS in Italy [24].

3.3.5. Albania

According to the outcomes of the @IT.2020 [6] study, in Albania, 14% of the patients visiting an Allergy Center are presenting PFAS, they are mainly sensitized to PR-10 and they present moderate/severe allergic rhinitis [6]. The most frequent PFAS reactions were to almond, followed by cherry, apple, melon, banana and sesame [6].

3.3.6. Greece

In the Greek population, the high frequency of allergic rhinitis contributes to increased sensitization to various allergens and is therefore also connected to a higher occurrence of PFAS [6]. An online survey on self-reported OAS found that nearly 26% of the adult population experienced relevant symptoms [40]. The data from the @IT.2020 [6] study showed no PR-10 sensitivity but a low

occurrence of sensitization to nsLTP and profilin [6]. In a study with IgE-detected profilin, its prevalence in the atopic adult population was found to be 11% [41]. In the same study, OAS (mainly PFAS) was reported by 29.9% of the examined cohort, with no statistically significant correlation between sensitization to profilin and OAS [41]. OAS-PFAS in Greece is mainly attributed to peach, kiwi, melon, banana, almond and walnut [6,41]. Culprit foods might pose the suspicion of primary sensitization to PR-10 (and PR-5) allergens, however Greece is country with limited vegetation in trees or plants that produce PR-10 homologs, while there is vegetation of plants that produce PR-5 homologs [41].

3.3.7. Türkiye

In Türkiye, studies conducted in Ankara, Izmir, and Istanbul have shown similar outcomes, with approximately 14% of adult patients with allergic rhinitis presenting with PFAS [6,42]. The age of onset of PFAS symptoms is relatively late, around 26 years, and there is a low incidence of comorbidities [6]. PR-10 is not detected in pollen-allergic patients [6]. Most adults with allergic rhinitis and PFAS are sensitized to pollen of Grasses and Weeds, however sensitization to tree pollen was associated with the highest rates of PFAS [42,43]. The foods that most frequently induce PFAS are kiwi, peach, tomato, apricot, eggplant, walnut, sesame, melon, and watermelon. [6,42,43].

3.4. Allergens Causing PFAS in South Europe

3.4.1. Profilins

Profilin is one of proteins that cause PFAS in the South European area. Profilins like Phl p12 in Timothy grass, Art v4 in Mugwort, Pla a3 in Plane tree and Ole e2 in Olive tree can serve as the primary sensitizers in this area [41,44]. Sensitization in them may trigger PFAS in about 50% of sensitised patients, with foods like melon, watermelon, citron fruits, banana, pineapple, tomato, zucchini, mustard, hazelnut, tomato, persimmon, muskmelon, Apiaceae (celery, carrot, fennel) and Rosaceae (apple, pear, peach, apricot, plum) [4,44,45].

3.4.2. Pathogenesis-Related Class 10 Proteins

Sensitization to PR-10-like proteins is mainly caused by the pollen of Fagales, like Birch, Hazel, Chestnut, Beech, Oak and Alder [46]. Bet v1 is the major pollen allergen of Birch and represents the archetype of all PR-10-like allergens [47]. Although PR-10-like allergens are one of the most significant causes of PFAS in Europe, sensitization is not observed in the Mediterranean coastal regions, since Fagales do not grow in this region. Individuals in most central parts of the Southern European countries that are sensitized to their pollen, manifest OAS up to 70% after consuming fruits and vegetables of the Rosaceae (apple, peach), Actinidiaceae (kiwi), Corylaceae (hazelnut), Fabaceae (soy, peanut) and Apiaceae (celery, carrot) families [48]. Similarity of Bet v1 with the food allergens Cor a 1, Ara h 8, Gly m 4, Mal d 1 and Pru p 1 explains this cross-reaction [48].

3.4.3. Thaumatin-Like Proteins

Several members of the Thaumatin-like proteins (TLPs) (*PR-5 proteins*) plays an important role in the plant's defense against pathogens. TLP family have been identified as major allergens in Cupressaceae pollens, such as Jun a 3, Cup a 3, and Cry j 3, as well as in plant foods such as cherry, apple, kiwi, banana, grape, sapodilla, and bell pepper. Recombinant TLPs have been characterized as important allergens of bell pepper, several fruits (kiwi, apple, cherry, and grape) as well as of cypress, mountain cedar, and Japanese cedar pollens. Despite the vast experimental data, the clinical relevance of TLPs is still debated [34,49].

3.4.4. Non-Specific Lipid Transfer Proteins (nsLTPs)

Sensitisation to non-specific lipid transfer proteins (nsLTP) can be connected to clinical symptoms ranging from local manifestations to anaphylaxis. Sensitization typically occurs through ingestion of foods containing these proteins (e.g., peel of peach, walnut, apple) [50], although sensitization via inhalation is also possible in some cases [51,52]. nsLTPs are far more resistant to heat and gastric enzymes than profilins and PR-10s. This is why LTPs are responsible for most cases of systemic reactions following sensitisation through the gastrointestinal track [51,52]. They are considered one of the PFAS causes in Southern Europe and the Mediterranean area. Allergens of the nsLTP family are found in *Parietaria*, *Artemisia*, *Platanus* and *Olea* pollen, but they show rather low (*Artemisia* and *Platanus*) or absent (*Parietaria* and *Olea*) cross-reactivity with Pru p 3 as a consequence of the lower sequence identity (<35%), and different lengths [53]. In many patients food allergy symptoms are observed after ingestion of the skin of fruits of the Rosaceae family (Mal d 3-apple, Pru p 3-peach), but also with peanut, soybean, walnut and wheat [13]. It has been proposed that the severity of nsLTP-related allergic reactions is related to concomitant allergies to ≥ 3 plant food groups [54].

3.4.5. Gibberellin-Regulated Protein (GRP)

Of specific interest for Southern Europe is well-documented PFAS has been observed between peach and Cypress pollen. The culprit allergens belong to the Gibberellin-regulated protein (GRP) family, specifically BP14 from cypress pollen and Pru p 7 from peach [55].

3.5. Cross-Reactivity Between Aeroallergens and Food Allergens in Southern Europe

PFAS (Pollen-Food Allergy Syndrome) is clearly influenced by local airborne allergens, which act as primary sensitizers, as well as by the dietary habits of the local population. The Mediterranean climate, characterized by mild winters and dry summers with relatively high temperatures, supports a diverse range of vegetation typical of Southern Europe and the Mediterranean region. Common plants in this area include Grass, Olive and Cypress and weeds like *Parietaria*, *Plantago*, *Chenopodium*, *Salsola kali*, *Mugwort* and *Ragweed*.

Aerobiological sampling of pollen concentrations in Mediterranean cities has identified three distinct "pollen seasons" [56]:

1. Mild winter season (December-March) with Cypress as the prevailing pollen
2. Spring-Summer season (March-July) with Grass, Olive and weeds as prevailing pollen
3. Autumn period with *Parietaria* and *Artemisia*

An interesting review on the topic, highlights numerous associations between aeroallergens and foods of plant origin within this geographical area, many of them implicated in PFAS [57]. The region is particularly known for olive tree growing, and sensitization to the Olive profilin Ole e2, has been linked to PFAS to peach (*Prunus persica*), pear (*Pyrus communis*), melon (*Cucumis melo*) and kiwi (*Actinidia deliciosa*) [57]. The profilin Cyn d 12 from Bermuda grass (*Cynodon dactylon*) is cross-reactive with profilins from tomato (*Sola l1*) and cantaloupe (*Cuc m2*) [58]. On the other hand, the profilin of *Mugwort* (*Art v4*) is associated with PFAS involving Apiaceae foods such as celery (*Api g4*), carrot (*Dau c4*) and various spices, a cross-reaction often referred as Celery-Mugwort-Spice syndrome [57,59].

Fruits of the Cucurbitaceae family - including watermelon, cantaloupe, honeydew melon, zucchini and cucumber - are widely consumed during summer in South Europe. PFAS to Cucurbitaceae as well as to Musaceae family (e.g., bananas), is commonly observed in individuals sensitized to *Ragweed* (*Ambrosia artemisiifolia*), a phenomenon known as the Ragweed-Melon-Banana association [57,59,60]. PFAS to melon, banana and peach has also been linked to respiratory sensitization to the profilin of *Chenopodium album*, while sensitization to *Plantago lanceolata* pollen has also been associated with PFAS to melon [57,59].

Finally, pistachio (*Pistacia vera*), a popular tree nut in Italy, Greece, Türkiye and Cyprus have been implicated in PFAS due to cross-reactivity to *Parietaria* sensitization [61].

4. Discussion

Southern Europe's unique aeroallergen exposure - dominated by Oleaceae, Cupressaceae, Poaceae, Urticaceae, Chenopodiaceae, Plantaginaceae and Asteraceae - plays a crucial role in the pathogenesis of PFAS [62]. Cross-reactivity between aeroallergens and food allergens is a major driver of PFAS. In Southern Europe, the GRP allergens in Cypress pollen and nsLTPs in Olive pollen show significant cross-reactivity with common foods such as peach, melon, and other fruits. This interaction between environmental and dietary allergens is central to the distinct manifestation of PFAS in Mediterranean populations.

Climate change is emerging as a contributing factor to the rising prevalence of PFAS. Extended pollen seasons, shifts in vegetation patterns (notably the spread of Ragweed), and increased aeroallergen exposure may exacerbate both the incidence and severity of PFAS in Southern Europe, highlighting the need for ongoing surveillance and adaptive healthcare strategies [63,64].

The prevalence of PFAS in adult populations across Southern Europe shows significant variation [38]. One contributing factor to the inconsistencies in epidemiological data is the underestimation of the condition, which partly explains the observed differences in prevalence between children and adults. However, PFAS appears to be less severe in Southern Europe compared to Central and Northern Europe [38]. This disparity may be attributed to the limited blooming of the Betulaceae family, particularly birch trees, in coastal Southern Europe [19,62].

Region-specific diagnostic and therapeutic approaches are essential for managing PFAS. In Mediterranean countries, molecular diagnostics targeting nsLTPs (e.g., Pru p3) — which are strongly associated with systemic reactions — along with profilins and PR-10 proteins, should be prioritized. Component-resolved diagnostics (CRD) can enhance the accuracy of PFAS diagnosis by identifying primary sensitizations and distinguishing them from cross-reactivity. Incorporating molecular diagnostics and CRD into routine clinical practice is critical for improving diagnostic precision and effectively managing complex multisensitization profiles [65].

In the era of CRD, microarrays containing many different allergen components are very helpful in allergy diagnosis. The ImmunoCAP ISAC test is the most used and studied multiplex array to date, offering 112 molecular components [66]. The ALEX2 multiplex array is a relatively new multiplex allergy test which analyses more than 120 allergen extracts and 170 molecular components [66]. Advanced informatics tools, called expert systems, have also been developed to support the interpretation of allergy tests based on microarray technology [67]. Such state-of-the-art technology can assist allergy diagnosis of cross-reactions in poly-sensitized patients [57].

In conclusion, this review highlights the unique characteristics of PFAS in Southern Europe, influenced by regional aeroallergen profiles, dietary habits, and environmental factors. Addressing these gaps and utilizing advanced molecular diagnostic tools can significantly improve PFAS management and patient outcomes in this region.

Abbreviations

The following abbreviations are used in this manuscript:

CRD	Component-resolved diagnostics
GRP	Gibberellin-regulated protein
LTPs	Lipid transfer proteins
nsLTPs	Non-specific lipid transfer proteins
OAS	Oral Allergy Syndrome
PFAS	Pollen-food Allergy Syndrome
PR-10	Pathogenesis-related class 10 protein
PR-5	Pathogenesis-related class 5 protein
TLPs	Thaumatococcus-like proteins

References

1. Nwaru, B.I.; Hickstein, L.; Panesear, S.S.; Muraro, A.; Werfel, T.; Cardona, V.; Dubois, A.E.J.; Halken, S.; Hoffmann-Sommergruber, K.; Poulsen, L.K.; et al. The epidemiology of food allergy in Europe: a systematic review and meta-analysis. *Allergy* 2014, 69, 62-75. DOI: 10.1111/all.12305
2. Amlot, P.L.; Kemeny, D.M.; Zachary, C.; Parkes, P.; and Lessof, M.H. Oral allergy syndrome (OAS): symptoms of IgE-mediated hypersensitivity to foods. *Clinical & Experimental Allergy* 1987, 17(1), 33-42. DOI: 10.1111/j.1365-2222.1987.tb02317.x
3. Ortolani, C.; Ispano, M.; Pastorello, E.; Bigi, A.; Ansaloni, R. The oral allergy syndrome. *Annals of Allergy* 1988, 61, 47-52.
4. Alessandri, C.; Ferrara, R.; Bernardi, M.L.; Zennaro, D.; Tuppo, L.; Giangrieco, I.; Ricciardi, T.; Tamburrini, M.; Ciardiello, M.A.; Mari, A. Molecular approach to a patient's tailored diagnosis of the oral allergy syndrome. *Clin Transl Allergy* 2020, 10, 22. DOI: 10.1186/s13601-020-00329-8.
5. Skypala, I.J.; Hunter, H.; Krishna, M.T.; Rey-Garcia, H.; Till, S.J.; du Toit, G.; Angier, E.; Baker, S.; Stoenchev, K.V.; Luyt, D.K. BSACI guideline for the diagnosis and management of pollen food syndrome in the UK. *Clin Exp Allergy* 2022, 52(9), 1018-1034. DOI: 10.1111/cea.14208.
6. Lipp, T.; Acar Şahin, A.; Aggelidis, X.; Arasi, S.; Barbalace, A.; Bourgoin, A.; Bregu, B.; Brighetti, M.A.; Caeiro, E.; Caglayan Sozmen, S.; et al. Heterogeneity of pollen food allergy syndrome in seven Southern European countries: The @IT.2020 multicenter study. *Allergy* 2021, 76(10), 3041-3052. DOI: 10.1111/all.14742.
7. Mastroiilli, C.; Cardinale, F.; Giannetti, A.; Caffarelli, C. Pollen-Food Allergy Syndrome: A not so Rare Disease in Childhood. *Medicina (Kaunas)* 2019, 55(10), 641. DOI: 10.3390/medicina55100641.
8. Seidler CA, Zeindi R, Fernández-Quintero ML, Tollinger M, Liedl KR. Allergenicity and conformational diversity of allergens. *Allergies* 2024, 4(1), 1-16.
9. Miller, D.; Lee, M. Gastrointestinal stability of plant-based allergens and implications for systemic allergic reactions. *Clinical Immunology* 2017, 55(2), 210-222.
10. Worm, M.; Jappe, U.; Kleine-Tebbe, J.; Schäfer, C.; Reese, I.; Saloga, J.; Treudler, R.; Zuberbier, T.; Wassmann, A.; Fuchs, T.; et al. Food allergies resulting from immunological cross-reactivity with inhalant allergens. *Allergo J Int.* 2014; 23, 1-16.
11. Johnson, A.; et al. Food pollen syndrome: The clinical burden and immune mechanisms. *Food Allergy Journal* 2021, 7(2), 112-124.
12. Nguyen, T.; Chang, P. Class 1 food allergens and the pathogenesis of systemic reactions. *J. Allergy Immunol.* 2017, 139(6), 1830-1838.
13. Carlson, G.; Coop, C. Pollen food allergy syndrome (PFAS): A review of current available literature. *Ann. Allergy Asthma Immunol.* 2019, 123(4), 359-365. DOI: 10.1016/j.anai.2019.07.022.
14. Kim, M.A.; Kim, D.K.; Yang, H.J.; Yoo, Y.; Ahn, Y.; Park, H.S.; Lee, H.J.; Jeong, Y.Y.; Kim, B.S.; Bae, W.Y.; et al. Erratum: Pollen-Food Allergy Syndrome in Korean Pollinosis Patients: A Nationwide Survey. *Allergy Asthma Immunol. Res.* 2019, 11(3), 441-442. DOI: 10.4168/aaair.2019.11.3.441.
15. Kiguchi, T.; Yamamoto-Hanada, K.; Saito-Abe, M.; Sato, M.; Irahara, M.; Ogita, H.; Miyagi, Y.; Inuzuka, Y.; Toyokuni, K.; Nishimura, K.; et al. Pollen-food allergy syndrome and component sensitization in adolescents: A Japanese population-based study. *PLoS ONE* 2021, 16(4). DOI: 10.1371/journal.pone.0249649.
16. Movsiyan, M.R.; Hakobyan, A.V.; Gambarov, S.S. Pollen Food Allergy Syndrome (PFAS) Among Young Armenian Adults. *J. Allergy Clin. Immunol.* 2019, 142(2), AB433. DOI: 10.1016/j.jaci.2018.12.981.
17. Ma, S.; Sicherer, S.H.; Nowak-Węgrzyn, A. A survey on the management of pollen-food allergy syndrome in allergy practices. *J. Allergy Clin. Immunol.* 2003, 112(4), 784-788. DOI: 10.1016/S0091-6749(03)02008-6.
18. Brown, C.E.; Katelaris, C.H. The prevalence of the oral allergy syndrome and pollen-food syndrome in an atopic paediatric population in south-west Sydney. *J. Paediatrics Child Health* 2014, 50(10), 795-800. DOI: 10.1111/jpc.12658.
19. Biedermann, T.; Winther, L.; Till, S.J.; Panzner, P.; Knulst, A.; Valovirta, E. Birch pollen allergy in Europe. *Allergy* 2019, 74(7), 1237-1248. DOI: 10.1111/all.13758.

20. Osterballe, M.; Hansen, T.K.; Mortz, C.G.; Bindeslev-Jensen, C. The clinical relevance of sensitization to pollen-related fruits and vegetables in unselected pollen-sensitized adults. *Allergy* 2005, 60(2), 218–225. DOI: 10.1111/j.1398-9995.2005.00674.x.
21. Cuesta-Herranz, J.; Lázaro, M.; Figueredo, E.; Igea, J.M.; Umpiérrez, A.; De-Las-Heras, M. Allergy to plant-derived fresh foods in a birch- and ragweed-free area. *Clin. Exp. Allergy* 2000, 30(10), 1411–1416. DOI: 10.1046/j.1365-2222.2000.00868.x.
22. Westman, M.; Stjärne, P.; Asarnoj, A.; Kull, I.; van Hage, M.; Wickman, M.; Toskala, E. Natural course and comorbidities of allergic and nonallergic rhinitis in children. *J. Allergy Clin. Immunol.* 2012, 129(2), 403–408. DOI: 10.1016/j.jaci.2011.09.036.
23. Ludman, S.; Jafari-Mamaghani, M.; Ebling, R.; Fox, A.T.; Lack, G.; Du Toit, G. Pollen food syndrome amongst children with seasonal allergic rhinitis attending allergy clinic. *Pediatr. Allergy Immunol.* 2016, 27(2), 134–140. DOI: 10.1111/pai.12504.
24. Mastrorilli, C.; Tripodi, S.; Caffarelli, C.; Perna, S.; Di Rienzo-Busino, A.; Sfika, I.; Asero, R.; Dondi, A.; Bianchi, A.; Povesi Dascola, C.; et al. Endotypes of pollen-food syndrome in children with seasonal allergic rhinoconjunctivitis: a molecular classification. *Allergy* 2016, 71(8), 1181–1191. DOI: 10.1111/all.12888.
25. Ivković-Jureković, I. Oral allergy syndrome in children. *Int. Dent. J.* 2020, 65(3), 164–168. DOI: 10.1111/idj.12164.
26. Loraud, C.; de Ménonville, C.T.; Bourgoin-Heck, M.; Cottel, N.; Wanin, S.; Just, J. Emergence of pollen food allergy syndrome in asthmatic children in Paris. *Pediatr. Allergy Immunol.* 2021, 32(4), 702–708. DOI: 10.1111/pai.13435.
27. Guvenir, H.; Dibek Misirlioglu, E.; Buyuktiryaki, B.; Zabun, M.M.; Capanoglu, M.; Toyran, M.; Civelek, E.; Kocabas, C.N. Frequency and clinical features of pollen-food syndrome in children. *Allergol. Immunopathol* 2020, 48(1), 78–83. DOI: 10.1016/j.aller.2019.07.010.
28. Lozoya-Ibáñez, C.; Morgado-Nunes, S.; Rodrigues, A.; Lobo, C.; Taborda-Barata, L. Prevalence and clinical features of adverse food reactions in Portuguese adults. *All. Asthma Clin. Immunol.* 2016, 12: 36. DOI: 10.1186/s13223-016-0139-8.
29. Pereira, C.; Valero, A.; Loureiro, C.; Dávila, I.; Martínez-Cócera, C.; Murio, C.; Rico, P.; Palomino, R. Iberian study of aeroallergens sensitization in allergic rhinitis. *Eur. Annals Allergy Clin. Immunol.* 2006, 38(6), 186–194.
30. Tavares, B.; Machado, D.; Loureiro, G.; Cemlyn-Jones, J.; Pereira, C. Sensitization to profilin in the Central region of Portugal. *Sci. Total Environ.* 2008, 407(1), 273–278. DOI: 10.1016/j.scitotenv.2008.08.013
31. Alvarado, M.I.; Pérez, M. Study of food allergy in the Spanish population. *Allergol. Immunopathol. (Madr)* 2006, 34(5), 185–193. DOI: 10.1157/13094025.
32. Fernández-Rivas, M. Food Allergy in Alergológica-2005. *J. Invest. Allergol. Clin. Immunol.* 2009, 19(2), 37–44.
33. Barber, D.; de la Torre, F.; Feo, F.; Florido, F.; Guardia, P.; Moreno, C.; Quiralte, J.; Lombardero, M.; Villalba, M.; Salcedo, G.; et al. Understanding patient sensitization profiles in complex pollen areas: A molecular epidemiological study. *Allergy* 2008, 63(11), 1550–1558. DOI: 10.1111/j.1398-9995.2008.01807.x.
34. Fernández-Rivas, M.; Bolhaar, S.; González-Mancebo, E.; Asero, R.; van Leeuwen, A.; Bohle, B.; Ma, Y.; Ebner, C.; Rigby, N.; Sancho, A.I.; et al. Apple allergy across Europe: How allergen sensitization profiles determine the clinical expression of allergies to plant foods. *J. Allergy Clin. Immunol* 2006, 118(2), 481–488. DOI: 10.1016/j.jaci.2006.05.012.
35. Pedrosa, M.; Guerrero-Sanchez, V.M.; Canales-Bueno, N.; Loli-Ausejo, D.; Castillejo, M.Á.; Quirce, S.; Jorriñ-Novo, J.V.; Rodríguez-Pérez, R. Quercus ilex pollen allergen, Que i 1, responsible for pollen food allergy syndrome caused by fruits in Spanish allergic patients. *Clin. Exp. Allergy* 2020, 50(7), 815–823. DOI: 10.1111/cea.13679.
36. Pauli, G.; Oster, J.P.; Deviller, P.; Heiss, S.; Bessot, J.C.; Susani, M.; Ferreira, F.; Kraft, D.; Valenta, R. Skin testing with recombinant allergens rBet v 1 and birch profilin, rBet v 2: diagnostic value for birch pollen and associated allergic. *J. Allergy Clin. Immunol.* 1996, 97(5), 1100–1109. DOI: 10.1016/s0091-6749(96)70264-6.

37. Sénéchal, H.; Šantrůček, J.; Melčová, M.; Svoboda, P.; Zídková, J.; Charpin, D.; Guilloux, L.; Shahali, Y.; Selva, M.A.; Couderc, R.; et al. A new allergen family involved in pollen food-associated syndrome: Snakin/gibberellin-regulated proteins. *J. Allergy Clin. Immunol.* 2018, 141(1), 411-414. DOI: 10.1016/j.jaci.2017.06.041.
38. Asero, R.; Antonicelli, L.; Arena, A.; Bommarito, L.; Caruso, B.; Crivellaro, M.; De Carli, M.; Della Torre, E.; Della Torre, F.; Heffler, E.; et al. EpidemAAITO: Features of food allergy in Italian adults attending allergy clinics: a multi-centre study. *Clin. Exp. Allergy* 2009, 39(4), 547-555. DOI: 10.1111/j.1365-2222.2008.03167.x
39. Ciprandi, G.; Comite, P.; Mussap, M.; De Amici, M.; Quaglini, S.; Barocci, F.; Marsegia, G.L.; Scala, E. Profiles of birch sensitization (Bet v1, Bet v2, and Bet v4) and Oral Allergy Syndrome Across Italy. *J. Investig. Allergol. Clin. Immunol.* 2016, 26(4), 244-248. DOI: 10.18176/jiaci.0041.
40. Kalogeromitros, D.; Makris, M.P.; Chliva, C.; Sergeantanis, T.N.; Church, M.K.; Maurer, M.; Psaltopoulou, T. An internet survey on self-reported food allergy in Greece: Clinical aspects and lack of appropriate medical consultation. *J. Eur. Acad. Dermatol. Venereol.* 2012, 27(5), 558-564. DOI: 10.1111/j.1468-3083.2012.04482.x.
41. Iliopoulou, A.; Petrodimitopoulou, M.; Konstantakopoulou, M.; Pasioti, M.; Papadopoulou, A.; Mikos, N.; Kompoti, E.; Korakianitis, I.; Kontogianni, M.; Pitsios, C. Profilin sensitization and its clinical relevance to a population of atopic adults in Greece. *Revue Française d'Allergologie* 2018, 58(2), 72-76. DOI: 10.1016/j.reval.2017.11.001.
42. Özdemir, E.; Damadoğlu, E.; Karakaya, G.; Kalyoncu, A.F. Prevalence and clinical features of pollen-food allergy syndrome in adults with seasonal allergic rhinitis. *Eur. Rev. Med. Pharmacol. Sci.* 2023, 27(1), 103-109. DOI: 10.26355/eurrev_202301_30858.
43. Özdemir, S.K.; Özgüçlü, S. Pollen food allergy syndrome in Turkey: Clinical characteristics and evaluation of its association with skin test reactivity to pollens. *Asian Pac. J. Allergy Immunol.* 2018, 36(2), 77-81. DOI: 10.12932/AP0881.
44. Santos, A.; Van Ree, R. Profilins: Mimickers of allergy or relevant allergens? *Int. Arch. Allergy Immunol.* 2011, 155(3), 191-204. DOI: 10.1159/000321178.
45. Nucera, E.; Aruanno, A.; Rizzi, A.; Pecora, V.; Patriarca, G.; Buonomo, A.; Mezzacappa, S.; Schiavino, D. Profilin desensitization: A case series. *Int. J. Immunopathol. Pharmacol.* 2016, 29(3), 529-536. DOI: 10.1177/0394632015621926.
46. Barni, S.; Caimmi, D.; Chiera, F.; Comberiati, P.; Mastroilli, C.; Pelosi, U.; Paravati, F.; Marsegia, G.L.; Arasi, S. Phenotypes and Endotypes of Peach Allergy: What Is New? *Nutrients* 2022, 14(5), 998. DOI: 10.3390/nu14050998.
47. Breiteneder, H.; Kraft, D. The History and Science of the major Birch pollen allergen Bet v1. *Biomolecules* 2023, 13(7), 1151. DOI: 10.3390/biom13071151.
48. Scala, E.; Abeni, D.; Cecchi, L.; Guerra, E.C.; Locanto, M.; Pirrotta, L.; Giani, M.; Asero, R. Molecular recognition profiles and clinical patterns of PR-10 sensitization in a birch-free mediterranean area. *Int. Arch. Allergy Immunol.* 2017, 173(3), 138-146. DOI: 10.1159/000477565.
49. Hassan, A.K.G.; Venkatesh, Y.P. An overview of fruit allergy and the causative allergens. *Eur. Ann. Allergy Clin. Immunol.* 2015, 47(6), 180-187.
50. Ridolo, E.; Barone, A.; Ottoni, M.; Peveri, S.; Montagni, M.; Nicoletta, F. Factors and co-factors influencing clinical manifestations in nsLTPs allergy: between the good and the bad. *Front Allergy.* 2023, 4, 1253304. doi: 10.3389/falgy.2023.1253304
51. Amador, V.C.; Santos-Silva, C.A.D.; Vilela, L.M.B.; Oliveira-Lima, M.; de Santana Rêgo, M.; Roldan-Filho, R.S.; Oliveira-Silva, R.L.; Lemos, A.B.; de Oliveira, W.D.; Ferreira-Neto, J.R.C.; et al. Lipid transfer proteins (LTPs)—Structure, Diversity and Roles beyond Antimicrobial Activity. *Antibiotics (Basel)* 2021, 10(11), 1281. DOI: 10.3390/antibiotics10111281.
52. Poncet, P.; Sénéchal, H.; Charpin, D. Update on pollen-food allergy syndrome. *Expert Rev. Clin. Immunol.* 2020, 16(6), 561-578. DOI: 10.1080/1744666X.2020.1774366.
53. Pastorello, E.A.; Monza, M.; Pravettoni, V.; Longhi, R.; Bonara, P.; Scibilia, J.; Primavesi, L.; Scorza, R. Characterization of the T-cell epitopes of the major peach allergen Pru p 3. *Int. Arch. Allergy Immunol.* 2010, 153(1), 1-12. DOI:10.1159/000301573.

54. Zambrabo Ibarra, G.; Rodriguez Mazariego, M.E.; Lopez Tovar, C.; Blanco López, M.; Baeza Ochoa, M.L. Clinical and sensitization profile in peach allergy due to LTP sensitization. *Front Allergy* 2024, 5, 1477364. DOI: 10.3389/falgy.2024.1477364.
55. Sénéchal, H.; Keykhosravi, S.; Couderc, R.; Selva, M.A.; Shahali, Y.; Aizawa, T.; Busnel, J.M.; Arif, R.; Mercier, I.; Pham-Thi, N.; et al. Pollen/Fruit Syndrome: Clinical Relevance of the Cypress Pollen Allergenic Gibberellin-Regulated Protein. *Allergy Asthma Immunol. Res.* 2019, 11(1), 143-151. DOI: 10.4168/aair.2019.11.1.143.
56. D'Amato, G.; Cecchi, L.; Bonini, S.; Nunes, C.; Annesi-Maesano, I.; Behrendt, H.; Liccardi, G.; Popov, T.; van Cauwenberge, P. Allergenic pollen and pollen allergy in Europe. *Allergy* 2007, 62(9), 976-960. DOI: 10.1111/j.1398-9995.2007.01393.x.
57. Popescu, F.D. Cross-reactivity between aeroallergens and food allergens. *World J Methodol.* 2015, 5(2), 31-50. DOI: 10.5662/wjm.v5.i2.31.
58. Sankian, M.; Varasteh, A.; Pazouki, N.; Mahmoudi, M. Sequence homology: A poor predictive value for profilins cross-reactivity. *Clin. Mol. Allergy* 2005, 3, 13. DOI: 10.1186/1476-7961-3-13.
59. Egger, M.; Mutschlechner, S.; Wopfner, N.; Gadermaier, G.; Briza, P.; Ferreira, F. Pollen-food syndromes associated with weed pollinosis: an update from the molecular point of view. *Allergy* 2006, 61(4), 461-476. DOI: 10.1111/j.1398-9995.2006.00994.x.
60. Asero, R.; Mistrello, G.; Amato, S. The nature of melon allergy in ragweed-allergic subjects: a study of 1000 patients. *Allergy Asthma Proc.* 2011, 32(1), 64-67. DOI: 10.2500/aap.2011.32.3416.
61. Liccardi, G.; Russo, M.; Mistrello, G.; Falagiani, P.; D'Amato, M.; D'Amato, G. Sensitization to pistachio is common in Parietaria allergy. *Allergy* 1999, 54(6), 643-645. DOI: 10.1034/j.1398-9995.1999.00041.x.
62. D' Amato, G.; Lobefalo, G. *Allergenic pollens in the southern Mediterranean area.* *J. Allergy Clin. Immunol.* 1989, 83(1), 116-122. DOI: 10.1016/0091-6749(89)90485-5.
63. Lake, I.R.; Jones, N.R.; Agnew, M.; Goodess, C.M.; Giorgi, F.; Hamaoui-Laguel, L.; Semenov, M.A.; Solmon, F.; Storkey, J.; Vautard, R.; et al. *Climate change and future pollen allergy in Europe.* *Environ Health Perspect* 2017, 125(3), 385-391. DOI: 10.1289/EHP173.
64. Paudel, B.; Chu, T.; Chen, M.; Sampath, V.; Prunicki, M.; Nadeau, K.C. *Increased duration of pollen and mold exposure are linked to climate change.* *Sci Rep* 2021, 11(1), 12816. DOI: 10.1038/s41598-021-92178-z.
65. Canonica, G.W.; Ansotegui, I.J.; Pawankar, R.; Schmid-Grendelmeier, P.; van Hage, M.; Baena-Cagnani, C.E.; Melioli, G.; Nunes, C.; Passalacqua, G.; Rosenwasser, L.; et al. *A WAO - ARIA - GA²LEN consensus document on molecular-based allergy diagnostics.* *World Allergy Organ J.* 2013, 6(1), 17. DOI: 10.1186/1939-4551-6-17.
66. Sonneveld, L.J.H.; Emons, J.A.M.; Arends, N.J.T.; Landzaat, L.J.; Veenbergen, S.; Schreurs, M.W.J. *ALEX versus ISAC multiplex array in analyzing food allergy in atopic children.* *Clin. Mol. Allergy* 2022, 20(1), 10. DOI: 10.1186/s12948-022-00177-w.
67. Melioli, G.; Spenser, C.; Reggiardo, G.; Passalacqua, G.; Compalati, E.; Rogkakou, A.; Riccio, A.M.; Di Leo, E.; Nettis, E.; Canonica, G.W. Allergenius, an expert system for the interpretation of allergen microarray results. *World Allergy Organ J.* 2014, 7(1), 15. DOI: 10.1186/1939-4551-7-15.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.