Eur Ann Allergy Clin Immunol Vol 47, N 6, 180-187, 2015

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An overview of fruit allergy and the causative allergens

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Key words

Allergens; cross-reactivity; fruit allergy; oral allergy syndrome; tropical fruits.

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Summary

Plant allergens, being one of the most widespread allergenic substances, are hard to avoid. Hence, their identification and characterization are of prime importance for the diagnosis and treatment of food allergy. The reported allergies to fruits mainly evoke oral allergy syndrome caused by the presence of cross-reactive IgE to certain pollens and thus, allergy to fruits has also been linked to particular pollens. Many fruit allergies are being studied for their causative allergens, and are being characterized. Some tropical or exotic fruits are responsible for region-specific allergies for which only limited information is available, and generally lack allergen characterization. From a survey of the literature on fruit allergy, it is clear that some common fruits (apple, peach, musk melon, kiwi fruit, cherry, grape, strawberry, banana, custard apple, mango and pomegranate) and their allergens appear to be at the center of current research on food allergy. The present review focuses on common fruits reported as allergenic and their identified allergens; a brief description of allergens from six rare/tropical fruits is also covered.

Abbreviations: LTP, lipid transfer protein; NRL, natural rubber latex; nsLTP, non-specific LTP; OAS, oral allergy syndrome; PR-, pathogenesis-related; STP, skin prick test; TLP, thaumatin-like protein.

Introduction

Food allergy constitutes adverse immune response against food proteins that generally are harmless. From objectively confirmed results, ~5-8% children and 2-3% adults suffer from food allergy. Allergy to vegetables have been described for celery, asparagus, avocado, bell pepper, cabbage, carrot, fennel, lettuce, potato, pumpkin, turnip and zucchini (1-3). An enquiry into the fruits causing allergy leads one to a listing of 12-15 fruits to be commonly associated. Most of these are available worldwide in vegetable and fruit markets; however, a few rare fruits, especially tropical fruits and berries also can be observed to cause allergy in susceptible individuals.

The reported fruit allergic reactions are frequently observed to be associated with oral allergy syndrome (OAS) conjoined with pollen-fruit-vegetable syndrome, triggered upon consumption of raw vegetables or fresh fruits. This is most commonly attributed to cross-reacting, homologous proteins found in plant foods and pollens. Since conserved proteins and distinct epitopes of proteins are found throughout the plant kingdom, expression of homologous proteins in plant foods is not surprising (4-6).
Regional variations have been observed in OAS. In a study of 274 adults in England who were allergic to at least one pollen (birch, grass, and/or mugwort), 34% were sensitive to apple, 25% to potato, 23% each to carrot and celery, 22% to peach, and 16% to melon (7). In contrast, OAS is most commonly due to hazelnut, kiwi and apple in Denmark (8). Pollen-allergic adults in Sweden most often reported symptoms with hazelnut, apple, tomato, carrot, and peanut (9). In Spain, peach is the most common fruit which causes allergy (10).

Pollen-food syndromes have been observed to be associated with specific plants. One of them is birch-fruit-vegetable syndrome. Foods belonging to the family Rosaceae, which include apple, pear, peach and almond, most commonly cause symptoms in birch-allergic patients. Another is celery-birch-mugwort-spice syndrome; celery has been found to have cross-reactivity with both birch and mugwort pollens. In areas where birch trees are prevalent, celery allergy is due to Bet v 1 homologs. However, celery allergy does exist in birch-free areas; in these cases, mugwort pollen allergens may be the primary sensitizer (4). Bet v 1 and profilins have also been identified in various spices (11), including anise (Pim a 1 and 2), coriander (Cor s 1 and 2), cumin (Cum c 1 and 2), fennel (Foe v 1 and 2), and parsley (Pet c 1 and 2). Cross-reactivity between mugwort and mustard has also been demonstrated, and accordingly, celery-birch-mugwort-spice syndrome has been used to describe these cross-reactivities (12). Celery root (which is mainly consumed in Switzerland) has been associated with systemic symptoms in the "mugwort-celery-spice syndrome" (13), whereas celery stick is more often associated with OAS in birch pollen-allergic subjects (14).

Melon-induced OAS in ragweed-allergic subjects has been observed to be associated with profilin sensitization (15). Such cross-reaction syndromes have also been observed for mugwort-peach association, plantain-melon association, pellitory-pistachio association, goosefoot-fruit association, and Russian thistle-saffron association (16).

Latex-fruit syndrome was first reported by M'Raihi et al. (17), wherein an allergic reaction to banana was observed in a latex-allergic patient. Soon thereafter, cross-reactivity between latex and various fruits was demonstrated, and generally, this is termed latex-fruit syndrome (18). Some studies have reported that up to 88% of latex-allergic adults have evidence of specific IgE to plant-derived foods (19,20). Several homologous proteins are found to be present in allergenic plant foods as well as in latex which include Hev b 2 (β-1,3-glucanase), Hev b 11 (class I chitinase) and Hev b 8 (profilin) (4,21,22). Hev b 6 (prohevein) is the latex allergen that has received most attention as a possible cause of the latex-fruit allergy syndrome.

Different fruit processing conditions may induce alteration of immune-reactive epitopes on allergenic proteins. Processing was shown to destroy existing epitopes on a protein and generate new ones (formation of neoallergens) as a result of conformational changes (23). Upon surveying the fruit allergy reports, 10 to 12 common fruits and their allergens can be observed to be at the center of the current allergy research on fruits, which include apple, peach, kiwi, musk melon, grape, cherry, strawberry, banana, mango and pomegranate (listed in **table 1**). The present review focuses on such fruits reported as allergenic and the allergens identified from them; in addition, a brief account of some important rare fruits causing allergy is also covered.

Table 1 - *Common fruits and their identified allergens.*

Fruit	**Allergens [kDa - allergen name (nomenclature)]**
Apple (*Malus domestica*)	23.0 - TLP (Mal d 2) 17.5 - Bet v 1 homolog (Mal d 1) 14.0 - Profilin (Mal d 4) 9.0 - LTP (Mal d 3)
Peach (*Prunus persica*)	23.0 - TLP (Pru p 2) 17.5 - Bet v 1 homolog (Pru p 1) 14.0 - Profilin (Pru p 4) 9.0 - LTP (Pru p 3)
Musk melon (*Cucumis melo*)	67.0 - serine protease (Cuc m 1.01) 54.0 - serine protease (Cuc m 1.02) 36.0 - serine protease (Cuc m 1.03) 16.0 - PR-1 protein (Cuc m 3) 14.0 - Profilin (Cuc m 2)
Gold kiwi, green kiwi (*Actinidia chinensis*, *A. deliciosa*)	43.0 - Chitinase (Act d 3) 30.0 - Actinidin (Act d 1) 28.0 - Kiwellin (Act d 5) 23.0 - TLP (Act d 2) 11.0 - Cystatin (Act d 4)
Sweet cherry (*Prunus avium*)	23.0 - TLP (Pru av 2) 17.5 - Bet v 1 homolog (Pru av 1) 14.0 - Profilin (Pru av 4) 9.0 - LTP (Pru av 3)
Grape (*Vitis vinifera*)	30.0 - Chitinase, hevein-like (Vit v 5) 23.0 - TLP (Vit v TLP) 17.5 - Bet v 1 homolog (Vit v 8) 14.0 - Profilin (Vit v 4) 9.0 - LTP (Vit v 1)
Strawberry (*Fragaria ananassa*)	35.0 - Bet v 6 homolog (isoflavone reductase) 17.5 - Bet v 1 homolog (Fra a 1) 14.0 - Profilin (Fra a 4) 9.0 - LTP (Fra a 3)
Banana (*Musa acuminata*)	33.0 - β-1,3-glucanase (Mus a 5) 31.0 - Class I chitinase (Mus a 2) 21.0 - TLP (Mus a 4)
Custard apple (*Annona cherimola*)	45.0 - Class I chitinase (Ann c Chitinase)
Mango (*Anacardium occidentale*)	14.0 - Bet v 1-like (Man i 14kD) 30-45 Class I chitinase (Man i Chitinase)
Pomegranate (*Punica granatum*)	28.0 - PR-4 protein (Barwin family) 17.0 - PR-4 protein 16.0 - PR-4 protein 9.0 - LTP (Pun g 1)

Common fruits causing allergy and their allergens

Apple (Malus domestica**):** Allergy to apple, a fruit of the Rosaceae family, is usually presented with mild oropharyngeal symptoms. Mal d 1, homologous to the major birch pollen allergen Bet v 1 was the first apple allergen to be characterized (24). Later, other allergens were identified which include the thaumatin-like protein (TLP; Mal d 2), the non-specific lipid transfer protein (nsLTP; Mal d 3) and the profilin (Mal d 4).

In Northern and Central Europe, the occurrence of allergy to apple is frequently related to birch pollinosis, and sensitization is due to cross-reactivity between Bet v 1 and Mal d 1, whereas in Southern Europe this fruit allergy is observed together with allergy to peach caused by the allergens Pru p 3 and Mal d 3. Symptoms related to Mal d 1 are generally mild and local, representative of a chemically-labile protein. Mal d 3, on the other hand, is a highly stable protein due to the presence of four disulfide bonds. Mal d 3 and its homologs in other fruits and vegetables have been repeatedly detected as the main elicitors for true food allergy. Systemic manifestations mainly occur in the Mediterranean area and are observed to be based on cross-reactivity between apple LTP and peach LTP, with the latter considered as the primary sensitizer. LTP allergenicity is not reduced by high-temperature processing (25,26). Little is known about the way of sensitization to Mal d 2 (TLP). However, due to the presence of 8 conserved disulfide bridges, TLPs are expected to be resistant to pH or heat. Mal d 4 is a minor allergen and seems to be pollinosis-related; Bet v 2, the birch pollen profilin, sensitizes approximately 20% of the pollen-allergic patients. Profilins seem to be highly cross-reactive allergens with other fruits and vegetables of the Rosaceae, Vitaceae and Solanaceae families as well as with several pollens.

Peach (Prunus persica**):** The two fruits from Rosaceae most frequently involved in allergy cases are apple and peach. Different clinical phenotypes of peach allergy are observed across Europe in relation to different allergen sensitization patterns to the peach allergens. In a series of studies on Rosaceae fruit allergy in the Mediterranean area, peach has been shown as the first triggering food to subsequently associate with other Rosaceae fruits such as apple, due to cross-reactivity of their LTPs (27). In areas rich in birch trees of Central and Northern Europe, peach allergy is linked to birch pollinosis and apple allergy. These patients present mild oropharyngeal symptoms upon peach ingestion. As in the case of apple, 4 homologous allergens have been identified in peach so far: Pru p 1 (a Bet v 1 homolog), Pru p 2 (a TLP), Pru p 3 (a profilin) and Pru p 4 (a LTP) (28, 29).

Musk melon (Cucumis melo**):** As a member of the Cucurbitaceae family which includes several warm season vegetables (squash, cucumber and pumpkin) and fruits (watermelon), musk melon has been reported as a frequent cause of fruit allergy, both in some areas from the U.S. and the European Union. Primary melon allergy is extremely rare, and most cases of melon allergy occur in pollen-allergic subjects. Profilin (Cuc m 2) has been identified as a major allergen from this fruit (30). Other allergens described from this fruit are cucumisin (Cuc m 1, a subtilisin-like protease), and Cuc m 3, a 16 kDa pathogenesis-related (PR) protein belonging to the PR-1 family (31); no plant allergen homologous to Cuc m 3 has been detected till date. The Cuc m 1 serine protease is present in the melon extract in several molecular forms which arise during the process of maturation and subsequently as degradation fragments and, similar to Hev b 6, they have been named Cuc m 1.01 (67 kDa), Cuc m 1.02 (54 kDa) and Cuc m 1.03 (36 kDa); cucumisin and its several N-terminal fragments are major allergens of melon. The ubiquitous distribution of this protein family (cucumisin-like proteases) in many plant species, its high structural similarity and the inhibition data suggest its potential role as a panallergen in plant foods (31).

Kiwi (Actinidia **spp.):** A popular fruit, very rich in vitamin C, is available in two varieties: one with green flesh and the other with yellow flesh. Allergy to green kiwifruit (*A. deliciosa*) was the first to be documented in the early 1980s, and has been reported increasingly in recent years. Moreover, a closely related species, gold kiwi fruit (*A. chinensis*) became available in the international market in 1999 and shares IgE cross-reactivity and the presence of common allergens with green kiwifruit (32). Although allergy to kiwifruit is commonly associated with mild and local symptoms (mainly OAS) and with hypersensitivity to pollens, severe anaphylactic reactions also occur frequently. Further, kiwi allergy also has to be considered in relationship with the latex-fruit syndrome, together with sensitization to avocado, chestnut and banana, which are the main plant foods linked to latex allergy (32).

Among the several putative kiwifruit allergens detected, only two of them have been studied sufficiently in different groups of kiwi-allergic patients till now. Act d 1 (originally Act c 1) corresponds to the 30 kDa thiol-protease actinidin, which is well established as a major kiwi allergen (33). Act d 2 is a 24 kDa TLP, whose sensitization prevalence is still controversial. Besides, N-terminal amino acid sequences of putative relevant allergens, namely an 11 kDa cystatin (Act d 4), a 28 kDa kiwellin (Act d 5), 43 and 45 kDa chitinases (Act d 3) have been reported. Class I chitinases with an N-terminal hevein-like domain and latex hevein have been identified as the major cross-reactive components involved in this latex-fruit syndrome (34). Identification of major allergens in kiwifruit has so far resulted in conflicting and confusing results both in terms of number and relevance of allergens. In fact, different studies reported different dominant allergens, probably due to differences in both experimental procedures and study population used (32).

Cherry (Prunus avium**):** Allergy to cherry fruit is often reported in the context of allergy to other fruits of the Rosaceae family and pollinosis to trees because of cross-reactive allergens. Allergic reactions to cherry are reported by 19-29% of birch pollen-allergic patients (35). Pru av 2, identified as a TLP from sweet cherry, was recognized by the majority of cherry-allergic patients. Pollen-related cherry allergy is caused by the presence of cross-reactive IgE epitopes on homologous proteins. Four allergens from sweet cherry have been identified so far. Pru av 1 and Pru av 4 are homologous to the birch pollen allergens Bet v 1 and Bet v 2, respectively, and are in part responsible for the cross-reactivity between birch pollen and cherry. Pru av 3 is a nsLTP sharing high amino acid sequence identities with nsLTPs from other Rosaceae fruits. Pru av 2 was first identified in 1996 as the most abundant soluble protein (29 kDa) in ripe cherries accumulating during the ripening process. Later, TLP (23 kDa) from cherry was described as a potential major allergen and named as Pru a 2, which was revised as Pru av 2 (36).

Grape (Vitis vinifera**):** As one of the oldest cultivated plants all over the world, it grows in a temperate climate, especially around the Mediterranean, and its fruit, the grape, is consumed either directly or as processed products (juice, jam and wine). Western Europe is the world's biggest producer of grapes; France, Italy and Spain are the major producers of wine that is consumed throughout the world. Allergic reactions to wine are commonly believed to be caused mainly by sulfites (37). Giannoccaro et al. (38) reported a patient allergic to grape and cherry. Pastorello et al. (39) characterized the major allergens of grape as endochitinase 4A (~30 kDa) and a LTP that was homologous to and cross-reactive with peach LTP; however, a 24 kDa TLP was found to be a minor allergen. In another study, severe allergic reactions to grapes have been described as part of a LTP-associated clinical syndrome (40).

Endochitinase 4A is very likely the allergen in *vino novello* (young wine) and *vino Fragolino.* Researchers have observed several patients with severe allergic reactions after eating grapes and, in some of them, also after drinking two particular kinds of red wine, namely *vino Fragolino* and *vino novello.* Some technical differences in the process of making non-aged wine might explain why the patients were allergic only to *vino novello* or *vino Fragolino.* Polymerization of polyphenols causes the tiny residual proteinaceous material in red wines to coalesce, so that it can be filtered off once the wine has aged, thus theoretically explaining why the patients tolerated older wine. Grape chitinases account for 50% of the soluble proteins in grapes, persisting through the vinification process. Another protein persisting in wine throughout vinification is the 24 kDa TLP, which has been found as another important allergen in grapes. The identification of a 9 kDa LTP as a major grape allergen seems very interesting because it could explain why grape allergy is often associated with allergic reactions to fruits, such as peach and cherry (39).

Strawberry (Fragaria ananassa**):** Nicknamed an 'accessory' fruit due to its seeds on the outside, strawberry is not only eaten fresh, but also used as a common ingredient in many food products such as jam, yogurt, ice cream, and breakfast cereals; strawberry is an important ingredient in the food industry. The strawberry Fra a 1 allergen is a homolog of the major birch pollen allergen Bet v 1. Mass spectrometric analysis indicated the presence of strawberry homologs to the Bet v 1 allergen in both the 20 and the 18 kDa protein bands. They are synthesized by red ripe strawberry fruits while white strawberry fruits of a mutant genotype, which is known to be tolerated by individuals affected by strawberry allergy, are devoid of them (41-43). The presence of a strawberry homolog to the 35 kDa Bet v 6 allergen, an isoflavone reductase, was also suggested to be a strawberry allergen. A 9 kDa LTP (Fra a 3) with 74% homology to apple LTP (Mal d 3) has been detected, which could be a possible strawberry allergen (44).

Banana (Musa acuminata**):** Allergy to banana is relatively frequent; the relevance of banana as a source of food allergy was confirmed in two patients by double-blind food challenge. It has been observed that 20-50% of patients allergic to natural rubber latex (NRL) have experienced symptoms after eating banana. Even though evidence for cross-reacting allergens in NRL and banana has also been reported (45), most cases of banana allergy are associated with profilin sensitization; banana-latex association is, by far, less frequent. Three major allergens from banana have been identified (46-48): Mus a 2 (31 kDa class I chitinase), Mus a 4 (21 kDa TLP), and Mus a 5 (33 kDa β-1,3-glucanase).

Custard apple (Annona cherimola**):** Allergic cases reported for custard apple (also known as cherimoya) have, for most of the cases, been in cross-reaction to latex. Cross-reactivity with latex allergy was found for 40-45 kDa proteins; the 45 kDa protein was identified as chitinase. It has also been reported that the N-terminal hevein-like domain of the chitinase is responsible for cross-reactivity with latex (49). The first case of allergy to custard apple was reported in 1997 wherein a 20-25 kDa band was detected. A 14 kDa acyl carrier protein was also reported as an allergen but not confirmed. Several reports of allergy to custard apple have appeared in the literature (50-52). The 20-25 kDa protein identified as the allergen by IgE-immunoblotting is likely to be a TLP.

Mango (Anacardium occidentale**):** This delicious fruit belongs to the Anacardiaceae family (*Sumac* species), which also includes cashews and pistachios. Rubin and Shapiro (53) were the first to report an anaphylactic reaction following the ingestion of mango. Renner et al. (54) identified 2 major allergens with a molecular mass of 27 kDa in two patients, in addition to a 15 kDa allergen in one patient and a 32 kDa allergen in another. Mango profilin has been shown to cross-react with birch pollen profilin Bet v 2 (55).

Pomegranate (Punica granatum**):** This fruit is commonly consumed in raw and processed forms such as juice, wines, flavors, and extracts, but has rarely been reported to cause immediate hypersensitivity after ingestion. Allergy to pomegranate was first reported by Igea et al. (56) wherein an IgE-mediated allergy could not be demonstrated. An extremely rare case of anaphylaxis to mannitol present in pomegranate (0.25 g per 100 g edible portion) was described by Hegde et al. (57); the presence of mannitol-specific IgE was further demonstrated in the serum of the allergic subject (58). Cross-reactivity has been demonstrated for LTPs present in different fruits including pomegranate (59). By 2-D electrophoresis, Bolla et al. (60) have separated different nsLTP isoforms possessing different IgE-binding properties, which might reflect peculiar allergenic potencies; the contribution of Pru p 3 to prime sensitization is not central as in other plant nsLTPs. Currently, it appears that nsLTP is the major pomegranate allergen (60).

Important allergens causing fruit allergy

Birch pollen-associated allergy in relation to fruits is a well-known clinical phenomenon especially in northern Europe. Following a primary sensitization to birch pollen allergen, a subsequent IgE cross-reaction with homologous proteins in the consumed fruit occurs. Bet v 1, the major birch pollen allergen, shares common epitopes with major food allergens in a large number of different fruits and berries, e.g., cherry (Pru av 1), apple (Mal d 1), pear (Pyr c 1) and peach (Pru p 1). Patients suffering from type I hypersensitivity caused by birch pollen frequently demonstrate allergy to many fruits.

Plant nsLTPs are a widely distributed superfamily of related proteins (PR-14 defense proteins). They are divided into two subfamilies according to their molecular masses: the 9 kDa nsLTP1 and the 7 kDa nsLTP2; several nsLTPs with allergenic activity have been identified in fruits and pollens. The most frequently implicated foods belong to the Rosaceae fruits, but nsLTPs with allergenic activity have also been detected in tree nuts, peanut, lupine, maize, mustard, fennel, and several other fruits and vegetables.

The family of TLPs (PR-5 defense proteins) plays an important role in the plant's defense against pathogens. Several members of the 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 TLP is still debated because hypersensitivity to this allergen is exceedingly rare in an isolated form (23).

The latex-fruit syndrome is the result of cross-reactivity between NRL proteins and fruit proteins. Class 1 chitinases (Hev b 6, hevein-like proteins), β-1,3-glucanases (Hev b 2), and other cross-reactive proteins have been implicated. The commonly reported cross-reactive foods include banana, avocado, kiwi and chestnut. The group of defense-related plant proteins, class 1 chitinases, cross-react with the pan allergen hevein. Cross-reactivity with these proteins is noted for banana, avocado, kiwi, chestnut, papaya, tomato, cherimoya, passion fruit, mango and wheat. Prohevein (Hev b 6) behaves as a major allergen, since it reacts with IgE in most sera of subjects with latex allergy (4).

Plant allergens, being one of the most widespread allergenic substances, are hard to avoid. Therefore, their identification and characterization aid in the diagnosis and treatment of allergic diseases. Although serum IgE level is low in the general population, those with hereditary risk of atopy produce excessive levels of IgE, and in conjunction with the relatively high occurrence of the conserved proteins and epitopes in plant-derived foods, completes the disease triangle resulting in sensitization and allergic reactions. In most cases, protocols for the diagnosis of food allergy make use of whole food extracts. However, depending on the experimental procedure used and on the food characteristics (e.g., the ripening stage of a fruit), whole food extracts may be variable in both the number and amount of the allergenic components; this heterogeneity may be at least one of the causes of some conflicting and confusing results reported in the field of allergy. Moreover, results obtained by using whole food extracts do not provide information about individual sensitivity towards single allergenic components of the investigated food, which should be particularly useful in planning and monitoring desensitizing immunotherapy. Availability of purified and characterized allergens would help solving these clinical problems, and also allow controlled and reproducible production of hypoallergenic derivatives (61-63).

Allergy caused by fruits with lower incidence and rare/tropical fruits

Apart from the common fruits available in the vegetable and fruit market, many allergic reactions have been reported for some common fruits as well as for tropical and region-specific fruits. Since only limited number of cases is encountered, the causative allergens have not been identified in many cases as characterization of the allergens is lacking. Despite the low incidence of allergy to these fruits, isolation and characterization of some allergens have been carried out. Allergy to some common fruits with a lower incidence of allergy including rare/tropical fruits is summarized in **table 2**. These include orange (64-66), mulberry (67, 68), lychee (69, 70), raspberry (71, 72), pineapple (73, 74) and sapodilla (75, 76). Since many tropical and exotic fruits are exported to other countries, increased consumption of these rare fruits is likely to cause a moderate increase in the incidence of these fruit allergy in future.

Table 2 - Allergens from fruits with low incidence of allergy and some rare/tropical fruits.

Fruit	Remarks	Reference
Orange (*Citrus sinensis*)	Germin-like glycoprotein (Cit s 1; 23.7 kDa), profilin (Cit s 2), LTP (Cit s 3)	64-66
Mulberry (*Morus alba, M. nigra*)	Bet v 1-related allergens (Mor a 1), nsLTP1 (Mor n 3), profilin (Mor a 4)	67, 68
Lychee (*Litchi chinensis*)	Profilin (Lit c 1), 35 kDa isoflavone reductase (Lit c IFR), 28 kDa triose-phosphate isomerase (Lit c TPI)	69, 70
Raspberry (*Rubus idaeus*)	Rub i 1 (Mal d 1 homolog), Rub i 3 (Mal d 3 homolog), 30 kDa protein (class III chitinase), cyclophilin (Bet v 7 homolog)	71, 72
Pineapple (*Ananas comosus*)	Systemic reactions; profilin (Ana c 1), bromelain (Ana c 2)	73, 74
Sapodilla (*Manilkara zapota*)	Mainly oral allergy syndrome; acidic TLP (Man za TLP 1), basic TLP (Man za TLP 2)	75, 76

Conclusions

It can be observed that most fruits available in the market elicit allergic reactions in susceptible individuals. The prevalence of fruit allergy appears to result from the increased imports and exports of fruits sensitizing susceptible individuals. It can also be observed that similar allergens are present in most of the fruits, and show structural similarity with homologous allergens from pollens and other vegetables/fruits. Although observations on the similarities and differences in allergenic structures may lead to many speculations regarding fruit allergens, substantial experimental data is required to establish allergen properties and uniqueness. Since the protein content of fruits is very low, a detailed study on the fruit proteins is lacking in many situations. The lack of patient data on rare fruit allergy makes it difficult to characterize new allergens form these fruits. Nonetheless, proteomic studies of all fruits should be performed to locate the many isoforms and differential expressions of fruit allergens which should pave the way for preparation of fruit extracts or recombinant allergens for fruit allergy diagnosis and immunotherapy.

Funding

Some of the research work described in this review has been investigated from funding provided to YPV by the Department of Science and Technology (DST; project# SP/SO/B48/97), New Delhi and the Council of Scientific and Industrial Research (CSIR; institutional projects MLP-0201, MLP-1407 and MLP-0094), New Delhi.

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