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DIAGNOSIS OF ALLERGY: IgE MEDIATED CROSS-REACTIONS AMONGST SELECTED ASTHMA ELICITORS

SYED M. HASNAIN[1*], ALANOUD ALQASSIM[1] AND ABDULRAHMAN AL-FRAYH[2]

[1]Department of Cell Biology, Allergy and Medical Aerobiology, King Faisal Specialist Hospital and Research Centre, P.O.Box 3354, Riyadh 11211, Saudi Arabia.

[2]Department of Pediatrics, College of Medicine, King Saud University, P.O.Box 2925 (39), Riyadh 11461, Saudi Arabia.

AUTHORS' CONTRIBUTIONS

This work was carried out in collaboration between all authors. Author SMH as the first author (corresponding author) has had the main idea in the developing, analyzing as well as writing review. Author AA contributed literature search as well as writing and formatting the tables. Author AAF also contributed in the discussion and adding to the review. All authors read and approved the final manuscript.

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ABSTRACT

IgE mediated allergic reactions to various foods such as fish, nuts, some fruits and vegetables are very common in both children and adults worldwide. Diagnoses of allergies particularly bronchial asthma, allergic rhinitis, urticaria and atopic dermatitis are generally conducted *in vivo* as Skin Prick Test (SPT) using different allergenic extracts. Review of data from various international publications on allergy related journals show that majority of allergic patients are diagnosed as mono-sensitized. The research was aimed at reviewing cross-reactivity pattern in SPT between various ingestant and inhalant allergens and its specific objective is the cross-reactivity between food items and pollen, fruits and pollen, vegetables and pollen as well as seafood and indoor allergens. The major identified proteins for each allergen were included.

The review of the data on SPT, cross-reactivity and the major protein, exhibit cross-reactivity between majority of common food items and pollen grains. The data also revealed 5 major proteins namely, profilin, Lipid Transfer Proteins (LTP), Pathogenesis-Related (PR) Protein, Tropomyosins and albumin in majority of allergens. The first 3 proteins were commonly shared by majority of food and pollen. The last 2 proteins were shared between the seafood and indoor allergens. It is therefore not inconceivable that the majority of poly-sensitizations are cross-reactivity of the major proteins found in all such allergens.

Clinical diagnosis in both adults and children are difficult as a result of cross-reactivity. The cross-reactivity does not confirm the primary sensitizer(s) but induces IgE mediated skin reactivity by allergens containing similar protein(s). The choice of allergens for immunotherapy should be carefully evaluated with possible cross-reacting allergens.

Keywords: Allergy diagnosis; skin prick test; asthma; allergens; cross-reactivity.

**Corresponding author: Email: hasnain@kfshrc.edu.sa;*
E-mail: CMijares@kfshrc.edu.sa;

1. INTRODUCTION

The common ingestant and inhalant allergens, responsible for IgE mediated sensitization and elicitation of respiratory and other generalized symptoms, include fish such as shrimps and lobsters; nuts such as peanuts and hazelnuts; fruits such as banana and kiwi fruits; vegetables such as corn and tomato, as well as, indoor allergens [1].

Allergy to plant derived food and pollen sensitization is one of most common cross-reacting syndromes [2]. Nuts, Fruits and vegetables are important sources of food allergy in both adults and children [3]. Inhalation of aeroallergens and/or ingestion of foods may induce allergic symptoms, and their sensitization pattern can be seen on Skin Prick Testing. The cross-reacting pollen and food components have been described for many plants. These includes birch-apple (*Betula verrucosa-Malus domestica*), mugwort-celery (*Artemisia vulgaris-Apium graveolens*), ragweed-banana (*Ambrosia-Musa x paradisiaca*) etc. Likewise, cross-reactivity for various indoor and animal origin allergens have been reported that includes, HDM mite-shrimp (*Dermatophagoides pteronyssinus/ farina-Penaeus aztecus*), cat-pork (*Felis domesticus-Sus scrofa domestica*), chicken-dog (*Gallus domesticus-canis domesticus*) [4]. The association between primary IgE sensitization with respiratory symptoms to inhaled allergens and food allergy due to cross-reactive components has been confirmed [5]. This association of food allergy with allergies to pollen and indoor allergens has been widely reported in recent years, and their cross-reactivity has been confirmed by various studies [6].

Indoor allergens such as house dust mites, cats, dogs, and cockroaches are another important inhalant source of allergenic proteins, causing allergic diseases [7]. The morbidity and mortality for asthma and allergies is increasing due to the increase in exposure to indoor allergens [8].

This review is an attempt to summarize some of the available data on cross-reactivity and the common proteins for common foods, fruits and vegetables with pollen grains and indoor allergens.

1.1 Cross-reactivity between Food and Pollen Allergens

Table 1, lists various food such as peanuts (*Arachis hypogaea*) [9], almonds (*Prunus dulcis*) [10], hazelnuts (*Corylus avellana*) [11] etc., along with their cross-reactive pollen type. For each food and cross-reactive pollen type, scientific names, characterized abbreviations as per International Union of Immunological Societies (IUIS) and major proteins identified are included. As allergic reaction, is an antigen antibody reaction or protein vs protein reaction, the major proteins found in each of these food items and pollen grains appear to be profiling [12]. In addition to profilin, there are few allergens containing LTP and a fewer with Glycoprotein and PR. The chosen food item and the corresponding pollen type are known to have cross-reactivity between them. The poly-sensitization of many allergic patients can be related to the presence of common proteins as presented in the table [13].

In addition, various food items including lentils (*Lens culinaris*) [14], Wheat (*Triticum aestivum*) [15], Saffron (*Saffron Crocus*) [16] etc. [16] containing additives and preservative can cause a generalized allergic reaction urticaria atopic dermatitis. In some patients, milk and milk products can cause intolerance and Gastrointestinal upset [17]. Pollen grains are generally airborne, can be inhaled with food or as food contaminant. Some food e.g. peanuts and shrimps can cause anaphylaxis, a fatal allergic reaction [18].

1.2 Cross-reactivity between Fruits and Pollen Allergens

Table 2, lists common fruits such as apple (*Malus domestica*) [24], banana (*Musa x paradisiaca*) and watermelon (*Citrullus lanatus)* [25] etc. along with their cross-reactive pollen. For each fruit and cross-reactive pollen type, scientific name, characterized abbreviations and major protein(s) identified are included.

A cross-reactivity pattern of some fruits including Apple (*Malus domestica*), orange (*Citrus reticulate*) [26], kiwi fruits (*Actinidia chinensis*) [27], banana (*Musa x paradisiaca*) [28], with inhalant pollen have been confirmed.

It is evident from the table that majority of fruits contained profilin, PR and LTP. Likewise, in majority of pollen grains, showing cross-reactivity with the common fruits, are profilin, followed by PR and LTP [29].

1.3 Cross-Reactivity between Vegetables and Pollen Allergens

Table 3 summarizes some vegetables and their cross-reactivity with various pollen allergens. The list includes asparagus (*Asparagus officinalis)* [40], carrot (*Daucus carota)* [41] and corn (*Zea mays)* [42] etc., with their corresponding cross-reactivity with pollen

allergen. From the table, it is evident that the majority of pollen grains with profilins can cross react with fruits showing two major proteins i.e. profilin and LTP.

1.4 Cross-Reactivity between Seafood and Indoor Allergens

Table 4 summarizes some seafood such as shrimp (*Penaeus aztecus*) [47], squid (*Todarodes pacificus*) [48], crawfish (*Procambarus clarkia*) [49] and bay lobster (*Thenus orientalis*) [50] and their corresponding cross-reactive indoor allergens. The cross-reactivity between the various seafood and indoor pollen grains indicate a different pattern than the food and pollen. In the case of seafood and indoor allergens the table shows most of the seafood had either tropomyosin or albumin as a major protein while the majority of indoor allergens had also tropomyosin and albumin [51]. It is interesting to note that major proteins found in different seafood and various indoor allergens are tropomyosin, a muscle protein.

It is therefore, obvious that the cross-reactivity within the fish or indoor allergens such as house dust mites is common because of the similar proteins [52].

2. DISCUSSION

Cross-reactivity can be defined as IgE mediated specific reactivity on a patient induced by similar allergens (proteins). As such quantitative information with relative affinity is desirable on cross-reactivity in the allergic population with specific allergens.

Most allergic patients react to more than one single allergen. This immunological phenomenon can be a multi-sensitization as a result of increased immunologic responsiveness (strong susceptibility) of a patient or a poly-sensitization as a result of cross-reacting allergens [53]. The cross-reactivity reflects the phylogenetic relations between organisms and this relation results in a high degree of homology in the primary structure of the protein i.e. amino acid sequence [53].

It is expected that clustering cross-reactive allergens may simplify diagnostic procedure and treatment modalities. As such, immunotherapy with one allergen is likely to relieve symptoms of the other allergens. Therefore, it is important to identify the primary sensitizing allergens, particularly for the therapeutic reasons as this will cover the widest spectrum of specificities.

The Tables 1-4 presented in this review describe cross-reactivity pattern of various allergenic groups and identify a limited number of major groups of proteins present in all of these allergens.

Exposure to homologous proteins can trigger reactions or may be clinically silent while provoking positive test responses for food-specific IgE antibody. Clinical evaluation requires a careful history laboratory test, and in some cases, oral food challenges [54]. Sometime, the problem caused by false positive SPT responses and/or RAST result with unreliable patient history, make the cross-reactivity issue more complicated [54]. In general, profilin purified from a grass pollen (*Lolium perenne*) by means of affinity purification, was shown to be cross-reactive with vegetable food like potato [55].

A proper classification of patients allergic to plants derived food is of great importance because the clinical features of allergic reaction to fruits and vegetables depend on the nature and characteristics of proteins responsible for sensitization. The risk of severe and life-threatening reaction is relevant if the sensitizing allergen is heat stable, pepsin resistant, such as LTP [56]. The example includes celery proteins cross-reactivity with mugwort pollen [56]. In contrast, patients sensitized to labile vegetable food proteins (birch pollen allergy), the consequences of the ingestion of allergenic food are less severe and result in oral allergy syndrome. However, severe local reaction including asthma and edema have been reported with inhalation of food particles [56].

Some workers have attempted to study skin prick test and the RASTS for some pollen plant food cross-reactive structure [57]. In this study, birch pollen sensitization was reliably diagnosed compared to whole birch pollen extract. In contrast, Recombinant Bet v 2 proved to be reactively poor reagent for studying sensitization to profilins. Comparison of RASTS result with rBet v 2 and its natural counterpart confirmed that the recombinant profilin has significantly lower IgE binding capacity [57].

The allergenic potential of a protein, either from food or pollen needs to be understood in terms of immunogenicity and cross-reactivity. The first one reflects the potential of a protein to induce IgE antibodies, while the second one is the reactivity of IgE antibodies with the target protein. In addition to the above, the relation between IgE binding potential and patients' symptoms is of interest [58].

Table 1. Cross-reactivity between food and pollen allergens

Food type	Scientific name	Allergen abbreviation	Major protein	Pollen type	Scientific name	Allergen abbreviation	Major protein
Peanut [9]	*Arachis hypogaea*	Ara h 5	Profilins	Hybrid Plane	*Platanus acerifolia*	Pla a 3	LTP
		Ara h 8	PR	Alder	*Alnus glutinosa*	Aln g 1	Profilins
				Birch weeping	*Betula verrucosa*	Bet v 1	PR
						Bet v 2	Profilins
				Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
Almond [10]	*Prunus dulcis*	Pru du 1	PR	Alder	*Alnus glutinosa*	Aln g 1	Profilins
		Pru du 4	Profilins	Birch weeping	*Betula verrucosa*	Bet v 1	PR
						Bet v 2	Profilins
Hazelnut [11]	*Corylus avellana*	Cor a 2	Profilins	Alder	*Alnus glutinosa*	Aln g 1	Profilins
		Cor a 8	LTP	Birch weeping	*Betula verrucosa*	Bet v 1	PR
		Cor a 1,5	PR			Bet v 2	Profilins
Lentil [14]	*Lens culinaris*	Len c 3	LTP	Hybrid Plane	*Platanus acerifolia*	Pla a 3	LTP
Wheat [15]	*Triticum aestivum*	Tri a 14	LTP	Hybrid Plane	*Platanus acerifolia*	Pla a 3	LTP
Saffron [16]	*Saffron Crocus*	Cro s 2	Profilins	Hybrid Plane	*Platanus acerifolia*	Pla a 3	LTP
		Cro s 3	LTP	Alder	*Alnus glutinosa*	Aln g 1	Profilins
				Birch weeping	*Betula verrucosa*	Bet v 1	PR
						Bet v 2	Profilins
Aniseed [19]	*Pimpinella anisum*	Pim a 1	Profilins	Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
				Birch weeping	*Betula verrucosa*	Bet v 1	PR
						Bet v 2	Profilins
Cumin [19]	*Cuminum cyminum*	Cum c 2	Profilins	Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
				Birch weeping	*Betula verrucosa*	Bet v 1	PR
						Bet v 2	Profilins
Celery [20]	*Apium graveolens*	Api g 4	Profilins	Hybrid Plane	*Platanus acerifolia*	Pla a 3	LTP
		Api g 5	Glycoprotein	Alder	*Alnus glutinosa*	Aln g 1	Profilins
		Api g 1	PR	Birch weeping	*Betula verrucosa*	Bet v 1	PR
		Api g 2	LTP			Bet v 2	Profilins
				Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
Soybean [21]	*Glycine max*	Gly m 3	Profilins	Alder	*Alnus glutinosa*	Aln g 1	Profilins
		Gly m 4	PR	Birch weeping	*Betula verrucosa*	Bet v 1	PR
						Bet v 2	Profilins
				Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
Mustard [22]	*Brassica rapa*	Bra r 8	Profilins	Alder	*Alnus glutinosa*	Aln g 1	Profilins
				Birch weeping	*Betula verrucosa*	Bet v 1	PR
						Bet v 2	Profilins
Bean [23]	*Phaseolus vulgaris*	Pha v 3	LTP	Hybrid Plane	*Platanus acerifolia*	Pla a 3	LTP

Table 2. Cross-reactivity between Fruit and Pollen allergens

Food type	Scientific name	Allergen abbreviation	Major protein	Pollen type	Scientific name	Allergen abbreviation	Major protein
Apple [24]	*Malus domestica*	Mal d 1	PR	Birch weeping	*Betula verrucosa*	Bet v 1	PR
		Mal d 4	Profilins			Bet v 2	Profilins
		Mal d 3	LTP	Common Ragweed	*Ambrosia artemisiifolia*	Amb a 8	Profilins
				Rye-grass	*Lolium longiflorum*	Lil l	Profilins
				Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
						Art v 3	LTP
Watermelon [25]	*Citrullus lanatus*	Cit la 2	Profilins	Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
						Art v 3	LTP
				Birch weeping	*Betula verrucosa*	Bet v 1	PR
						Bet v 2	Profilins
Orange [26]	*Citrus reticulata*	Cit r 3	LTP	Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
						Art v 3	LTP
				Hybrid Plane	*Platanus acerifolia*	Pla a 3	LTP
Kiwi [27]	*Actinidia chinensis*		Glycoprotein	Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
		Act c 10	LTP			Art v 3	LTP
				Hybrid Plane	*Platanus acerifolia*	Pla a 3	LTP
Banana [28]	*Musa x paradisiaca*			Birch weeping	*Betula verrucosa*	Bet v 1	PR
		Mus xp 1	Profilins			Bet v 2	Profilins
				Goose-foot	*Chenopodium murale*		
				Lambs Quarters	*Chenopodium album*	Che a 2	Profilins
				Hybrid Plane	*Platanus acerifolia*	Pla a 1	
Peach [30]	*Prunus persica*	Pru p 1	PR	Birch weeping	*Betula verrucosa*	Bet v 1	PR
		Pru p 3	LTP			Bet v 2	Profilins
		Pru p 2	Profilins	Alder	*Alnus*	Aln g 1	PR
		Pru p 4	Profilins	Lambs Quarters	*Chenopodium album*	Che a 2	Profilins
Cherry [31]	*Prunus avium*	Pru av 1	PR	Alder	*Alnus*	Aln g 1	PR
		Pru av 3	LTP 45	Birch weeping	*Betula verrucosa*	Bet v 1	PR
		Pru av 4	Profilins			Bet v 2	Profilins
Apricot [32]	*Prunus armeniaca*	Pru ar 3	LTP	Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
		Pru ar 4	LTP			Art v 3	LTP
				Hybrid Plane	*Platanus acerifolia*	Pla a 3	LTP
Grape [33]	*Vitls vinlfera*	Vit v 1	LTP	Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
		Vit v 4	Profilins			Art v 3	LTP
				Hybrid Plane	*Platanus acerifolia*	Pla a 3	LTP

Food type	Scientific name	Allergen abbreviation	Major protein	Pollen type	Scientific name	Allergen abbreviation	Major protein
Lemon [34]	*Citrus limonum*	Cit l 3	LTP	Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
						Art v 3	LTP
				Hybrid Plane	*Platanus acerifolia*	Pla a 3	LTP
Strawberry [35]	*Fragaria ananassa*	Fra a 3	LTP	Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
						Art v 3	LTP
				Hybrid Plane	*Platanus acerifolia*	Pla a 3	LTP
Pomegranate [36]	*Punica granatum*	Pun g 1	LTP	Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
						Art v 3	LTP
				Hybrid Plane	*Platanus acerifolia*	Pla a 3	LTP
Pineapple [37]	*Ananas comosus*	Ana c 1	Profilins	Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
						Art v 3	LTP
				Birch weeping	*Betula verrucosa*	Bet v 1	PR
						Bet v 2	Profilins
Mango [38]	*Mangifera indica*	Man i 3	Profilins	Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
						Art v 3	LTP
				Birch weeping	*Betula verrucosa*	Bet v 1	PR
						Bet v 2	Profilins
Pear [39]	*Pyrus communis*	Pyr c 3	LTP	Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
						Art v 3	LTP
				Hybrid Plane	*Platanus acerifolia*	Pla a 3	LTP

Table 3. Cross-reactivity between vegetable and pollen allergens

Food type	Scientific name	Allergen abbreviation	Major protein	Pollen type	Scientific name	Allergen abbreviation	Major protein
Asparagus [40]	*Asparagus officinalis*	Aspa o 1	LTP	Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
						Art v 3	LTP
				Hybrid Plane	*Platanus acerifolia*	Pla a 3	LTP
Carrot [41]	*Daucus carota*	Dau c 4	Profilins	Birch weeping	*Betula verrucosa*	Bet v 1	PR
						Bet v 2	Profilins
				Timothy grass	*Phleum pratense*	Phl p 12	Profilins
				Lambs Quarters	*Chenopodium album*	Che a 2	Profilins
Corn [42]	*Zea mays*	Zea m 14	LTP	Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
						Art v 3	LTP
				Hybrid Plane	*Platanus acerifolia*	Pla a 3	LTP
Cucumber [43]	*Cucumis sativus*	Cuc s 2	Profilins	Birch weeping	*Betula verrucosa*	Bet v 1	PR
						Bet v 2	Profilins
				Timothy grass	*Phleum pratense*	Phl p 12	Profilins
				Lambs Quarters	*Chenopodium album*	Che a 2	Profilins
Tomato [44]	*Lycopersicon esculentum*	Lyc e 1	Profilins	Birch weeping	*Betula verrucosa*	Bet v 1	PR
						Bet v 2	Profilins
				Timothy grass	*Phleum pratense*	Phl p 12	Profilins
Lettuce [45]	*Lactuca sativa*	Lac s 1	LTP	Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
						Art v 3	LTP
				Hybrid Plane	*Platanus acerifolia*	Pla a 3	LTP
Broccoli [46]	*Brassica oleracea*	Bra o 3	LTP	Mugwort	*Artemisia vulgaris*	Art v 4	Profilins
						Art v 3	LTP
				Hybrid Plane	*Platanus acerifolia*	Pla a 3	LTP

Table 4. Cross-reactivity between seafood and indoor allergens

Food type	Scientific name	Allergen abbreviation	Major protein	Indoor allergen type	Scientific name	Allergen abbreviation	Major protein
Shrimp [47]	*Penaeus aztecus*	Pen a 1	Tropomyosins	Cockroach	*Periplaneta americana*	Per a 7	Tropomyosins
				House dust mite	*Dermatophagoides pteronyssinus*	Der p 10	Tropomyosins
				House dust mite	*Dermatophagoides farinae*	Der f 10	Tropomyosins
Lobster [47]	*Homarus americanus*	Hom a 1	Tropomyosins	Cockroach	*Periplaneta americana*	Per a 7	Tropomyosins
				House dust mite	*Dermatophagoides pteronyssinus*	Der p 10	Tropomyosins
				House dust mite	*Dermatophagoides farinae*	Der f 10	Tropomyosins

Food type	Scientific name	Allergen abbreviation	Major protein	Indoor allergen type	Scientific name	Allergen abbreviation	Major protein
Crustaceans [47]	*Caligus clemensi*	Cal cl 1	Tropomyosins	Cockroach	*Periplaneta americana*	Per a 7	Tropomyosins
				House dust mite	*Dermatophagoides pteronyssinus*	Der p 10	Tropomyosins
				House dust mite	*Dermatophagoides farinae*	Der f 10	Tropomyosins
Squid [48]	*Todarodes pacificus*	Tod p 1	Tropomyosins	Cockroach	*Periplaneta americana*	Per a 7	Tropomyosins
				House dust mite	*Dermatophagoides pteronyssinus*	Der p 10	Tropomyosins
				House dust mite	*Dermatophagoides farinae*	Der f 10	Tropomyosins
Crawfish [49]	*Procambarus clarkii*	Pro cl 1	Tropomyosins	Cockroach	*Periplaneta americana*	Per a 7	Tropomyosins
				House dust mite	*Dermatophagoides pteronyssinus*	Der p 10	Tropomyosins
				House dust mite	*Dermatophagoides farinae*	Der f 10	Tropomyosins
Bay Lobster [50]	*Thenus orientalis*	The or 1	Tropomyosins	Cockroach	*Periplaneta americana*	Per a 7	Tropomyosins
				House dust mite	*Dermatophagoides pteronyssinus*	Der p 10	Tropomyosins
				House dust mite	*Dermatophagoides farinae*	Der f 10	Tropomyosins
Beef (cow's milk) [60]	*Bos domesticus*	Bos d 6	Albumin	Dog dander	*Canis domesticus*	Can f 3	Albumin
				Cat dander	*Felis domesticus*	Fel d 2	Albumin
Pork meat [61]	*Sus scrofa domestica*	Sus s 1	Albumin	Dog dander	*Canis domesticus*	Can f 3	Albumin
				Cat dander	*Felis domesticus*	Fel d 2	Albumin
Chicken [61]	*Gallus domesticus*	Gal d 5	Albumin	Dog dander	*Canis domesticus*	Can f 3	Albumin
				Cat dander	*Felis domesticus*	Fel d 2	Albumin
Snail [62]	*Helix aspersa*	hel a 1	Tropomyosins	Cockroach	*Periplaneta americana*	Per a 7	Tropomyosins
				House dust mite	*Dermatophagoides pteronyssinus*	Der p 10	Tropomyosins
				House dust mite	*Dermatophagoides farinae*	Der f 10	Tropomyosins
Tuna [63]	*Thunnus thynnus*	Thu t 4	Tropomyosins	Cockroach	*Periplaneta americana*	Per a 7	Tropomyosins
				House dust mite	*Dermatophagoides pteronyssinus*	Der p 10	Tropomyosins
				House dust mite	*Dermatophagoides farinae*	Der f 10	Tropomyosins
Tilapia [63]	*Oreochromis ossambicus*	Ore m 1	Albumin	Dog dander	*Canis domesticus*	Can f 3	Albumin
				Cat dander	*Felis domesticus*	Fel d 2	Albumin
Atlantic Salmon [64]	*Salmo salar*	Sal s 4	Tropomyosins	Cockroach	*Periplaneta americana*	Per a 7	Tropomyosins
				House dust mite	*Dermatophagoides pteronyssinus*	Der p 10	Tropomyosins
				House dust mite	*Dermatophagoides farinae*	Der f 10	Tropomyosins
Black Tiger Prawn [65]	*Penaeus monodon*	Pen m 1	Tropomyosins	Cockroach	*Periplaneta americana*	Per a 7	Tropomyosins
				House dust mite	*Dermatophagoides pteronyssinus*	Der p 10	Tropomyosins
				House dust mite	*Dermatophagoides farinae*	Der f 10	Tropomyosins
Calamari [66]	*Ommastrephes bartramii*	Omm b 1	Tropomyosins	Cockroach	*Periplaneta americana*	Per a 7	Tropomyosins
				House dust mite	*Dermatophagoides pteronyssinus*	Der p 10	Tropomyosins
				House dust mite	*Dermatophagoides farinae*	Der f 10	Tropomyosins

Protein nomenclature has been confusing in the understanding of protein structure for a long time. Proteins with the label, albumin, prove to have very different structures. An albumin is structurally very different from either serum albumin or milk albumin. The term pathogenesis related protein is used for a series of plant proteins involved in stress relation, comparable with the use of acute-phase proteins in mammals. Despite their common name, pathogenesis related proteins have almost no structural relationship at all [58].

The clinical relevance in association with allergen specific wheal size in Skin Prick Testing (SPT) has also been studied using pollen and indoor allergens [59]. This study described strong correlation between skin prick test wheal sizes in patient reported allergy symptom in exposure to allergen. The SPTs correlated well with physician diagnosed allergic rhinitis but the correlation was poorer for asthma and poorest for atopic dermatitis and food allergy. This is an expected finding as rhinoconjunctivitis is most often triggered by IgE mediated sensitization while in asthma other mechanism (e.g. increase bronchial responsiveness) play a major role.

Likewise, the literature to date, on the issue of immunogenicity, cross-reactivity and poly-sensitization in relation to clinical symptoms is very wide and variable, rather confusing. For example, in the food allergy, two types of allergy are mentioned: Class one food allergy where sensitization process occurs in the gastrointestinal tract. This food allergy is characteristically one of the manifestations of atopic syndrome in young children with cow's milk, eggs and legumes. However, as the immunity develop, these symptoms are replaced by other manifestation. Class two food allergy is seen in adult as a consequence of an allergic sensitization to inhalant allergen. The basis of this sensitization appears to be IgE cross-reactivity which may or may not show a clinical manifestation. During the digestion process, a food can cause oral allergy syndrome (birch-apple syndrome) or anaphylactic shock such as, mugwort-celery syndrome [67]. Such data are still emerging on the characterized proteins and their relationship or their ability to induce reactivity, similar to proteins found in other food or pollen. Profilins are cross-reactive plants derived allergens, known to cause multiple pollen sensitization as well as pollen and food associated allergy. But studies suggest partial or even lacking IgE cross-reactivity between certain profilins [5]. The study describes the extent of reactivity amongst profilins from Timothy, Birch, Latex and Celery was greater than cross-reactivity to Mugwort and Bellpepper profilins. The structural integrity of purified proteins was confirmed by circular dichroism spectroscopy. IgE ELISAs and ELISA inhibitions using sera from 22 profilin-sensitized allergic patients were carried out [5]. IgE binding proteins related to birch pollen, minor allergen, bet v6 have been found in many vegetables foods such as apple, peach, orange, lychee, strawberry, carrot and zucchini. Nevertheless, the occurrence of cross-reactive IgE antibodies is not correlated with the development of clinical food allergy. Profilins and cross-reactive carbohydrate determinants (CCD) responsible for approximately 10-20% of all pollen-allergic patients' sensitization, are also present in grass and weed pollen grains. The clinical relevance of sensitization to CCD is doubtful [3]. Patients with IgE to cross-reactive epitopes displayed allergic reactions to a greater number of plant foods than patients having IgE directed to species-specific epitopes [5].

3. CONCLUSION

The data indicate presence of a few major proteins shared by many airborne, indoor and food allergens. Data summarized in this publication provide an overall pattern of allergenic proteins present in various food and pollen dominated by profilins, LTP and PR. Likewise, fruits and pollen are also dominated by the above 3 protein groups. Almost same major proteins were found in vegetables and their cross-reacting pollen. Compared to this, a different pattern was seen between the cross-reacting seafood and indoor allergens. The major protein in both seafood and indoor allergens were tropomyosin.

The review of the literature provided interesting clue towards IgE mediated cross-reactivity patterns between various food and inhalants in *in vivo* SPT of allergenic subjects. However, our discussion remains inconclusive in relation to primary sensitizer in poly-sensitized patient vs positively reacting allergenic extracts. Since SPT reactions are simply indications of sensitizations or cross-reacting allergens, *in vivo* diagnosis and particularly immunotherapy treatment, based only on Skin Prick Testing or Prick to Prick testing, must be evaluated with symptoms correlation, season and timing of symptoms, dietary habit of the patient and the exposure possibility to both seasonal pollen grains and indoor allergens.

We, therefore conclude that, despite a huge amount of scientific information available in the medical literature, yet it is difficult to find an accurate answer whether different groups of major allergenic proteins have similarities in their biochemical and molecular structure and they act in the similar manner and induce similar immunological responses. Even more difficult is to understand clinical manifestations of

cross reacting proteins. Data on molecular aspects such as amino acid sequencing for many cross-reactive proteins are emerging and an answer can only be found upon successful conclusion of many such studies in the future.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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