Clinic Rev Allerg Immunol (2019) 57:39–54
https://doi.org/10.1007/s12016-017-8651-2

A Comprehensive Review on Mustard-Induced Allergy and Implications for Human Health

Akanksha Sharma[1,3] · **Alok K. Verma**[2] · **Rinkesh Kumar Gupta**[1] · **Neelabh**[4] · **Premendra D. Dwivedi**[1,3]

Published online: 20 November 2017

Abstract Mustard is widely used in a variety of foods/food products to enhance the flavor and nutritional value that subsequently raise the risk of hypersensitivity reactions. Mustard allergy has been reported for many years and is increasing gradually especially in the areas where its consumption is comparatively higher, and it may be considered among the most important food allergies. A number of relevant clinical studies focused on mustard-induced allergic manifestations are summarized in the current review. In addition, the knowledge regarding the immunological as well as biochemical characteristics of mustard allergens that have been known till date and their cross-reactivity with other food allergens have also been discussed here. Notably, mustard may also be present as a hidden allergen in foods; therefore, it is important to recognize food products that may contain mustard as it may pose potential risk for the allergic individuals. Additionally, the better understanding of the underlying mechanism in mustard allergy is a prerequisite for the development of specific therapeutic procedures. Conclusively, mustard sensitivity should be routinely tested in patients with idiopathic anaphylaxis for the safety of the allergic patients.

Keywords Mustard allergy · Cross-reactivity · Hidden allergen · Anaphylaxis

Abbreviations

APC	Antigen-presenting cells
SPT	Skin prick test
DBPCFC	Double-blind placebo-controlled food challenge
PFAS	Pollen-food allergy syndrome
LA	Latex allergy
NRL	Natural rubber latex
mAbs	Monoclonal antibodies
LTPs	Lipid transfer proteins
MW	Molecular weight

Introduction

The last few decades have witnessed an increased prevalence of the allergic diseases worldwide, and food allergy constitutes a major part of this increase [1, 2]. Our gastrointestinal tract is continuously exposed to a large number of antigenic loads in the form of either commensal bacteria, harmful antigens, or food antigens. There is a need to balance between the immune reactions and tolerogenic reactions. Failure of this balance or immune tolerance to food antigens results into a strong immune reaction against the ingested foods and may cause allergy-like symptoms. Basically, food allergy may be defined as a disorder characterized by adverse immune response upon the ingestion of even a tiny amount of food and food components in the susceptible individuals. It is important to note that not all the constituents of food are responsible for

✉ Premendra D. Dwivedi
pddwivedi@yahoo.com; pddwivedi@iitr.res.in

[1] Food Toxicology Laboratory, Food, Drug and Chemical Toxicology Group, CSIR-Indian Institute of Toxicology Research (CSIR-IITR), 31, Vishvigyan Bhawan, P.O. Box No. 80, Mahatma Gandhi Marg, Lucknow, Uttar Pradesh 226 001, India

[2] Department of Medicine, Section of Pulmonary Diseases, Tulane Eosinophilic Disorders Center, Tulane University School of Medicine, New Orleans, LA 70112,, USA

[3] Academy of Scientific and Innovative Research (AcSIR), CSIR-IITR, Lucknow, India

[4] Department of Zoology, Banaras Hindu University (BHU), Varanasi, Uttar Pradesh 221005,, India

the allergic reactions, but only a few proteins present in food are recognized by the immune system as foreign and are responsible for eliciting an immune response [3]. Food-induced allergic reactions are the consequence of the immunological responses against any food protein that may include effector cells, food-specific IgE antibodies, and cell-mediated reactions resulting into acute, sub-acute, and in some cases chronic reactions. Further, food-induced allergic reactions include symptoms involving the respiratory tract, gastrointestinal tract, and skin in the susceptible individuals [4, 5].

The anaphylactic reactions due to consumption of food affect a significant percentage of the population, and the prevalence of food allergy is estimated about 6–8% in children and 3–4% in adults [6]. The incidences of food allergy vary from country to country and depend on the food habits as well as lifestyle of a particular geographical area like soy allergy is common in Japan; peanut allergy in the UK, France, and North America; and sesame allergy in Israel [7]. The eight foods commonly known as the "Big Eight" account for about 90% of documented food allergy and includes peanuts, soybeans, cow's milk, hen's egg, fish, crustacean, wheat, and tree nuts. Out of these foods, cow's milk, eggs, wheat, soy, peanut, and fish are the main causes of food allergy in infancy and early childhood [8–10]; whereas peanut, tree nuts, and seafood are reported to be causative factors in 85% of severe reactions in grown-up children and adults [11, 12]. In addition to these common and potential allergens, few uncommon or unusual foods may also cause allergic reactions in sensitive individuals; these include mustard [13], sesame seeds [14], mango [15], red meat [16], avocados [17], kiwis [18], spices and condiments [19], banana [20], cereals [21], eggplant [22], and many others.

In the recent years, the scientific community and clinicians have focused their attention towards mustard allergy as the incidences are increasing day by day. Basically, mustard belongs to the Brassicaceae family that includes more than 3200 species and 375 genera together with some important vegetable crops. The most common varieties of mustard are as follows:

1. White mustard (*Brassica alba*; *syn.*: *B. hirta*, *Sinapis alba*), also known as yellow mustard and is cultivated for its pungent seeds. It is a common source of table mustard
2. Black mustard (*B. nigra*; *syn.*: *S. nigra*, *B. sinapioides*), a Eurasian annual variety of mustard with pungent odor and flavor is an important source of oil. Its seeds are used in the pharmaceutical industry for cataplasms because of their revulsive properties
3. Brown mustard (*B. juncea*; *syn.*: *B. integrifolia*), commonly known as oriental mustard, Chinese mustard, Indian mustard, leaf mustard, Sarepta mustard, and Asiatic mustard that is used as a spice and a potherb and for mustard oil.

Mustard is widely used in foods to enhance the flavor and for its nutritional values; therefore, there are chances of provoking allergic manifestations in susceptible individuals (Table 1) [23]. Foods formulated with mustard are expected to increase in popularity in the future due to its sensory attributes, its high protein content, and its functional properties (Table 2) [24, 25]. The widespread use of mustard in foods has raised concerns that mustard can cause IgE-mediated allergic reactions in sensitive individuals. Allergy to mustard depends upon the extent of its consumption, and prevalence is rather high in the areas where the consumption of mustard is more than in other parts of the world.

Scenario of Mustard-Induced Food Allergy Mustard allergy accounts for 1.1% of food allergies in children [26] and about 6–7% of total food allergies [27]. Mustard-induced anaphylaxis has also been reported over the last 20 years [28, 29].

In countries like France, mustard is extensively consumed in foods as sauce or food additive with the consequent risk of

Table 1 List of foods containing mustard

S. No.	List of foods
1.	Condiments
2.	Spices, flavoring, or seasoning
3.	Salad dressings (vinaigrettes and cruditées)
4.	Barbecue sauce
5.	Curry sauce
6.	Cumberland sauce
7.	Ketchup, tomato sauces
8.	Béarnaises
9.	Mayonnaises
10.	Pesto sauce
11.	Curries, chutneys
12.	Pickles and other pickled products
13.	Vegetables with vinegar
14.	Dehydrated soups
15.	Processed meat (sausages, salami etc.) including hamburgers/steakettes, Some fast food products
16.	Some appetizers
17.	Dehydrated mashed potatoes
18.	Some baby/toddlers pre packaged food
19.	Sprouted seeds
20.	Mustard powder (additive to foods)
21.	Mustard sauce (commercial)
22.	Salad dressing
23.	Salad oil
24.	Flours for flavoring fried fish or meat
25.	Lubricant

This list is taken from Monsalve et al. (2001) and from review—Mustard one of the ten priority food allergens, Government of Canada

Table 2 Mustard nutrient compositions

S. No.	Composition	Yellow mustard seeds (%)	Brown mustard seeds (%)	Black mustard seeds (%)
1.	Protein	30	26	23
2.	Fixed oil	29	32	36
3.	Carbohydrates	16	12	18
4.	Minerals	4	4	4
5.	Essential oils	2.3	0.78	0.8
6.	Phytin	2	2	3
7.	Fiber	9	7	6
8.	Ash	4	4	4
9.	H_2O	6	6	6

Source: Giuseppe Mazza. Functional Foods: Biochemical and Processing Aspects. *CRC Press* 1998;1:236–239. ISBN-1566764874, 9,781,566,764,872; Reference [25]

mustard allergy. Mustard is the fourth leading cause of food allergy in France after milk, eggs, and peanuts. In France, about 10% of school children are allergic to at least one or more food items and the most common food allergens include hen's egg (35%), peanut (24%), cow's milk (8%), mustard (6%), and fish (4%) [30–32]. Rance et al. investigated 36 children with positive mustard SPT. Children (51.8%) had atopic dermatitis and 37% experienced urticaria and/or angioedema. Children were allergic to one or more food items including peanut, egg, soy, hazelnut, beef, shrimp, wheat, avocado, and cow's milk [29]. Similarly, one more study from France included 378 children with food hypersensitivity and it was observed that five allergens accounted for 82% of confirmed food hypersensitivity: egg (51.8%), peanut (34.3%), milk (11.6%), mustard (8.9%), and codfish (7.1%) [33]. Another study conducted by Rance et al. included 42 children with cashew allergy. Out of these 42 children, 3 were sensitized to mustard [34]. A study on 163 asthmatic children with food allergy indicated that 6.9% were positive to mustard with mixed symptoms affecting the gastrointestinal tract, respiratory tract, and skin [35]. Mathelier-Fusadeet et al. reported seven cases of food-dependent exercise-induced anaphylaxis, and mustard was mentioned as one of the responsible foods [36]. Further, Andre et al. (1994) screened 580 patients with pathological reactions to foods and found that mustard (3%) is one of the foods that were responsible for anaphylactic reactions and it is often present as hidden allergen in commercial foods [37]. Similarly, Morisset et al. conducted a study in France for screening of mustard allergy in 30 subjects (3–20 years) by SPT using ground mustard seeds (*B. nigra*), mustard flour (*B. juncea*), metabisulfite-free strong mustard seasoning (*B. juncea*), and a commercialized allergenic extract (*B. nigra*) and it was observed that about 23.3% of the sensitized subjects were allergic to a routine dose of mustard [13]. Furthermore, a case study in France revealed that a 38-year-old woman with history of mustard allergy showed symptoms of anaphylaxis 20 min after ingestion of chicken dips containing mustard as an ingredient. SPT results showed positive reactions to mustard, coriander, and curry powder (which contained mustard). The woman had 56.3 kU/L mustard-specific serum IgE levels [38]. Additionally, in two individuals, life-threatening exercise-induced anaphylactic reactions to mustard have also been reported in France. One patient was allergic to wheat, parsley, tomato, carrot, peanut, and hazelnut while the other patient was allergic to soybean, peanut, hazelnut, and strawberry [39]. Further, a 51-year-old woman had two hospitalizations within 8 months for acute generalized urticaria, with lip and tongue edema and dyspnea, which appeared within 20 min of eating fillet of anchovy in sauce. SPT was done for mustard and fish that was positive to the former [40].

In Spain, where mustard is widely used, only a few reports are available in reference with mustard allergy and no large-scale studies have been carried out or published so far. A study conducted with 29 patients with history of mustard allergy underwent skin prick tests with mustard and were found positive. All patients had high levels of mustard-specific IgE (0.7 to > 100 kU/L). Out of 29 patients, 19 (66%) showed a systemic reaction after consumption of mustard, 10 (34%) had a local reaction, and 14 (48%) had anaphylaxis [41]. Similarly, a study was performed by Figueroa et al. in which 38 patients were screened for mustard allergy by SPT and 24 patients by double-blind placebo-controlled food challenges (DBPCFC). Out of the 24 subjects, 14 cases showed positive results to DBPCFC and showed significantly greater mustard SPT than those of controls [42]. Moreover, a 47-year-old woman with history of seasonal rhinoconjunctivitis showed symptoms of anaphylaxis like acute severe urticaria and facial angioedema together with nausea, vomiting, dyspnea, wheezing, chest tightness, and hoarseness after ingestion of vegetable sandwiches containing mayonnaise and mustard. Also, the serum levels of specific IgE against mustard were found to be greatly enhanced (23.6 kU/I) [43]. Another case study from Spain reported that ingestion of small amount of mustard sauce resulted into anaphylaxis in two individuals. A positive SPT reaction against mustard was evident in both persons [44]. Further, Domínguez et al. isolated allergen from mustard seed extracts by gel filtration and this allergen inhibited more than 60% of the binding of mustard-specific IgE from a pool of seven patients' sera. The allergenic activity was also confirmed by histamine release from whole blood from two sensitive patients [45].

Canada is the second largest producer and largest exporter (75–80%) of mustard, while the province of Saskatchewan produces 80% Canadian mustard [46]. Mustard is included in the list of priority food allergens in Canada since 2012. In Canada, mustard allergy is also very prevalent as it is very much utilized in various foods and food preparations [43].

India is also one of the largest consumers of mustard in the form of whole seeds, mustard powder, and mustard oil but hardly any data with regard to mustard allergy is available from India. A study conducted by Tripathi et al. (2001) revealed that out of 78 patients, 78% of subjects showed positive reaction to mustard allergen extract and 74% were SPT positive for mustard family pollen extract that suggest strong cross-reactivity [47]. According to EuroPrevall-INCO survey (a project that has been developed to evaluate the occurrence of food allergies in China, India, and Russia using the standardized methodology of the EuroPrevall protocol used for studies in the European Union), mustard is listed in 24 priority food allergens [48]. In a study, 1860 patients (12–62 years) were screened for food allergy using standard questionnaire and SPT. Eleven patients showed increased IgE levels against mustard [49]. Further, Singh et al. carried out SPT on 96 patients with history of sensitization to inhalant or food allergens with genetically modified (expressing choline oxidase (codA) gene from *Arthrobacter globiformis*) and native *B. juncea* leaf extracts. Of these, six patients were SPT positive to GM and native mustard extracts and ten patients showed 2.5–3 times higher specific IgE levels to GM and native mustard in comparison to negative controls [50].

Further, a case report from Italy revealed that one patient was admitted twice in a year after ingestion of pizza due to symptoms like acute urticaria with edema of the glottis. The patient was SPT positive for the Brassicaceae family (mustard, turnip, cabbage, and cauliflower). When the patient was injected with mustard antigen extracted from seeds of yellow and black mustard, an intense wheal and flare reaction was observed with shock and edema of glottis [28].

A 40-year-old Swedish woman who was working as a cook had eczema with profuse vesicular lesions. Prick test using crushed white and black mustard seeds in this woman showed positive results with marked wheal and flare reaction. She was also SPT positive for rape seed (*B. napus*) and was advised to avoid eating foods containing mustard and rape seed [51]. Two case reports of mustard allergy were also revealed from the study conducted by Gaig et al. In the first case, a 25-year-old woman showed urticaria with pertusis after ingestion of pomegranate. She was allergic to peach, grapes, banana, and mustard. In another case, a 3-year-old girl showed urticaria, facial angioedema, and experienced shortness of breath after eating pomegranate. SPT results were positive to mites, mustard, peanut, almonds, fig, peach, corn, and rice [52]. Connors et al. reported a case of mustard allergy wherein, a 50-year-old woman had symptoms of anaphylaxis following ingestion of a hamburger with mustard. She had a previous history of similar symptoms with ingestion of mustard [53].

One case report from USA showed that a 29-year-old man consumed quinoa dish and experienced an episode of facial flushing and angioedema together with urticaria, chest tightness, and vomiting within 30 min of consumption of the dish. Previously, he had consumed and tolerated quinoa without any reaction. The quinoa dish contained chicken, rice, avocado, ginger, onion, potatoes, tomato, nutmeg, yeast, soy, wheat, black pepper, thyme, and mustard seed. Skin prick test was positive to mustard and percutaneous skin testing was positive to soy [54]. Stricker et al. screened 168 patients having idiopathic anaphylaxis with a battery of 79 food-antigen skin prick tests, out of which 3 patients were SPT positive to mustard, and a positive clinical correlation with skin test and anaphylaxis was observed in the case of mustard [55]. A study conducted by Mailhol et al. included a total of 386 children with atopic dermatitis, out of which 69 children were diagnosed with food allergy, and prevalence of mustard allergy was 1% [56]. Furthermore, Asero et al. screened 49 patients monosensitized to LTPs and found that 4% of the people were SPT positive to mustard [57].

A study in Finland was conducted on 50 patients with spice extracts, and their potential to cause skin reactions were analyzed by SPT. Notable, mustard was reported as one of the major spices that cause skin reactions in sensitive individuals [58]. The case reports are summarized in Table 3.

Mustard-Induced Respiratory Allergies Individuals suffering from food allergy may also show symptoms of respiratory allergy (sneezing, coughing, rhinoconjunctivitis, and sometimes asthma) due to inhalation of a wide variety of plant-derived pollens. Some foods are responsible for inflammation of respiratory tract and cause allergic rhinitis/asthma-like symptoms in susceptible individuals. People suffering from pollinosis are more likely to develop food allergy and 30–60% of patients with pollen allergy in the European population do suffer with plant food allergy [59–61]. Little is known about the mustard-induced respiratory allergies as on date, and relatively few studies are available in this regard (Table 3). The explanation of these kinds of allergy can be given by cross-reactivity among plant foods and pollens.

A study conducted by Singh et al. investigated allergenicity of antigenic extracts of pollens of 4 species of Brassica and revealed that out of 159 atopic subjects, 21.4% were positive to at least one or other species of Brassica pollen, with the highest skin positivity (13.2%) to *B. campestris* extract [62]. Further, a study conducted by Toorenenbergen et al. reported that a patient working in spice factory experienced symptoms of rhinitis and shortness of breath. These symptoms became severe during Monday to Friday and relieved during weekends. It was noticed that due to exposure of spice dust, the person faced such problems [63]. A woman (ex-smoker) with history of rhinitis and asthma was found to be sensitive to yellow mustard allergen Sina2 (11S globulin/legumin) and rapeseeds. It was the first case indicating the involvement of mustard allergen (Sina2)-11S globulin in the etiology of asthma upon inhalation [64].

Moreover, a study conducted by Niinimaki et al. in Finland revealed that 49 patients allergic to birch pollen or mugwort pollen when subjected to SPT with extracts of different commonly used spices (coriander, caraway, cayenne and mustard) showed SPT-positive results with all these spices and mustard is one of the major causes of allergic reactions in these sensitive individuals [65]. A study by Morriset et al. reported that out of 30 subjects, 7 patients were allergic to mustard and 4 individuals (4/7 = 57%) showed symptoms of respiratory allergy, but symptoms were moderately severe [13]. An interesting prospective study in 38 mustard-sensitive patients was performed by Figueroa et al. suggesting the strong relationship between mustard hypersensitivity and mugwort pollen sensitization (97.4% of patients) [42].

Similarly, Yagami et al. demonstrated a case (22-year-old woman) of pollen-food allergy syndrome (PFAS) from melon and latex allergy (LA) to natural rubber latex (NRL) antigen. She was also allergic to birch pollen (Bet v 2), natural rubber latex allergen (Hev b 8), and timothy allergen (Phl p 12), as well as to some common spices including mustard seeds, cumin, fennel, dill, fenugreek, cayenne, ginger, cardamom, garlic, garam masala, and coconut milk with symptoms of atopic dermatitis, allergic rhinitis, and pollinosis [66]. Anguita et al. screened 12 olive orchard workers, who had a history of rhinitis and/or bronchial asthma, with SPT with *S. alba* pollen extract. The patients were found sensitized to *S. alba* pollen extract, and also showed a positive nasal challenge test response. Therefore, the authors concluded that *S. alba* pollen acts as occupational allergen for olive farmers [67].

Mustard-Induced Skin Allergies Mustard has the ability to provoke respiratory allergies. There are emerging evidences indicating the involvement of mustard in inducing skin allergies. Allylisothiocyanate (a volatile chemical), a major antigen of mustard oil, which is responsible for the pungent odor and flavor, is also capable of inciting contact dermatitis [68, 69]. A study conducted by Gaul et al. showed that a 61 years old Negro man developed symptoms of contact dermatitis on hands, forearms, face, and neck. Additionally, patch test was also found to be positive (8 cm patch) for household liniment that contained clove oil, wintergreen oil, synthetic mustard oil, sassafras oil, peppermint oil, and cajeput oil. Later on, allylisothiocyanate present in synthetic mustard oil was noticed as the main culprit in the liniment as 0.1% of mustard oil produced approximately 2 cm vesicular patch [70]. Similarly, a 34-year-old woman felt burning sensation and erythematous skin after application of compress crushed mustard seeds. Five days later, she ate German sausage having mustard as ingredient that resulted into serious exacerbation with development of bullae. Further, patch tests and prick tests were performed using 0.001 to 0.1% allylisothiocyanate, mustard seeds 1:100 to 1:1, and different commercially available mustard preparation. However, only allergic reaction with superficial necrosis was observed with 5% allylisothiocyanate [71].

In addition to allylisothiocyanate, some proteins from mustard are also responsible for causing allergic reactions in sensitive individuals. Leanizbarrutia et al. reported two cases of mustard allergy with severe anaphylaxis after eating small quantities of prepared mustard. Interestingly, when mustard extract was treated with proteolytic enzymes, its allergenic capacity was lost suggesting that proteins present in mustard extract were responsible for allergic responses [72]. Moreover, a case report showed that a 38-year-old female salad maker has a history of hand dermatitis for 2 years with itchy vesicular eruption on fingers and forearms. It was noticed that being a salad maker, she was continuously exposed (dermal exposure) to salad cream that contain various members of the mustard family. Patch test results showed + 1 reaction against 1% aqueous concentration of black mustard (*B. nigra*) and + 3 positive for two commercial mustards. In addition, RAST test was found positive for IgE against extract of black mustard [73]. Further, another case of occupational contact dermatitis came into existence when major fish stick factory workers in Northern Norway complained about the irritant reaction on skin, eyes, and upper airways. Some of them developed symptoms of eczema on the hands, arms, and face. Later, it was observed that 3 individuals out of 16 had immediate reaction to mustard and all the 3 persons had the history of atopic disease [74].

Another interesting case revealed that a 48-year-old woman with history of eczema and allergic contact dermatitis developed swelling, itching, and redness on her back after application of Chinese herbal medicine for the treatment of tracheitis. Patch test results showed only positive reaction (erythema and bulla) to white mustard seed [75]. As white mustard seeds are widely used in Chinese herbal medicine, persons with history of allergy should avoid its application. Furthermore, a study from Finland included 64 children with atopic dermatitis. These children were screened for sensitization with turnip rape and oilseed rape. Almost all the children (97%) were sensitized to mustard with total IgE values higher than controls [76]. Poikonenet et al. carried out a study on Finnish (14 children) and French children (14 children) to find out the scenario of turnip rape and mustard allergy among them and also the cross-reactivity between turnip rape and mustard. Oral challenge with turnip rape was positive in 14 (100%) Finnish subjects and 5 (36%) French children whereas mustard challenge was positive in 5 (36%) Finnish and 5 (36%) French children. Moreover, most of the children (both Finnish and French) had serum IgE against oilseed rape and mustard indicating towards the possible cross-reactivity among turnip rape, oilseed rape, and mustard [77].

A 54-year-old female working as a vegetable farmer presented with painful pruritic skin lesions on both hands

Table 3 Clinical data on mustard allergy in chronological order

S. No.	Patients	Mustard allergy	Clinical symptoms	Other allergy	Reference
1.	1	Mustard and heated mustard = SPT Positive	Dyspnea, swelling of the lips and eyelids	Allergy from mugwort, raw broccoli and heated broccoli	[97]
2.	1	Mustard seeds = SPT Positive	Facial flushing angioedema and generalized urticaria	Also SPT positive to soy	[54]
3.	159	21.4% patients were positive for at least one or other species of Brassica pollen	Allergic rhinitis, asthma, asthma with allergic rhinitis	27.6% cases = *Cyanodon* SPT positive 24.11% = *Amaranthus* SPT positive 21.4% = dust mite SPT positive 7.09% = *Morus* extract SPT positive	[62]
4.	386 children, (69 had FA)	4% (out of 69) SPT positive to mustard	Food allergy and atopic dermatitis	–	[56]
5.	11	Sin a 2 allergen = SPT positive	Contact urticaria, digestive symptoms, oral allergy syndrome, rhinoconjunctivitis	Patients also SPT positive to tree nuts (almond or hazelnut or pistachio or walnut)	[112]
6.	1	White mustard seeds = SPT positive	Allergic contact dermatitis	–	[75]
7.	6	Specific IgE for Sin a 4 allergen	NA	Sin a 4-specific serum also showed binding with Cuc m 2 (major melon allergen), Che a 2 (allergen of *Chenopodium album* pollen), and Bet v 2 (Birch pollen allergen)	[117]
8.	34	Sin a1 allergen (25 positive), Sin a 2 allergen (19 positive)	Asthma, angioedema, contact urticaria, oral allergy syndrome, digestive symptoms	Most of the patients were allergic to Rosaceae family (peach, apple, pear, apricot, plum, cherries, and strawberries), melon and peanut	[114]
9.	15	SPT Positive to mustard (13 patients)	Contact urticaria, angioedema, asthma, rhinoconjunctivitis, throat tightness, oral allergy syndrome	Patients were SPT positive to peach, nuts, legumes, peanut, melon, kiwi	[85]
10.	14 Finnish children and 14 French children	All were SPT positive to mustard	Atopic dermatitis	Finnish children were allergic to egg and wheat, milk, Birch, and grass pollen; French children were allergic to egg, milk, wheat and grass pollen	[77]
11.	1	Mustard seeds = SPT positive	Atopic dermatitis, allergic rhinitis, pollinosis, and PFAS	Allergic to melon, natural rubber latex (NRL) antigen, Bet v 2, Hev b 8, Phl p 12, cumin, fennel, dill, fenugreek, cayenne, ginger, cardamom, garlic, garam masala, and coconut milk	[66]
12.	64 children (43 boys and 23 girls)	97% children were SPT positive to mustard	Atopic dermatitis, asthma, and allergic rhinitis	Children were allergic to oilseed rape, turnip rape, and egg	[76]
13.	436	3 patients positive to mustard found in sauses and pizza	–	Patients were allergic to fruits, nuts, fish, shell fish, eggs, and legumes	[119]
14.	49 patients monosensitized to LTP	2 patients (4%) SPT positive to mustard		Patients were allergic to LTPs of different foods including fruits, seeds, garlic, onion, tomato	[57]
15.	12 olive orchard workers	SPT and nasal challenge positive to *S. alba* pollen extract	11 patients suffered from rhinitis and bronchial asthma and only 1 had rhinitis	–	[67]
16.	8	All SPT positive to rSin a 2 and nSin a 2 allergen	–	Three peptides described as epitopes in Ara h 3 were moderately conserved in Sin a 2; therefore, patients may be allergic to peanut.	[84]
17.	17 allergic patients to cabbage	All SPT positive to mustard	–	Patients were also allergic to mugwort pollen and peach	[116]
18.	96	SPT positive for native and GM mustard (6 patients)	10 patients showed 2.5–3 times higher specific IgE levels for native and GM mustard than negative control	–	[50]

Table 3 (continued)

S. No.	Patients	Mustard allergy	Clinical symptoms	Other allergy	Reference
19.	3	SPT positive to mustard (1)	–	–	[53]
20.	1	Patch test positive to different concentration of mustard oil	Patient had contact allergic dermatitis to the mustard oil (chiefly to allylisothiocyanate).	–	[81]
21.	13	SPT positive to mustard. Sera of all patients showed IgE binding at MW 14 kDa (Sin a1) and 51 kDa (Sin a2)	Oral allergy syndrome, asthma, angioedema, gastrointestinal symptoms, and anaphylaxis	–	[90]
22.	38	SPT positive to mustard (All)	Rhinitis, bronchial asthma, and atopic dermatitis	Patients were allergic to mugwort pollen (97.4%), nut (97.4%), leguminous (94.7%), corn (78.9%), and Rosaceae fruit (89.5%)	[42]
23.	42 children	3 children sensitized to mustard	–	7 children were allergic to pistachio, 5 to egg, 2 to shrimp, and 1 to cow milk	[34]
24.	30 (28 children and 2 adults)	23.3% were SPT positive to *Brassica nigra* and *B. juncea*	Asthma, abdominal pain, atopic dermatitis, angioedema, and digestive symptoms	–	[13]
25.	1	SPT positive to salad mustard (rucola)	Atopic dermatitis	Allergic to spinach and chives	[78]
26.	163 asthmatic children	6.9% children were DBPCFC positive to mustard	Cutaneous, respiratory, and gastrointestinal symptoms	Children were allergic to peanut, egg, cow's milk, codfish, shrimp, kiwi fruit, hazelnut, cashew nut, almond, and garlic	[35]
27.	29	All patients were SPT positive to mustard	19 (66%) had a systemic reaction, 10 (34%) had a local reaction, 14 (48%) had anaphylaxis	73% patients were allergic to mugwort and 67% to olive	[41]
28.	7	1 patient SPT positive to mustard	Food-dependant exercise-induced anaphylaxis	Patients were allergic to wheat, corn, barley, shrimp, apple, and paprika	[36]
29.	36 children	All were SPT positive to mustard. SBPCFC was used to diagnose mustard allergy	51.8% children had atopic dermatitis and 37% experienced urticaria and/or angioedema	Children were allergic to one or more food items including peanut, egg, soy, hazelnut, beef, shrimp, wheat, avocado, and cow's milk	[29]
30.	1	SPT positive to mustard	Acute generalized urticaria, with lip and tongue edema and dyspnea	–	[40]
31.	49 out of 544	All were SPT positive to mustard	Atopic dermatitis, angioedema, asthma, laryngeal edema, oral allergy syndrome	Screened patients also found allergic to egg, peanut, cow's milk, hazelnut, shrimp, kiwi fruit, and wheat	[32]
32.	34 out of 378	All were SPT positive to mustard	Atopic dermatitis, urticaria, edema, asthma, anaphylaxis, gastrointestinal symptoms, oral symptoms, rhinoconjunctivitis	Children were allergic to egg, peanut, milk, and codfish	[33]
33.	23 out of 142 children	Labial food challenges were given. All were SPT positive to mustard	Labial edema with contiguous urticaria	Screened children were also found allergic to egg white, peanut, cow's milk, cod, kiwi fruit, shrimp, chicken, peanut oil, hazel nuts, snails, apple, fennel, garlic, chili peppers, pepper, and duck.	[31]
34.	1	Patient allergic to rapeseed napins but sera showed IgE binding to Sin a 1. Sin a 1 also inhibited 60% of the IgE recognition of BnIII.	–	–	[102]
35.	19	2 SPT positive to mustard	Life-threatening exercise-induced anaphylactic reactions	One patient was allergic to wheat, parsley, tomato, carrot, peanut, and hazelnut while the other patient was allergic to soybean, peanut, hazelnut and strawberry.	[39]
36.	22 out of 49	Strong SPT positive to spices including mustard	Atopic dermatitis, respiratory symptoms, chronic hand eczema	–	[65]

Table 3 (continued)

S. No.	Patients	Mustard allergy	Clinical symptoms	Other allergy	Reference
37.	3	All were SPT positive to mustard	Anaphylactic symptoms	–	[96]
38.	1	SPT positive to mustard	Anaphylactic reaction	–	[38]
39.	580	3% were SPT positive to mustard	–	Screened patients were also allergic to celery (30%), crustaceans (17%), fish (13%), peanuts (12%), and mango (7%)	[37]
40.	2	SPT positive to mustard	Anaphylactic reactions	–	[118]
41.	2	SPT positive to mustard	Anaphylactic reactions	–	[44]
42.	2	1 SPT positive to mustard and 1 had serum-specific IgE against mustard	Acute severe urticaria and facial angioedema, nausea, vomiting, dyspnea, wheezing, chest tightness, and hoarseness	–	[43]
43.	1	Reaction due to allylisothiocyanate. SPT negative to mustard	Irritant contact dermatitis	–	[71]
44.	7	SPT positive to mustard. The allergenic activity was also demonstrated by REIA and histamine release assays	Angioedema, urticaria, or anaphylactic shock	–	[45]
45.	1	Patch testing with different parts of the plant (not with the seeds). Reaction to mustard oil	Contact dermatitis	–	[82]
46.	29 out of 50	SPT positive to mustard with cross-reactivity with birch pollen	Gastrointestinal pains, rhinitis, atopic dermatitis, and birch pollen allergy	22 patients were allergic to paprika, 29 for coriander, 31 for caraway, 20 for cayenne, and 4 for white pepper	[58]
47.	18	All patients were SPT positive	Bronchial asthma and allergic rhinitis; anaphylactic shock in two patients	–	[86] [87]
48.	2	SPT positive, anaphylactic reactions due to allylisothiocyanate	Severe anaphylaxis	–	[72]
49.	122	3 were SPT positive to mustard	Contact dermatitis	8 were SPT positive to fish	[74]
50.	1	SPT positive to mustard	Contact dermatitis to allylisothiocyanate	Also positive to cabbage	[73]
51.	102	7 patients were SPT positive to mustard	Anaphylactic symptoms	Patients were also allergic to cashew nut, celery, flaxseed, hops, mushroom, shrimp, sunflower, and walnut	[55]
52.	1	SPT and RAST positive to mustard	Urticaria and angioneurotic edema	–	[79]
53.	1	SPT positive to crushed seeds of black and white mustard	Vesicular hand eczema	SPT positive to rapeseed	[51]
54.	23 out of 71	SPT positive to mustard	–	Patients were also allergic to some common spices including turmeric (1), clove (1), ginger (1), white pepper (2), cardamom (2), cayenne (32), caraway (39), and coriander (42)	[80]
55.	1	SPT positive to seeds of *Brassica nigra* and *B. alba*	Acute giant urticaria with edema of the glottis	–	[28]

SPT skin prick test, *FA* food allergy, *PFAS* pollen-food allergy syndrome, *DBPCFC* double-blind placebo-controlled food challenge, *SBPCFC* single-blind, placebo-controlled food challenges, *RAST* radioallergosorbent test

(eczema). Later on, further experimental analysis using RAST, skin prick, and patch testing confirmed that the woman was allergic to salad mustard (rucola), spinach, and chives [78]. Further, a young woman had recurrent urticaria and angioneurotic edema upon ingestion of mustard and mayonnaise. By RAST, IgE-mediated allergy to mustard and botanically related plants was confirmed [79]. Similarly, Niinimäki et al. did scratch tests with common spices in 1120 atopic and 380 non-atopic patients. Mustard was one of the foods found responsible for the vast majority of the skin reactions [80].

An interesting case from India revealed that topical application of mustard oil caused Pityriasisrosea-like eruptions on skin. A 25-year-old man suffered from multiple, well-demarcated, erythematous, scaly plaques of oval shape of variable sizes, ranging approximately from 0.5 to 3 cm in width and 1 to 5 cm in length. He applied mustard oil for body massage after bathing and after removal of the application, the lesions were cleared. Later examination confirmed that the man was SPT positive to all concentrations of mustard oil [81]. A study conducted by Diamond et al. revealed that nasturtium, a plant that contains mustard oil, causes skin irritation and allergic contact dermatitis [82], (Table 3).

Major Mustard Allergens Mustard, a widely consumed spice, can elicit IgE-mediated allergic reactions in sensitive individuals. Four major allergens from yellow mustard (*S. alba* or *B. alba)* have been identified and characterized namely (a) Sin a 1—2S albumin,14 kDa [83]; (b) Sin a 2—11S globulin, 51 kDa [84]; (c) Sin a 3—lipid transfer protein, 12 kDa [85]; and (d) Sin a 4—profilin, 13–14 kDa [85]. The structure of the major mustard allergens is provided in Fig. 1.

Sin a 1 belongs to storage protein of the 2S albumin [86, 87]. 2S albumins is a group of seed storage proteins that are classified on the basis of their sedimentation coefficient [88] and are important for many crucial functions of plants including nutrient source (amino acids and carbon skeletons), germination, seedling growth, and host defense against fungal attack. In the last few decades, various members of this protein family have been identified as major food allergens and were characterized by their IgE-binding ability. Sin a 1 (from *S. alba*), Bra j 1 (from *B. juncea*), Ric c 1 (from *Ricinus communis*), Ber e 1 (from Brazil nut), and Sesi 1 (from *Sesamum indicum*) are some important allergens that have been identified and classified as 2S albumins.

Sin a 1: 2S albumin fraction of mustard extract, i.e., Sin a 1 has been found to be the most potent allergen of yellow mustard than other fractions [86]. This protein (14.1 kDa) is made up of 2 polypeptides consisting 39 and 88 amino acids respectively that are held together by means of 2 disulfide bonds. Epitope mapping studies of Sin a 1 using ten specific monoclonal antibodies (mAbs) revealed that this allergen contains two immunodominant regions to which all these mAbs were directed, and binding of mAbs to these regions significantly reduced the IgE binding to Sin a 1. In addition, one out of ten mAbs recognizes a continuous epitope on a large chain of protein that is also a characteristic of IgE-binding epitope. Only one tyrosine residue within this epitope is thought to be the immuno-dominant portion of the allergen [87].

Sin a 1 is considered as the most suitable diagnostic marker to identify the prevalence and sensitization of mustard as levels of specific IgE against mustard were almost comparable to that of specific IgE levels against Sin a 1 alone, suggesting that it is a major allergen of *S. alba.* Sin a 1 can interact with membrane lipids that enhance its uptake at the intestinal barrier and thereby increases the resistance of this allergen against protease digestion. Interestingly, it was also noticed that binding of Sin a 1 to B cells results into their activation via cross-linking of cell surface proteins that leads to humoral immune response [89].

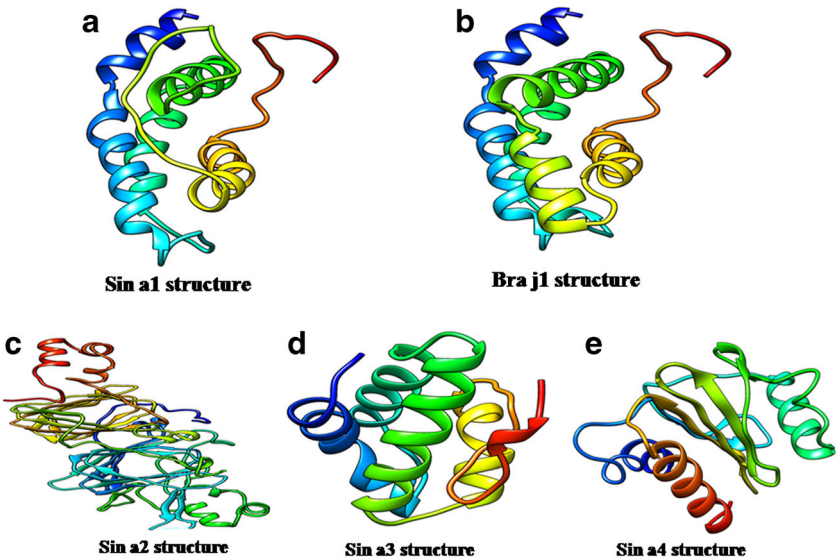

Fig. 1 The structural representation of major mustard allergens. **a** Sin a1. **b** Bra j1. **c** Sin a 2. **d** Sin a 3. **e** Sin a 4

Sin a 2: Sin a 2 was identified as the second major allergen from yellow mustard seeds using two-dimensional gel electrophoresis, mass spectrometry, and Edman degradation that belong to the 11S globulin family [90]. 11S globulins are salt-soluble proteins belonging to the family of seed storage proteins (Cupin superfamily). Sin a 2 (51 kDa) is composed of two polypeptides of 36 and 23 kDa linked by a disulfide bond. These two chains can be separated by treatment of reducing agents, but they retain their IgE-binding capacity even after separation [90]. In Sin a 2, the highly conserved asparaginyl cleavage site (characteristic of 11S globulin family) is located between positions $Asn^{297}$and Gly^{298}. In addition, out of five cysteine residues of Sin a 2, four are conserved in all allergenic 11S globulins. The major difference between Sin a 2 and other allergens of 11S globulin family is that the former contains a region enriched in Gln and Gly (positions 109 to 147) [84]. Sin a 2 is used as a marker to predict severity of symptoms. ELISA inhibition experiment with Sin a 1 and Sin a 2 revealed that incubation of Sin a1 with mustard-sensitive patients resulted into reduction of IgE binding (66.5% average inhibition) to mustard seed extract whereas preincubation of the patient's sera with Sin a 2 also resulted into reduced IgE binding (average 36.5% inhibition) to mustard seed extract. But, when sera were incubated with mixture of both the allergens, IgE binding to whole extract was abolished nearly by 90% [90].

Sin a 3 and Sin a 4: Other two allergens, Sin a 3 and Sin a 4, are present in very low amounts in yellow mustard seeds and belong to different families of panallergens. Sin a 3 belongs to non-specific lipid transfer protein (nsLTP) family that consists of a single chain of 92 amino acids with MW 12.3 kDa. Gastric and intestinal digestion of Sin a 3 resulted into partial proteolysis and the digested low-molecular-weight (MW) band retained IgE-binding ability up to 2 h [91].

Sin a 4 belongs to profilin plant family that contains a single chain of 14.2 kDa with 131 amino acids. Profilins from different plant species share highly conserved sequences and are major panallergens [92]. Gastric digestion of Sin a 4 resulted into approximately 80% digestion, but it retained its IgE-binding ability (20% residual activity) after 1 h of digestion. In contrast, intestinal digestion of Sin a 4 abolished its IgE reactivity [91]. When theoretical cleavage sites for pepsin were detected for mustard allergens using in silico approaches, it has been noticed that Sin a 4 has higher number of cleavage sites at the surface than Sin a 1 and Sin a 3 that make the former more liable to digestion than the latter ones. Theoretical cleavage sites for trypsin and chymotrypsin ($n = 14 + 8$) in Sin a 1 were more than pepsin ($n = 17$). In Sin a 3, all the cleavage sites for trypsin were located on the surface whereas only 55% sites for chymotrypsin were found on the surface of allergen. Sin a 4 displays cleavage sites inside and outside of structure for both the enzymes [91]. These results indicate that all mustard allergens are more prone to intestinal digestion rather than gastric digestion.

Bra j 1: Bra j 1, a major allergen from oriental mustard (*B. juncea*), consists of two polypeptides of 37 and 92 amino acids respectively linked by disulfide bonds. Bra j 1 is a member of 2S albumin family and is closely related to Sin a 1 from yellow mustard. González et al. reported that Bra j 1 was recognized by sera of mustard-sensitive patients. Moreover, five different fractions from *B. juncea* with MW in the range from 16 to 16.4 kDa were separated using ion exchange chromatography and observed that all these isoallergenic forms of Bra j 1 gave a single band using Sin a I-specific rabbit polyclonal serum [93]. These five isoallergenic forms named as Bra j 1A, Bra j 1B, Bra j 1C, Bra j 1D, and Bra j 1E [94] were recognized by monoclonal antibody 2B3 raised against Sin a 1. In addition, the sequence of Bra j 1 when aligned with Sin a 1 showed 89% sequence similarity [95]. The details of mustard allergens are provided in Table 4.

Cross-Reactivity of Mustard Allergens with Other Allergens People allergic to a specific food may also react to other food/environmental allergens due to the presence of homologous epitopes that may confuse the immune system and make it react against the allergen other than what they are allergic to. There are chances that mustard allergens show cross-reactivity to other members of Brassicaceae family and other plant families; therefore, it is important to understand the scenario of cross-reactivity of mustard with allergens of other related crops. However, little is known about the cross-reactivity between mustard seeds and leafy vegetables of Brassicaceae family but it has been shown that mustard did not show any cross-sensitivity with vegetables of the same family [96]. However, one case report suggested the involvement of broccoli (belongs to Brassicaceae family) in cross-reactivity with mustard. A 73-year-old Japanese male experienced dyspnea and swelling of the lips and eyelids after consumption of boiled broccoli. The person was SPT positive for raw broccoli (+ 4), heated broccoli (+ 4), mustard (3+), and heated mustard (+ 3) and therefore was advised to avoid consuming broccoli and mustard [97]. Moreover, the individuals who are allergic to one variety of mustard have the great probability of being sensitive to other varieties as well because there are structural similarities among allergens. The characterization of Sin a 1 and Bra j 1 revealed homologous epitopes between both allergens [84, 93, 95]; thus, the people allergic to yellow mustard are also sensitive for oriental mustard. In addition, Sin a 1 also shows a marked cross-reactivity with rape seed allergen Bn III [98]. Further, 2S albumins of 5 Brassica species (*B. campestris*, *B. oleracea*, *B. nigra*, *B. juncea*, and *B. carinata*) display more than 85% homology and significant similarity with some other 2S albumin fractions of Crucifereae family [99]. A study conducted by Asero et al. showed that 2S albumin from sunflower seed is cross-reactive to mustard 2S albumin, and therefore, it is necessary to carry out SPT for mustard in sunflower-sensitive patients

Table 4 Major mustard allergens

S. No.	Allergen	Molecular weight (kDa)	Protein family	Variety
1.	Sin a 1	14	2S albumin seed storage protein	*Sinapis alba* (yellow mustard)
2.	Sin a 2	51	11S globulin (legumin-like) seed storage protein	*S. alba* (yellow mustard)
3.	Sin a 3	12.3	Non-specific lipid transfer protein type 1	*S. alba* (yellow mustard)
4.	Sin a 4	13/14	Profilin	*S. alba* (yellow mustard)
5.	Bra j 1	14	2S albumin seed storage protein	*B. juncea* (Indian or oriental mustard)

[100]. Similarly, amino acid sequence of 2S albumin from *R. communis* showed the similarity with other 2S albumins including mustard (both to Bra j 1 and Sin a 1) and may cause cross-sensitization within the population [101]. Similarly, cross-reactivity between rapeseed allergen BnIII and Sin a 1 was also observed as Sin a 1 was recognized by the IgE antibodies present in the serum of the rapeseed allergic patient [102].

Many allergens from the 11S protein family have been identified and characterized including Ara h 3 from peanut [103], Lup a 11S globulin from Lupin [104], Cic a 11S globulin from chickpea [105], Cor a 9 from hazelnut [106], glycinins G1-G2 from soybean [107], Ber e 2 from Brazil nut [108], and Ana o 2 from cashew nut [109]. Some studies revealed that 11S globulins may play an important role in the cross-reactivity between coconut and walnut [110], among buckwheat, poppy, and hazelnut [111] and between peanut and different seeds spices. Sin a 2 from mustard belongs to 11S globulin family of proteins and shares IgG epitopes with allergenic 11S globulins from tree nuts (almond, hazelnut, pistachio, and walnut), but not from peanut. The IgG binding of Sin a 2 was reduced when sera of mustard-sensitive patients were incubated with almond extract (77% inhibition), walnut extract (60% inhibition), hazelnut extract (53% inhibition), and pistachio extract (43% inhibition). Similarly, the IgE-binding ability of Sin a 2 was also reduced by incubating the mustard-sensitive patient's sera with almond extract (63% inhibition), walnut extract (49% inhibition), pistachio extract (34% inhibition), peanut (32% inhibition), and hazelnut (15% inhibition). These research findings indicate that Sin a 2 is sensitizing allergen of mustard that shares conserved IgE epitopes with other allergenic 11S globulins that play an important role in the cross-reactivity among mustard, tree nuts and peanut.

The patients that had Sin a 2-specific IgE in their sera also showed positive specific IgE to the cross-reactive mustard allergens (panallergens) Sin a 3 and to Sin a 4 [112]. Further, it has also been found that people with mustard allergy also show symptoms against some pollens like birch, mugwort, and ragweed. Some researchers believe that mustard allergy is strongly associated with mugwort allergy called as mustard-mugwort allergy syndrome. Figueroa et al. conducted a study on 38 Spanish patients and reported that about 97.4% of patients with mustard allergy were also allergic to mugwort pollen with partial cross-reactivity confirmed by inhibition assay. In addition, all patients were also allergic to other members of Brassicaceae family, nuts (97.4%), leguminous crops (94.7%), corn (78.9%), and Rosaceae fruit (89.5%) that may be explained by cross-reactivity among allergens [42]. The potential cross-reactivity between mugwort and mustard may be due to LTPs (Art v 3, Sin a 3) and profilins (Art v 4, Sin a 4) [113]. Both Sin a 3 and Sin a 4 are associated with cross-reactivity with many pollens and plant-derived foods of Rosaceae family [114].

Sin a 3 shows 65% similarity with N-terminal sequence of Bra o 3 (nsLTP from cabbage), 50–55% similarity with Pru p 3 (nsLTP from peach), Mal d 3 (nsLTP from apple), Prua v 3 (nsLTP from cherry), Fra a 3 (pathogenesis-related PR-10 protein), and Cor a 8 (nsLTP from hazelnut). Substantial evidence now exists to indicate that the IgE-binding ability of Sin a 3 with sera of mustard-sensitive patients is reduced by both peach pulp and peel extracts [85, 115, 116]. Therefore, it may be possible that Sin a 3 is a key allergen responsible for the cross-reactivity of mustard extract with other allergens. Another mustard allergen Sin a 4 shows around 80% similarity with Cuc m 2 (profilin from melon) and Pru p 4 (profilin from peach), and the cross-reactivity is confirmed by ELISA inhibition as the IgE-binding capacity of Sin a 4 to mustard-sensitive patients' sera is inhibited by preincubation with melon extract. Moreover, it has been found that Sin a 4 (profilin) has sequence similarity with other profilins including Che a 2 from chenopod, Bet v 2 from birch, and Cuc m 2 from melon. Additionally, Sin a 4-specific antiserum is reactive to these profilins suggesting its involvement in cross-reactivity [117].

Mustard as a Hidden Allergen Although mustard allergy is not as prevalent as other food allergies and affect a small population, symptoms and severity caused by mustard allergens have been demonstrated by many published reports [14, 29, 41, 44, 96, 118], suggesting that mustard may cause severe anaphylactic reactions that need urgent medical treatment. Mustard may be present as a hidden ingredient in many prepared or prepackaged foods (Table 1) as it is widely used in the food formulations for its pungency, thickening, and stabilizing abilities. Hidden allergens or masked allergens are

present in such tiny amounts that sometimes it may be undetectable and cause mild to severe reactions in the previously sensitized individuals. Some allergenic reactions may occur due to the presence of food ingredients consumed in very small amounts (flavorings, honey, cinnamon, lupin, grass pea). The flavorings include mustard, paprika, ginger, oregano, and especially garlic as hidden allergens that sometimes can result in serious reactions. Mustard has also been found in sauces and pizza as hidden allergen [38]. Allergic reactions due to the ingestion of uncommon foods including mustard are usually overlooked as they are very difficult to identify and diagnose [119]. A major problem is how to avoid hidden allergens in the commercial or packaged foods, as reactions occur after ingesting the foods accidently or unknowingly that are responsible for the allergic symptoms. The presence of hidden allergens in foods is not always intentional; their presence is due to many reasons like misleading labels, contamination of foods with allergenic ingredients, carelessness, and listing of ingredients using uncommon term [119].

The Effect of Food Processing on Mustard Allergens It is well established that protein function (including enzymatic activity), stability (including resistance to proteolytic digestion), and glycosylation patterns may have significant impact on both immunogenicity and hence on the allergenic potential of that particular protein [120]. However, in the case of food allergy, the impact of food processing and food matrix should also be considered while looking towards the allergic potential. Food processing techniques may suppress food allergic reactions by destroying some epitopes but do not completely abolish the allergenic potential of allergens. The type of processing methods also affects the allergenic properties such as roasting reduces the allergenicity of most of the foods but in case of peanut, it results into enhanced allergenicity. Some common processing techniques include heating (thermal processing), enzymatic hydrolysis, acid hydrolysis, physical treatments (such as high-pressure processing or extrusion), the use of preservatives, changes in pH, or combination of two or more of these [121, 122].

At present, no effective preventive treatments exist for mustard allergy or for other food allergies. Hence, susceptible individuals are advised to strictly avoid mustard as whole or mustard-containing foods within their diet [6, 123]. However, novel alternate strategies need to be studied, including use of different thermal processing methods (roasting, autoclaving, boiling, and acid digestion). Most of the mustard allergens are heat resistant. A study demonstrated that Bra j 1, a major allergen from oriental mustard, is denatured at 82 °C [124].

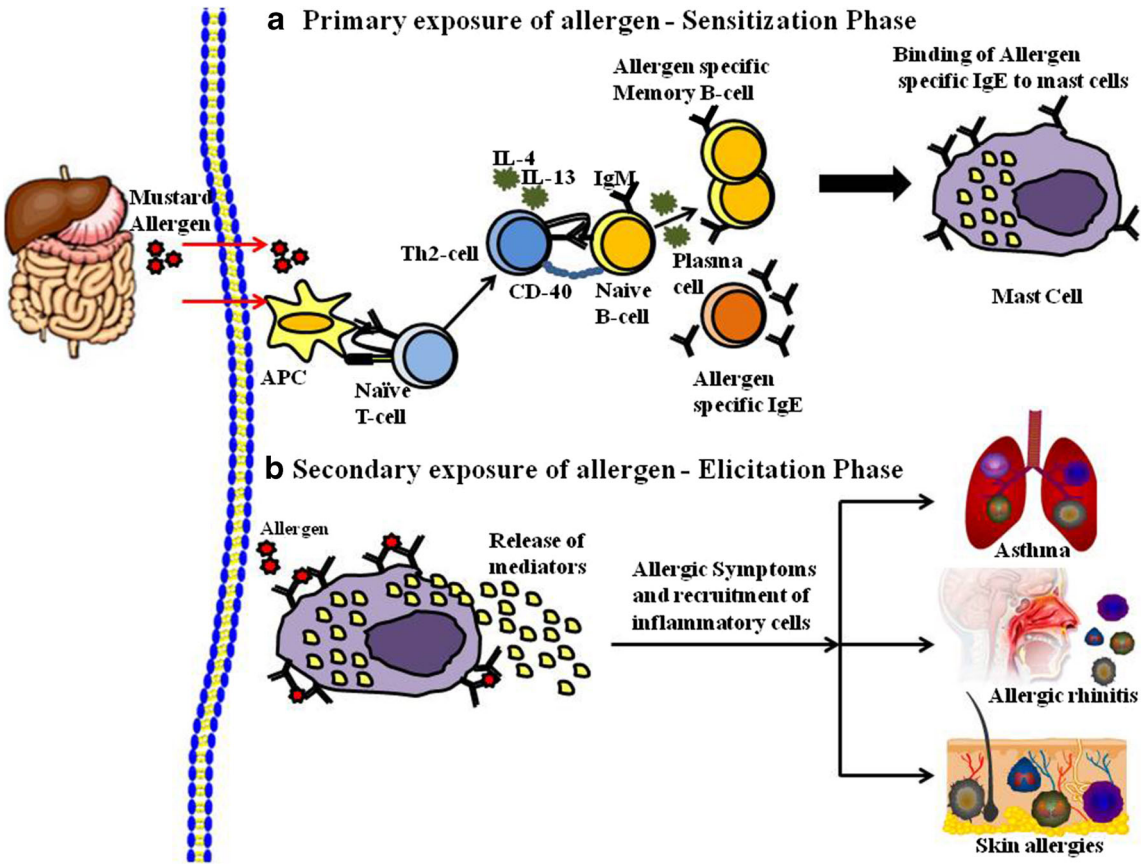

Fig. 2 The probable mechanism of mustard allergen-induced allergic manifestations in different organs that may lead to asthma, allergic rhinitis, atopic dermatitis, and other associated allergic disorders.

Heat resistance of allergens may be explained by their interaction with other food matrix constituents and thereby forming a more stable structure [95] as well as by disulfide bonds that contribute to form more stable structures. In addition, allergic proteins from mustard remain intact after gastric and intestinal digestion up to 60 min of digestibility period (pH 2 with pepsin and pH 6.8 with pancreatin, respectively) [125]. However, a combination of physical and thermal treatment (e.g., extrusion) may be beneficial in suppressing the allergenicity of mustard seed allergens. Glycosylation and glycation of mustard allergens may also play an important role in the alleviation of mustard-induced allergy. Microbial fermentation and enzymatic or acid hydrolysis can also have the potential to reduce the allergenicity to such an extent that reactions will not be elicited.

Conclusions

A number of reports are available on mustard hypersensitivity in the literature, but there no systematic review on mustard allergy and its major allergens. The current review provides the most relevant clinical studies on mustard allergy, the immunological and biochemical characteristics of mustard allergens that have been accumulated till date. The structural similarity of major mustard allergens with other allergenic proteins that may be involved in cross-reactive reactions, and the different processing techniques that have the potential to reduce the allergenic potential of different mustard allergens have been elucidated in this review. The better understanding of mustard-induced allergic manifestations and exploring the underlying mechanism will be helpful to develop therapeutic options.

Importantly, the current review may be beneficial for clinicians and researchers regarding the better understanding of mustard allergy and to know the probable cross-reactivity of mustard allergens with other allergens from same or different plant families. This will help the allergist and gastroenterologist to establish easy and early diagnosis of mustard allergy especially in the case of idiopathic anaphylaxis for the safety of the susceptible individuals. As avoidance of allergic food is considered the best treatment in the case of allergy, detailed understanding of mustard allergens and the effect of different processing techniques on these mustard allergens will reduce the incidence of mustard-induced allergic manifestations and thereby reduce the length of hospital stay. The information provided in the current review may pave the way to develop more general approaches and immunomodulatory therapies by allergist and gastroenterologist to treat mustard allergy that would be advantageous particularly for those patients who are allergic to multiple allergens. Conclusively, the understanding of mustard allergy will be useful to improve clinical management and quality of life of patients.

The probable underlying mechanism induced by mustard allergens is summarized in Fig. 2.

Acknowledgements The authors wish to thank Professor Alok Dhawan, Director, CSIR-IITR for his encouragement and support. Financial support from CSIR Research Grant InDepth (BSC-0111) is acknowledged. Dr. Akanksha Sharma is grateful to the Council of Scientific and Industrial Research, New Delhi, for the award of her Senior Research Fellowship. She conveys her gratitude to the Academy of Scientific and Innovative Research (AcSIR), New Delhi. Mr. Rinkesh Kumar Gupta and Neelabh are thankful to the Indian Council of Medical Research (ICMR), New Delhi, for the award of their Senior Research Fellowship. This is CSIR-IITR manuscript no-3481.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

References

1. Waddell L (2011) Living with food allergy. J Fam Health Care 21(4):21–28
2. Wang J, Sampson HA (2011) Food allergy. J Clin Invest 121(3): 827–835
3. Kumar S, Verma AK, Das M, Dwivedi PD (2012) Molecular mechanisms of IgE mediated food allergy. Int Immunopharmacol 13: 432–439
4. Sicherer SH, Sampson HA (2009) Food allergy: recent advances in pathophysiology and treatment. Annu Rev Med 60:261–277
5. Sicherer SH, Sampson HA (2010) Food allergy. J Allergy ClinImmunol 125:S116–S125
6. Sampson HA (2004) Update on food allergy. J Allergy Clin Immunol 113:805–819
7. Dalal I, Binson I, Reifen R, Amitai Z, Shohat T, Rahmani S, Levine A, Ballin A, Somekh E (2002) Food allergy is a matter of geography after all: sesame as a major cause of severe IgE-mediated food allergic reactions among infants and young children in Israel. Allergy 57:362–365
8. Sampson HA, Albergo R (1984) Comparison of results of skin tests, RAST, and double-blind, placebo-controlled food challenges in children with atopic dermatitis. J Allergy Clin Immunol 74:26–33
9. Burks AW, James JM, Hiegel A, Wilson G, Wheeler JG, Jones SM, Zuerlein N (1998) Atopic dermatitis and food hypersensitivity reactions. J Pediatr 132:132–136
10. Niggemann B, Sielaff B, Beyer K, Binder C, Wahn U (1999) Outcome of double-blind, placebo-controlled food challenge tests in 107 children with atopic dermatitis. Clin Exp Allergy 29:91–96
11. Sampson HA (1999) Food allergy. Part 1: immunopathogenesis and clinical disorders. J Allergy Clin Immunol 103:717–728
12. Sicherer SH, Sampson HA (1999) Food hypersensitivity and atopic dermatitis: pathophysiology, epidemiology, diagnosis, and management. J Allergy Clin Immunol 104:S114–S122
13. Morisset M, Moneret-Vautrin DA, Maadi F, Frémont S, Guénard L, Croizier A, Kanny G (2003) Prospective study of mustard allergy: first study with double-blind placebo-controlled food challenge trials (24 cases). Allergy 58:295–299
14. Kanny G, De Hauteclocque C, Moneret-Vautrin DA (1996) Sesame seed and sesame seed oil contain masked allergens of growing importance. Allergy 51:952–957

15. Sareen R, Shah A (2011) Hypersensitivity manifestations to the fruit mango. Asia Pac Allergy 1:43–49
16. Hamsten C, Starkhammar M, Tran TA, Johansson M, Bengtsson U, Ahlén G, Sällberg M, Grönlund H, van Hage M (2013) Identification of galactose-α-1,3-galactose in the gastrointestinal tract of the tick Ixodesricinus; possible relationship with red meat allergy. Allergy 68:549–552
17. Sowka S, Hsieh LS, Krebitz M, Akasawa A, Martin BM, Starrett D, Peterbauer CK, Scheiner O, Breiteneder H (1998) Identification and cloning of prs a 1, a 32-kDa endochitinase and major allergen of avocado, and its expression in the yeast *Pichia pastoris*. J Biol Chem 273:28091–28097
18. Lucas JS, Grimshaw KE, Collins K, Warner JO, Hourihane JO (2004) Kiwi fruit is a significant allergen and is associated with differing patterns of reactivity in children and adults. Clin Exp Allergy 34:1115–1121
19. Moneret-Vautrin DA, Morisset M, Lemerdy P, Croizier A, Kanny G (2002) Food allergy and IgE sensitization caused by spices: CICBAA data (based on 589 cases of food allergy). Allerg Immunol (Paris) 34:135–140
20. Delbourg MF, Guilloux L, Moneret-Vautrin DA, Ville G (1996) Hypersensitivity to banana in latex-allergic patients. Identification of two major banana allergens of 33 and 37 kD. Ann Allergy Asthma Immunol 76:321–326
21. Räsänen L, Lehto M, Turjanmaa K, Savolainen J, Reunala T (1994) Allergy to ingested cereals in atopic children. Allergy 49: 871–876
22. Pramod SN, Venkatesh YP (2008) Allergy to eggplant (*Solanum melongena*) caused by a putative secondary metabolite. J Investig Allergol Clin Immunol 18:59–62
23. Monsalve RI, Villalba M, Rodriguez R (2001) Allergy to mustard seeds: the importance of 2S albumins as food allergens. Internet Symposium Food Allergens 3:57–69
24. Sharma A, Kumar S, Gupta R, Roy R, Gupta K, Verma AK, Chaudhari BP, Das M, Dwivedi PD (2014) Elucidation of immediate type I reactions in native and GM mustard (Brassica spp.) Food Res Int 64:810–821
25. Giuseppe M (1998) Functional foods: biochemical and processing aspects. CRC Press 1:236–239 ISBN-1566764874, 9781566764872
26. Moneret-Vautrin DA (2001) Epidemiology of food allergies and relative prevalence of trophallergens. Cahiers de Nutrition et de Dietetique 36:247–252
27. EFSA (2004) Opinion of the scientific panel on dietetic products, nutrition and allergies on a request from the Commission relating to the evaluation of allergic foods for labeling purposes. The EFSA J 32:1–197. https://doi.org/10.2903/J.efsa.2004.32
28. Panconesi E, Sertoli A, Fabberi P, Giorgini S, Spallanzani P (1980) Anaphylactic shock from mustard after ingestion of pizza. Contact Dermatitis 6:294–295
29. Rancé F, Dutau G, Abbal M (2000) Mustard allergy in children. Allergy 55:496–500
30. Molkhou P (2003) The problems of the child with food allergies. Eur Ann Allergy Clin Immunol 35:7–8
31. Rance F, Dutau G (1997) Labial food challenge in children with food allergy. Pediatr Allergy Immunol 8:41–44
32. Rance F, Kanny G, Datau G, Moneret-Vautrin DA (1999a) Food hypersensitivity in children: clinical aspects and distribution of allergens. Pediatr Allergy Immunol 10:33–38
33. Rance F, Kanny G, Dutau G, Moneret-Vautrin DA (1999b) Food allergens in children. Arch Pediatr 6:61S–66S
34. Rancé F, Bidat E, Bourrier T, Sabouraud D (2003) Cashew allergy: observations of 42 children without associated peanut allergy. Allergy 58:1311–1314
35. Rancé F, Dutau G (2002) Asthma and food allergy: report of 163 pediatric cases. Arch Pediatr 9(Suppl 3):402s–407s
36. Mathelier-Fusade P, Vermeulen C, Leynadier F (2002) Responsibility of food in exercise-induced anaphylaxis: 7 cases. Ann Dermatol Venereol 129:694–697
37. André F, André C, Colin L, Cacaraci F, Cavagna S (1994) Role of new allergens and of allergens consumption in the increased incidence of food sensitizations in France. Toxicology 93:77–83
38. Kanny G, Fremont S, Talhouarne G, Nicolas JP, Moneret-Vautrin DA (1995) Anaphylaxis to mustard as a masked allergen in "chicken dips". Ann Allergy Asthma Immunol 75:340–342
39. Guinnepain MT, Eloit C, Raffard M, Burnet-Moret MJ, Rassemont R, Laurent J (1996) Exercise-induced anaphylaxis: useful screening of food sensitization. Ann Allergy Asthma Immunol 77:491–496
40. le Coz CJ, Ball C (2000) Contact urticaria syndrome from mustard in anchovy fillet sauce. Contact Dermatitis 42:114–115
41. Caballero T, San-Martín MS, Padial MA, Contreras J, Cabañas R, Barranco P, López-Serrano MC (2002) Clinical characteristics of patients with mustard hypersensitivity. Ann Allergy Asthma Immunol 89:166–171
42. Figueroa J, Blanco C, Dumpiérrez AG, Almeida L, Ortega N, Castillo R, Navarro L, Pérez E, Gallego MD, Carrillo T (2005) Mustard allergy confirmed by double-blind placebo-controlled food challenges: clinical features and cross-reactivity with mugwort pollen and plant-derived foods. Allergy 60:48–55
43. Vidal C, Díaz C, Sáez A, Rodriguez M, Iglesias A (1991) Anaphylaxis to mustard. Postgrad Med J 67:404
44. Monreal P, Botey J, Pena M, Marin A, Eseverri JL (1992) Mustard allergy. Two anaphylactic reactions to ingestion of mustard sauce. Ann Allergy 69:317–320
45. Domínguez J, Cuevas M, Ureña V, Muñoz T, Moneo I (1990) Purification and characterization of an allergen of mustard seed. Ann Allergy 64:352–357
46. Marambe HK, McIntosh TC, Cheng B, Wanasundara JPD (2014) Quantification of major 2S allergen protein of yellow mustard using anti-Sin a 1 epitope antibody. Food Control 44:233–241
47. Tripathi DM, Kumar S, Gupta A, Mehta N. A prospective study of mustard allergy in allergic rhinitis cases http://www.bhj.org.in/journal/2001_4302_apr01/org_261.htm
48. Wong GW, Mahesh PA, Ogorodova L, Leung TF, Fedorova O, Holla AD, Fernandez-Rivas M, Clare Mills EN, Kummeling I, van Ree R, Yazdanbakhsh M, Burney P (2010) The EuroPrevall-INCO surveys on the prevalence of food allergies in children from China, India and Russia: the study methodology. Allergy 65:385–390
49. Kumar R, Kumari D, Srivastava P, Khare V, Fakhr H, Arora N, Gaur SN, Singh BP (2010) Identification of IgE-mediated food allergy and allergens in older children and adults with asthma and allergic rhinitis. Indian J Chest Dis Allied Sci 52:217–224
50. Singh AK, Mehta AK, Sridhara S, Gaur SN, Singh BP, Sarma PU, Arora N (2006) Allergenicity assessment of transgenic mustard (*Brassica juncea*) expressing bacterial codA gene. Allergy 61: 491–497
51. Meding B (1985) Immediate hypersensitivity to mustard and rape. Contact Dermatitis 13:121–122
52. Gaig P, Bartolomé B, Lleonart R, García-Ortega P, Palacios R, Richart C (1999) Allergy to pomegranate (*Punicagranatum*). Allergy 54:287–288
53. Connors LA, Yang WH, Lacuesta GA (2006) Case reports of seed anaphylaxis: mustard, flax and sunflower seed. [Abstract] J Allergy Clin Immunol
54. Cuervo-Pardo L, Gonzalez-Estrada A, Fernandez J (2015) Anaphylaxis after home-made quinoa dinner: hold the mustard. BMJ Case Rep. https://doi.org/10.1136/bcr-2014-208980
55. Stricker WE, Anorve-Lopez E, Reed CE (1986) Food skin testing in patients with idiopathic anaphylaxis. J Allergy Clin Immunol 77:516–519

56. Mailhol C, Giordano-Labadie F, Lauwers-Cances V, Ammoury A, Paul C, Rance F (2014) Point prevalence and risk factors for food allergy in a cohort of 386 children with atopic dermatitis attending a multidisciplinary dermatology/paediatric allergy clinic. Eur J Dermatol 24:63–69
57. Asero R, Mistrello G, Roncarolo D, Amato S (2007) Detection of some safe plant-derived foods for LTP-allergic patients. Int Arch Allergy Immunol 144:57–63
58. Niinimäki A, Björkstén F, Puukka M, Tolonen K, Hannuksela M (1989) Spice allergy: results of skin prick tests and RAST with spice extracts. Allergy 44:60–65
59. Bircher AJ, Van Melle G, Haller E, Curty B, Frei PC (1994) IgE to food allergens are highly prevalent in patients allergic to pollens, with and without symptoms of food allergy. Clin Exp Allergy 24: 367–374
60. Osterballe M, Hansen TK, Mortz CG, Høst A, Bindslev-Jensen C (2005) The prevalence of food hypersensitivity in an unselected population of children and adults. Pediatr Allergy Immunol 16: 567–573
61. Ghunaim N, Grönlund H, Kronqvist M, Grönneberg R, Söderström L, Ahlstedt S, van Hage-Hamsten M (2005) Antibody profiles and self-reported symptoms to pollen-related food allergens in grass pollen-allergic patients from northern Europe. Allergy 60:185–191
62. Singh A, Shahi S, Katiyar RK, Gaur S, Jain V (2014) Hypersensitivity to pollen of four different species of Brassica: a clinico-immunologic evaluation in patients of respiratory allergy in India. Asia Pac Allergy 4:197–205
63. vanToorenenbergen AW, Dieges PH (1985) Immunoglobulin E antibodies against coriander and other spices. J Allergy Clin Immunol 76:477–481
64. Compés E, Palomares O, Fernández-Nieto M, Escudero C, Cuesta-Herranz J (2007) Allergy to turnip seeds in a bird fancier. Allergy 62:1472–1473
65. Niinimäki A, Hannuksela M, Mäkinen-Kiljunen S (1995) Skin prick tests and in vitro immunoassays with native spices and spice extracts. Ann Allergy Asthma Immunol 75:280–286
66. Yagami A, Nakazawa Y, Suzuki K, Matsunaga K (2009) Curry spice allergy associated with pollen-food allergy syndrome and latex fruit-syndrome. J Dermatol 36:45–49
67. Anguita JL, Palacios L, Ruiz-Valenzuela L, Bartolomé B, López-Urbano MJ, Sáenz de San Pedro B, Cano E, Quiralte J (2007) An occupational respiratory allergy caused by Sinapis alba pollen in olive farmers. Allergy 62:447–450
68. Ritschell, R. L., Fowler J (2001) In Fisher's contact dermatitis: 5th edition. Lippincott, Williams and Wlikins, Philadelphia 5:382–782
69. Pasricha JS, Gupta R, Gupta SK (1985) Contact hypersensitivity to mustard khal and mustard oil. Indian. J Dermatol Venereol Leprol 51:108–110
70. Gaul LE (1964) Contact dermatitis from synthetic oil of mustard. Arch Dermatol 90:158–159
71. Kohl PK, Frosch PJ (1990) Irritant contact dermatitis induced by a mustard compress. Contact Dermatitis 23:189–190
72. Leanizbarrutia I, Muñoz D, Fernández de Corrès L (1987) Cutaneous allergy to mustard. Contact Dermatitis 17:262–263
73. Dannaker CJ, White IR (1987) Cutaneous allergy to mustard in a salad maker. Contact Dermatitis 16:212–214
74. Kavli G, Moseng D (1987) Contact urticaria from mustard in fish-stick production. Contact Dermatitis 17:153–155
75. Li J, Jin HZ (2013) Allergic contact dermatitis caused by Chinese herbal medicine, white mustard seed. J Dermatol 40:69–70
76. Poikonen S, Puumalainen TJ, Kautiainen H, Palosuo T, Reunala T, Turjanmaa K (2008) Sensitization to turnip rape and oilseed rape in children with atopic dermatitis: a case-control study. Pediatr Allergy Immunol 19:408–411
77. Poikonen S, Rancé F, Puumalainen TJ, Le Manach G, Reunala T, Turjanmaa K (2009) Sensitization and allergy to turnip rape: a comparison between the Finnish and French children with atopic dermatitis. Acta Paediatr 98:310–315
78. Roller E, Meller S, Homey B, Ruzicka T, Neumann NJ (2003) Contact dermatitis caused by spinach, hedge mustard and chives. Hautarzt 54:374–375
79. Widström L, Johansson SG (1986) IgE-mediated anaphylaxis to mustard. Acta Derm Venereol 66:70–71
80. Niinimäki A, Hannuksela M (1981) Immediate skin test reactions to spices. Allergy 36:487–493
81. Zawar V (2005) Pityriasisrosea-like eruptions due to mustard oil application. Indian J Dermatol Venereol Leprol 71:282–284
82. Diamond SP, Wiener SG, Marks JG Jr (1990) Allergic contact dermatitis to nasturtium. Dermatol Clin 8:77–80
83. Palomares O, Cuesta-Herranz J, Rodriguez R, Villalba M (2005a) A recombinant precursor of the mustard allergen Sin a 1 retains the biochemical and immunological features of the heterodimeric native protein. Int Arch Allerg Immunol 137:18–26
84. Palomares O, Vereda A, Cuesta-Herranz J, Villalba M, Rodríguez R (2007) Cloning, sequencing, and recombinant production of Sin a 2, an allergenic 11S globulin from yellow mustard seeds. J Allergy Clin Immunol 119:1189–1196
85. Sirvent S, Palomares O, Vereda A, Villalba M, Cuesta-Herranz J, Rodríguez R (2009) nsLTP and profilin are allergens in mustard seeds: cloning, sequencing and recombinant production of Sin a 3 and Sin a 4. Clin Exp Allergy 39:1929–1936
86. Menéndez-Arias L, Moneo I, Domínguez J, Rodríguez R (1988) Primary structure of the major allergen of yellow mustard (*Sinapis alba L.*) seed, Sin a I. Eur J Biochem 177:159–166
87. Menendez-Arias L, Dominguez J, Moneo I, Rodriguez R (1990) Epitope mapping of the major allergen from yellow mustard seeds, Sin a I. Mol Immunol 27:143–150
88. Youle RJ, Huang HC (1981) Occurrence of low molecular weight and high cysteine containing albumin storage proteins in oilseeds of diverse species. Am J Bot 68:44–48
89. Oñaderra M, Monsalve RI, Mancheño JM, Villalba M, Martinez del Pozo A, Gavilanes JG, Rodriguez R (1994) Food mustard allergen interaction with phospholipid vesicles. Eur J Biochem 225:609–615
90. Palomares O, Cuesta-Herranz J, Vereda A, Sirvent S, Villalba M, Rodríguez R (2005b) Isolation and identification of an 11S globulin as a new major allergen in mustard seeds. Ann Allergy Asthma Immunol 94:586–592
91. Sirvent S, Palomares O, Cuesta-Herranz J, Villalba M, Rodríguez R (2012a) Analysis of the structural and immunological stability of 2S albumin, nonspecific lipid transfer protein, and profilin allergens from mustard seeds. J Agric Food Chem 60:6011–6018
92. vanRee R, Fernández-Rivas M, Cuevas M, van Wijngaarden M, Aalberse RC (1995) Pollen-related allergy to peach and apple: an important role for profilin. J Allergy Clin Immunol 95:726–734
93. González de la Peña MA, Menéndez-Arias L, Monsalve RI, Rodríguez R (1991) Isolation and characterization of a major allergen from oriental mustard seeds, BrajI. Int Arch Allergy Appl Immunol 96:263–270
94. Allergen nomenclature. IUIS/WHO Allergen Nomenclature Subcommittee (1994) Bull World Health Organ 72:797–806
95. Monsalve RI, Gonzalez de la Peña MA, Menendez-Arias L, Lopez-Otin C, Villalba M, Rodriguez R (1993) Characterization of a new oriental-mustard (*Brassica juncea*) allergen, Bra j IE: detection of an allergenic epitope. Biochem J 293:625–632
96. Jorro G, Morales C, Brasó JV, Peláez A (1995) Mustard allergy: three cases of systemic reaction to ingestion of mustard sauce. J Investig Allergol Clin Immunol 5:54–56

97. Sugita Y, Makino T, Mizawa M, Shimizu T (2016) Mugwort-mustard allergy syndrome due to broccoli consumption. Case Rep Dermatol Med 2016:8413767
98. Bartolomé B, Méndez JD, Armentia A, Vallverdú A, Palacios R (1997) Allergens from Brazil nut: immunochemical characterization. Allergol Immunopathol (Madr) 25:135–144
99. Dasgupta J, Dasgupta S, Ghosh S, Roy B, Mandal RK (1995) Deduced amino acid sequence of 2S storage protein from Brassica species and their conserved structural features. Indian J Biochem Biophys 32:378–384
100. Asero R, Mistrello G, Roncarolo D, Amato S (2002) Allergenic similarities of 2S albumins. Allergy 57:62–63
101. Bashir ME, Hubatsch I, Leinenbach HP, Zeppezauer M, Panzani RC, Hussein IH (1998) Ric c 1 and Ric c 3, the allergenic 2S albumin storage proteins of *Ricinuscommunis*: complete primary structures and phylogenetic relationships. Int Arch Allergy Immunol 115:73–82
102. Monsalve RI, González de la Peña MA, López-Otín C, Fiandor A, Fernández C, Villalba M, Rodríguez R (1997) Detection, isolation and complete amino acid sequence of an aeroallergenic protein from rapeseed flour. Clin Exp Allergy 27:833–841
103. Burks AW, Williams LW, Connaughton C, Cockrell G, O'Brien TJ, Helm RM (1992) Identification and characterization of a second major peanut allergen, Ara h II, with use of the sera of patients with atopic dermatitis and positive peanut challenge. J Allergy Clin Immunol 90:962–969
104. Magni C, Herndl A, Sironi E, Scarafoni A, Ballabio C, Restani P, Bernardini R, Novembre E, Vierucci A, Duranti M (2005) One- and two-dimensional electrophoretic identification of IgE-binding polypeptides of *Lupinusalbus* and other legume seeds. J Agric Food Chem 53:4567–4571
105. Karamloo F, Wangorsch A, Kasahara H, Davin LB, Haustein D, Lewis NG, Vieths S (2001) Phenylcoumaran benzylic ether and isoflavonoid reductases are a new class of cross-reactive allergens in birch pollen, fruits and vegetables. Eur J Biochem 268:5310–5320
106. Beyer K, Grishina G, Bardina L, Grishin A, Sampson HA (2002) Identification of an 11S globulin as a major hazelnut food allergen in hazelnut-induced systemic reactions. J Allergy Clin Immunol 110:517–523
107. Helm RM, Cockrell G, Connaughton C, Sampson HA, Bannon GA, Beilinson V, Nielsen NC, Burks AW (2000) A soybean G2 glycinin allergen. 2. Epitope mapping and three-dimensional modeling. Int Arch Allergy Immunol 123:213–219
108. Pastorello EA, Farioli L, Pravettoni V, Ispano M, Conti A, Ansaloni R, Rotondo F, Incorvaia C, Bengtsson A, Rivolta F, Trambaioli C, Previdi M, Ortolani C (1998) Sensitization to the major allergen of Brazil nut is correlated with the clinical expression of allergy. J Allergy Clin Immunol 102:1021–1027
109. Teuber SS, Sathe SK, Peterson WR, Roux KH (2002) Characterization of the soluble allergenic proteins of cashew nut (*Anacardiumoccidentale L.*) J Agric Food Chem 50:6543–6549
110. Manso L, Pastor C, Pérez-Gordo M, Cases B, Sastre J, Cuesta-Herranz J (2010) Cross-reactivity between coconut and lentil related to a 7S globulin and an 11S globulin. Allergy 65:1487–1488
111. Varga EM, Kollmann D, Zach M, Bohle B (2011) Anaphylaxis to buckwheat in an atopic child: a risk factor for severe allergy to nuts and seeds? Int Arch Allergy Immunol 156:112–116
112. Sirvent S, Akotenou M, Cuesta-Herranz J, Vereda A, Rodríguez R, Villalba M, Palomares O (2012b) The 11S globulin Sin a 2 from yellow mustard seeds shows IgE cross-reactivity with homologous counterparts from tree nuts and peanut. Clin Transl Allergy 2:23
113. Egger M, Mutschlechner S, Wopfner N, Gadermaier G, Briza P, Ferreira F (2006) Pollen-food syndromes associated with weed pollinosis: an update from the molecular point of view. Allergy 61:461–476
114. Vereda A, Sirvent S, Villalba M, Rodríguez R, Cuesta-Herranz J, Palomares O (2011) Improvement of mustard (Sinapis alba) allergy diagnosis and management by linking clinical features and component-resolved approaches. J Allergy Clin Immunol 127:1304–1307
115. Asero R, Mistrello G, Roncarolo D, de Vries SC, Gautier MF, Ciurana CL, Verbeek E, Mohammadi T, Knul-Brettlova V, Akkerdaas JH, Bulder I, Aalberse RC, van Ree R (2001) Lipid transfer protein: a pan-allergen in plant-derived foods that is highly resistant to pepsin digestion. Int Arch Allergy Immunol 124:67–69
116. Palacín A, Cumplido J, Figueroa J, Ahrazem O, Sánchez-Monge R, Carrillo T, Salcedo G, Blanco C (2006) Cabbage lipid transfer protein Bra o 3 is a major allergen responsible for cross-reactivity between plant foods and pollens. J Allergy Clin Immunol 117:1423–1429
117. Sirvent S, Tordesillas L, Villalba M, Díaz-Perales A, Cuesta-Herranz J, Salcedo G, Rodríguez R (2011) Pollen and plant food profilin allergens show equivalent IgE reactivity. Ann Allergy Asthma Immunol 106:429–435
118. Malet A, Valero A, Lluch M, Bescos M, Amat P, Serra E (1993) Hypersensitivity to mustard seed. Allergy 48:62–63
119. Añíbarro B, Seoane FJ, Múgica MV (2007) Involvement of hidden allergens in food allergic reactions. J Investig Allergol Clin Immunol 17:168–172
120. Huby RDJ, Dearman RJ, Kimber I (2000) Why are some proteins allergens? Toxicol. Science 55:235–246
121. Scientific opinion on the evaluation of allergenic foods and food ingredients for labelling purposes (2014) EFSA J 12:3894
122. Mills EN, Mackie AR (2008) The impact of processing on allergenicity of food. Curr Opin Allergy Clin Immunol 8:249–253
123. Rancé F (2003) Mustard allergy as a new food allergy. Allergy 58:287–288
124. Jyothi TC, Singh SA, Rao AG (2007) Conformation of Napin (*Brassica juncea*) in salts and monohydric alcohols: contribution of electrostatic and hydrophobic interactions. J Agric Food Chem 55:4229–4236
125. Thomas K, Aalbers M, Bannon GA, Bartels M, Dearman RJ, Esdaile DJ, TJ F, Glatt CM, Hadfield N, Hatzos C, Hefle SL, Heylings JR, Goodman RE, Henry B, Herouet C, Holsapple M, Ladics GS, Landry TD, MacIntosh SC, Rice EA, Privalle LS, Steiner HY, Teshima R, Van Ree R, Woolhiser M, Zawodny J (2004) A multi-laboratory evaluation of a common in vitro pepsin digestion assay protocol used in assessing the safety of novel proteins. Regul Toxicol Pharmacol 39:87–98