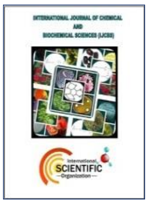
International Journal of Chemical and Biochemical Sciences

Journal Home page: www.iscientific.org/Journal.html



Latex and plant food allergens, its clinical effects and diagnosis: A review

Ravi Kant Upadhyay

Department of Zoology, D. D. U. Gorakhpur University, Gorakhpur, Uttar Pradesh 273 009

Abstract

Plant latex allergens show extensive cross reactivity to cause multiple sensitization and evoke different types of allergic disorders. Many plant-derived foods such as fruits, vegetables, and legumes induce latex-fruit syndrome or pollen-food allergy or allergic hypersensitivity. Mainly fruit latex contains acetogenins, profilins, and chitinases which showed cross-reactivity due to presence of C-terminal catalytic domain similar to hevein and enhanced IgE binding to different epitopes due to presence of HLDs. In addition, multiple allergen exposure from plant pollens and pollen-food-latex complexes, cause high allergic sensitization and cause serious allergic diseases. In such allergies profilins are dominant allergens/ proteins which induce multiple sensitization, responsible and generate cross reactivity and induce secretion of IgE antibodies in allergic patients. More specially, occupational allergens such as hevein and its related proteins persist for longer time in the medium and evoke different types of allergic reactions in exposed persons. However, to avoid allergic complications such as anaphylactic shock, immediate type hypersensitivity and serious latex related allergic disorders in health care workers protective devices are to be used and to minimize the allergen inhalation should be minimized. In the present review article latex allergen induced clinical effects; diagnosis and immunotherapy are explained in detail .To reduce the risk exposure of occupational allergens should be minimized.

Key words: Plant latex, food allergens, allergic reactions, hypersensitivity, immunodiagnosis

Full length article Received: 30-12-2012 Revised: 09-01-2013 Accepted: 15-01-2013 Available online: 31-01-2013

**Corresponding Author*, e-mail: rkupadhya@yahoo.com

1. Introduction

Plant latex is a mixture of many pharmaceutically active substances which possess very high medicinal value. Mainly latex allergens or its derivatives [1] are hazardous chemicals that upon direct exposure cause allergic reactions and induce immediate-type hypersensitivity in man [2,3] As every one of us get direct or indirect exposure to latex or latex made materials in our daily life and show allergic sensitivity differently. Many people are allergic to latex particularly to natural latex rubber or non-vulcanized rubber. Such people are highly sensitive to plant latex and its products as they show shock upon direct exposure [4] More especially children with spina bifida are found to be highly sensitive and allergic to natural latex rubber. In addition allergen induced sensitization is also found prevalent in doctors and nurses who inevitably use natural rubber gloves, catheters and tubes during daily operations. In addition people those who have faced multiple surgeries also get longer exposure to latex materials and show latex related allergies. Latex allergy is also evoked by inhalation of airborne[5] occupational allergens in health care workers [6].For example donning powder that is applied to the surface of latex gloves and abraded automobile-tire dust both persist in the atmosphere for longer duration. Upon inhalation these allergens reach into the lungs, sensitize alveoli and provoke asthma. Besides this, pollens are also important allergens that also cause respiratory allergy in morning and evening walkers. Mainly plant latex contains few important allergens such as acetogenins, profilins, heveins and chitinases which persist in to the final products evoke different types of allergic reactions and sensitization in exposed persons. But due to presence of latex proteins plants protect itself from insect attacks; grazing animals and these proteins serve as effective defense material. Few plants such as *Aristalochea bracteata* and *Adathoda vasica* contain distasteful latex which protects them from goat and other animals. Latex of *Semecarpus anacardium* is poisonous to animals that cause severe toxicity and induce anaphylactic reactions in animals.

2. Latex defense

Several latex proteins, including cysteine proteases and chitin-related proteins, have been shown to play important role in plant-insect interactions. Interaction between mulberry plant (*Morus* spp.) and silkworm (*Bombyx mori*) is an old model system of plant–insect interaction in which plant latex and its ingredients mainly sugar-mimic alkaloids and proteins play key role in operating defense against herbivorous insects. Due to presence of some enzymatic proteins, plant latex is considered as analogous to animal venom because it provides defense against herbivorous insects [7] and phytopathogenic fungi [8]. Similarly, both osmatin and thumatin proteins isolated from *Calatropis procera*, were found active against fungi *Fusarium solini* (IC_{50} 67µg/ml), *Neurospora (*$IC_{50}C$ 57.5 µg/ml), and *Collettricum gloesoriodes* 32.1µg/ml) [9] while *Pulmera rubra,* and *Euphorbia tirucallai* latex proteins showed activity against phytopathogens [8]. Similarly, tirucallol a triterpene from *Euphorbia* lacteal latex showed anti-inflammatory effect [10] and a protein peroxidase class III isolated from *Euphorbia characias* acts as a catalytic enzyme [11]. More specifically, plant latex contains defense protein MLX56 and cardenoides which operate inducible defense in infected plants [12]. These proteins also showed complicated molecular interactions to herbivores [13]. Plants possess unique defense molecules mainly chitinases which effect insect skin [14]. However, both papain and cysteine proteases found in Papaya latex [15] and chitinases occur in mulberry latex play a crucial role in defense against herbivorous insects.[16] Similar defense against insects is also found in latex of Apocynaceae plants due to presence of cardenolides and other defense proteins. It is an example of parallel defense which was evolved during long evolution through inter-specific interactions between insects and plants. Contrary to this, herbivores have also developed sophisticated adaptations at molecular, physiological, or behavioral level against latex-borne defenses. In addition this, latex-borne defense system also function as transport system for carrying defense substances between distant locations [17]. Contrary to this, vein cutting behavior in insects counter play latex defense [18].

3. Major plant food allergens and its clinical effects:

Few people are highly sensitive to fruit latex and show extensive cross-reactivity to various kinds of plant-derived foods such as fruits, vegetables, and legumes [19] and develop "latex-fruit syndrome" or allergic hypersensitivity [20]. Similarly, pollen-food latex also cause allergic syndrome which is notably visualized in form of itching and pruritus around the oral cavity. It is called "oral allergy syndrome" (OAS). In addition, multiple allergen exposure from plant pollens and pollen-food-latex complexes, cause high allergic sensitization and results in serious allergic diseases.[21] In such allergies profilins are main proteins which induce multiple sensitization and pollen-food-latex syndromes[[20]. or food allergy in man [23]. (Table 1) Profilins are dominant allergens responsible for the cross-reactivity to fruits and pollens [22] and induce secretion of IgE in allergic patients [24]. Similar to profilins class I chitinases show cross-reactivity due to presence of C-terminal catalytic domain [25] similar to hevein and enhanced IgE binding to different epitopesdue to presence of HLDs [25]. It is also confirmed by both the sequence alignments as well as the comparison of the amounts of allergen specific IgE level synthesized after sensitization. Profilin isoforms are also identified which express in several organisms and show amino acid sequence similarity up to 54 and 83% [26]. Even small changes in amino acid sequence can alter the biochemical properties of profilin substantially. For example single amino acid substitutions affect the binding of these proteins to other ligands [27-30]. Therefore, characterizing the biochemical properties of each profilin is highly important to decide the type of allergic reaction, rate of sensitization and to know its potential cellular function. Plant profilins, are originally similar to birch pollen allergens and plant panallergens [31], exist and encoded by large multigene families [32,33]. These are also isolated from Arabidopsis and maize [34-36]. Plants possess two classes of profilins class I and class II. Class I profilins, obtained from native endosperm and Class II profilins fruit and latex which show higher affinity for poly-L-proline and sequestered more monomeric actin than did class I profilins. In addition few recombinant protein, ZmPRO5 also have been made which act like class I profilins [37]. Profilins are highly cross-reactive allergens which bind IgE antibodies of almost 20% of plant-allergic patients. These proteins show wider cross-reactivity with other plant profilins due to presence of linear and conformational epitopes. Profilins are considered as mimickers of allergy [21], show extensive cross-reactivity [38], induce delayed type hyper-sensitization [5] and cause IgE-mediated allergic disorders [39] by making significant elevation in the level of latex-specific serum immunoglobulin IgE [1]. However, IgE mediated fruit allergens also induce atopic eczema, asthma, rhinitis and multiple anaphylactic shock [40, 41] and utricaria in females [42]. It is a common disease with marked effects on quality of life (QOL) occurs in general population [42]. Food and vegetable allergy cause direct sensitization of gastrointestinal tract [43]. Latex allergens function as antigens [44] and possess common epitopes for IgE antibodies [45]. These also show lysozyme activity [46], However, many latex allergens such as patatin [47], papatins [48], pepper allergens [20] Hev b 6.02 [49, 50] show enormous *in vivo* sensitization [49] and cross reactivity [51] (Palomares et al., 2005). Similarly, class I chitinases [52], from banana, avocado [48], *Ficus bengalensis* induce allergy [38] (Table 1). Similarly 1, 3-beta glucanase and Prsa 32 kDa endochitinases [53, 54] induce allergy and express insect chitinase genes [55]. Similar chitinase gene activity is reported in hevein protein isolated from elderberry fruits [56]. Similarly LTP from *H. brasilensis* [57] and Bet v 1 [22] cross react with IgE antibodies and show high clinical relevance [22]. Similarly, exposure to rohevein, hevein from natural rubber latex cause allergy in children [58] and show very high cross reactivity [59]. Moreover, protein glycosylation plays important role in allergy [60]. Allergens are a group of protein or proteins bound substances having molecular weight between 15,000 to 40,000, while allergenicity is a consequence of a complex series of interactions involving not only the allergen but also dose, sensitizing route, and genetic constituent of the recipient. In nature plants possess diverse forms of allergens in different plant families, but all have single important function i.e. protection from herbivorous insects. However, Few important allergens such as rye and timothy grass pollen, ragweed pollen, birch pollen, fruit latex, legume proteins, plant hairs and different types of vegetables proteins have been identified that impose clinical effects in man. Besides this, animal toxins, enzymes, leather, fur and bird and insect wings possess different types of allergens. Each of these allergens has been shown to a multi-allergen system containing a number of allergen components. Ragweed pollen is a major pollen allergen which suspend in the air in large amounts, inhaled and out wall of pollen particles is dissolved by enzymes in the mucous secretions, releasing the allergenic substances. Chemical fraction of ragweed has revealed a variety of substances most of which are not allergenic but are capable of eliciting an IgM or IgG response. Till the date so many fruit allergens Hev b 2 (endo-β-1,3-glucanase) [20, 51, 61] Hev b 6.02 (hevein) [62], Hev b 7 (patatin-like protein) [46], Hev b 8 (profilin) [63], and Hev b 12 (non-specific lipid-transfer protein) [64], Hev b 11 [65], Pers a 1 [66], and Cas s 5 [67] have been isolated from rubber plant, banana, avocado, chestnut, and kiwi fruits. These latex-fruit allergens showed very high cross-reactivity and cause latex-fruit syndrome. Similarly, several plant-derived class I chitinases from avocado [48] tobacco [54] were isolated which contain N-terminal domains with high sequence similarities to hevein and designated as hevein-like domains (HLDs). Contrary to this, class II chitinases, lack HLD and possess low-affinity to IgE binding sites [68, 69]. Similarly another hevein-like minor allergen agglutinin (Tri a 18) was isolated from wheat that contains four hevein-like domains [70]. It is currently believed that hevein Hev b 6.02 is the sensitizing agent in the hevein-HLD cross-reactivity. It is a major allergen which also occurs in high concentration in certain fruits and an important elicitor of latex associated plant food allergy due to its cross-reactivity to HLDs of class I chitinases [68, 71]. A similar latex protein concerned to ripening of fruits Act d 11 was identified [72] and other natural allergens such as Hev b 6, Hev b 3 and Hev b 7/13 were isolated by Khan et al. [73] from *Hevea brasilensis*. Hevea is a major allergen that shows functional similarity to heat shock protein (81 kDa), proteasome subunit (30 kDa), protease inhibitor (8 kDa), hevamine A (43 kDa) and glyceraldehyde-3-phosphate dehydrogenase (37 kDa) function like catalytic proteins [74] Similarly, Hemmer et al, 2010 [75] have identified Bet v 1- allergen from fig (*Ficus carica*) and other Moraceae fruits such as *Ficus benjamina*, mulberry (*Morus alba*), jackfruit (*Artocarpus heterophyllus*) by using western blot inhibition techniques. Both Fig and other Moraceae fruits contain allergens homologous to Bet v 1 and represent clinically relevant birch pollen-associated foods [75]. In addition, few nonspecific lipid transfer proteins (LTPs) which act as important allergens in fruits, vegetables, nuts, pollen, and latex are isolated. These proteins showed IgE reactivity and induce systemic symptoms [76]. A similar lipid transfer protein homolog of an IgE-binding antigen was isolated from Japanese cedar pollen by Ibrahim et al. [77]. Japanese cedar (*Cryptomeria japonica*) pollen is a major cause of seasonal rhinitis and conjunctivitis in Japan. It is an important clinical aspect that how allergens do sensitization and show cross reactivity to each other? It is possible that allergens may cause sensitization due to presence of glycoproteins carrying cross-reactive carbohydrate determinants (CCDs) which generate allergic symptoms in patients with or without reactivity of their IgE molecules [78]. Hence, for clinical establishment of latex-fruit syndrome, there is a need to explore new allergen families which might be more cross-reactive.

4. Occupational allergens

Natural rubber latex is a major occupational allergen that imposes various clinical effects in health care workers [6].NRL generates hypersensitivity, occupational asthma [2] contact allergic dermatitis in man [79] (Table 2). Occupational allergens cause severe health problems in rubber latex industry workers in many developing countries [80]. Natural rubber latex contains more than 200 proteins of which 13 have been identified as allergens and cause Type–I latex allergy [81]. Patients with type - I allergic sensitivity also show increased risk of type–I sensitization to aeroallergens [8]. Recently two allergens Hev b1 and hevamine are screened as major allergens among health care workers [82] mainly hospital staff who suffer with occupational asthma a[2]. Both Hev b1 and hevamine are mainly added in latex gloves as indicator allergens but they show serious consequences after a prolonged exposure. Similarly, anthraquinone a glycosideisolated from *C. procera* [83], glycolipids from*Aleo vera* and *Hevea brasiliensis* function as skin irritant and generate allergy [84]. Besides this, occupational groups such as zoo keepers, animal shop workers, bird keepers and hatchery people get exposure of bird and animal origin allergens and show various clinical health hazards [85] (Table 2). Birds mainly contribute allergic and contagious diseases due to exposure of feather and egg proteins. These allergens create complexity of occupational exposure and cause non-specific irritant effects in man and have to need hygiene and medical prophylaxis [85]. Thioureas are used as additives in rubber products as anti-degradants for natural rubber latex which are uncommon cause of allergic contact dermatitis [79]. Allergic contact dermatitis (ACD) is a well-recognized immune-mediated disease often associated with the use of vulcanization accelerator-containing latex and nitrile gloves [86]. Similarly, agricultural field workers get exposure of grass and weed origin allergens and tobacco industry workers to tobacco allergens and show heavy asthmatic sensitization. In addition honey bee and yellow jacket venom do mono-sensitization in patients [87].

5. Diagnosis

Mostly latex substances/chemicals act as antigens that upon regular exposure evoke allergic responses in man. However, for accurate diagnosis of serum samples and for successful treatment of allergic diseases, latex allergen should be identified more accurately. It can be detected by measuring level of allergen specific IgE antibodies in blood serum of patient. It is also determined by measuring allergen concentration in natural rubber latex [88] and in serum samples of experimental models [89]. More specifically, blood tests are used to measure levels of allergen specific IgE generated after use of various foods, exposure to inhalants, medications, latex and venoms. These tests provide both IgE positive and negative reactions to latex and non-latex proteins. More specifically it can be also measured by IgE epitopes analysis of hevein pre-protein, latex allergen [90-91] and by counting B cell epitopes of prohevein [92]. In addition, epitopes present on the major latex allergens such as Hev b2 and 1,3 beta-glucanase fruit allergen [61]can be determined by using IgG as blocking antibodies [50]. Same method is used to determine Hev b 6.02 and hevein induced effects in patients mainly in adults [88, 93, 94 .Similarly, recombinant latex allergens also express similar epitopes on B cells and behave like natural proteins [89]. Besides this, prick tests and IgE based ELISA are also used to determine the level of allergen in young people [95] those who take fruits in diet such as banana avocado chest nut and kiwi. In addition both tests are used to measuring cross reactivity between major haevin and hevin like domain (HLDs) occur in fruit class I chitinases [96]. IgE response to HLDs is elicited by hevein as sensing allergen in most cases [96]. In addition, allergic cross reactivity and sensitization profile in children is also determined by basophil activation test and by IgE measurements [97] while occupational type I allergies can be detected by using skin prick test [73, 98]. But sensitivity and specificity of above tests is influenced by patient-specific factors. However, secondary effects of few hidden occupational allergens which also cause hypersensitivity remain undetected by normal methods [6]. But identification of clinically relevant cross-sensitization between two allergen scan be done by using immunoblot inhibition or ImmunoCAP inhibition analyses [99] of patients serum [95]. Both EAST-inhibition and immunoblotting-inhibition assays confirm the existence of cross-reactivity between two allergens of different origin such as natural tobacco allergens and smoking induced allergens. Sometimes outcome of IgE measurement could not provide better results and show limited clinical relevance [100]. In such cases few newer methods such as CRD microarray and IPQCM are used. These highly specific microarray based immunoassays provide greater resolution of presence of allergens and workout asymptomatic sensitization [101]. IPQCM bioassay is based on development of a rubber elongation factor surface imprinted polymer quartz crystal microbalance sensor (IPQCM) and help to determine the concentration of Hev b1 in natural rubber latex products [102] while, presence of pollen allergens in pollinosis patients is detected by component resolved diagnosis (CRD) by using micro-array technology [103]. Furthermore, diagnosis of allergic sensitization can be measured by presence of an irritant allergen in plant latex by inter-digitated capacitance (IDC) transducer [102]. Moreover, CRD microarray is a reliable test for diagnosis of PFAS [103]. Further, to identify novel allergens with potential involvement in latex fruit syndrome are identified by immunoblot analysis [21] while profilin or nSLTPs based immune assays are used to diagnose of grass and pollen weed allergy in patients [40]. These assays can specially detect nonspecific lipid transfer proteins (LTPs) or allergens in fruits, vegetables, nuts, pollen, and latex [76, 77]. All the above confirmatory tests can diagnose an allergic disorder, and immediate allergic reactions in allergic patients [104]. In addition a marker effect generated by *C. japonica* pollen showed clinical conjunctival allergen challenge (CAC) and impose high sensitivity in patients with latex allergy. Both of these methods may become better diagnostic option in cases with uncertain diagnosis and might be used for the development of future molecular diagnostics and immunotherapeutic methods [105]. In addition latex allergy and its sensitization can be determined by using promoter polymorphisms in interleukins 13 and 18 (IL13 and IL18) in health care workers [106]. It is a molecular method which is based on single-nucleotide polymorphisms in genes encoding IL13 and IL18. These genes encoding IL13 and IL18 occur at an increased frequency in NRL allergic patients with spina bifida (SB) or bladder exstrophy (BE) [106].

6. Immunotherapy and prophylaxis

It is well known that latex and its derivatives persist for longer duration in environment, from where these are inhaled by patients, transport to reach in blood and after getting a regular exposure cause severe latex allergy. However, for removal of allergic symptoms immunotherapy is considered to be best therapy under use. It reduces asthma symptoms, improves bronchial hyper-reactivity, and kick off both local and systemic adverse effects [107]. Mainly, latex sublingual immunotherapy is helpful to reduce latex generated clinical effects in health care workers [108]. It significantly reduce symptoms [108] and shows better clinical efficacy in early age children mainly those who faced allergic asthma and rhinitis [109, 110] It is much safer for children below 5 years of age, with a lower limit of 3 years. Latex allergy is a preventable disorder if proper action is being taken, and to avoid use of powdered latex gloves, catheters and other clinical materials made up of latex. In addition, latex allergy incidences can be reduced among health care workers by using powder free gloves [111] or having low protein/allergen contents [112]. For industry people there must be instructions to decrease the level of latex allergen so then occupational groups may get lesser and lesser exposure. Powdered latex gloves or latex gloves with high allergen content are to be forbidden [113] and hospitals should implement the policies to restrict or ban the use of devices made of natural rubber latex in health care as precautionary measures against the perceived risk of NRL allergy [114]. Thus use of low protein, low allergenic powder free gloves can significantly decrease the prevalence of Type I allergic reactions to NRL [114] NRL is a common cause of allergic contact dermatitis [115]. Allergen avoidance in children is found very effective in terms of primary prevention of an allergic disorder [111]. Patients those who show positive reaction to natural rubber latex also show fruit allergies with a cross reactivity to latex [19]. But it is also advised to keep away spina bifida patients from latex exposure because it causes very high sensitization, evoke atopy and allergic diseases in patients [116]. Children with spin bifida have shown a disease inherited risk for NRL generated hypersensitivity, latex allergy and occupational asthma [2]. Latex exposure avoidance prevents latex allergen sensitization and its spreading to susceptible population mainly caused by inhalation of airborne allergens. Initial step to control type–I hypersensitivities is to identify the offending allergen and completely avoid the contact and exposure of it, if become possible.

Table 1: Showing major food allergens, its source, common name and type

Allergen code	Species scientific name	Common name	Allergen Type	Description
Act c 10	*Actinidia chinensis*	Gold Kiwi fruit	foods	nsLTP1
Act c 8.0101	*Actinidia chinensis*	Gold Kiwi fruit	foods	Pathogenesis-related protein PR-10
Act d 9	*Actinidia deliciosa*	Kiwi fruit	foods	Profilin
Ana o 1	*Anacardium occidentale*	cashew foods nut;	vicilin-like protein;	legumin-like protein
Ama r 2	*Amaranthus retroflexus*	Redroot	pigweed weed	Profilin
Ama r 2.0101	*Amaranthus retroflexus*	Redroot	pigweed weed	Profilin
Amb a 1	*Ambrosia artemisiifolia*	short ragweed weed	ragweed weed	antigen E; AgE
Amb a 10	*Ambrosia artemisiifolia*	short ragweed weed	Asterales	Polcalcin-like protein (4 EF-hands)
Ana c 1	*Ananas comosus*	pineapple	foods	profilin
Ana c 2	*Ananas comosus*	pineapple	foods	bromelain
Api g 1.0201	*Apium graveolens*	celery	foods	Api g 2
Ara h 2.0101	*Arachis hypogaea*	peanut	foods	Conglutin
Ara h 5	*Arachis hypogaea*	peanut	foods	profilin
Ara h 6	*Arachis hypogaea*	peanut	foods	homolog: conglutin
Ara h 7	*Arachis hypogaea*	peanut	foods	homolog: conglutin
Aspa o 1	*Asparagus officinalis*	asparagus	foods	lipid transfer protein
Aspa o 1.01	*Asparagus officinalis*	asparagus	foods	Nonspecific lipid transfer protein
Ber e 1	*Bertholletia excels*	Brazil nut	foods	2S albumin
Ber e 2	*Bertholletia excels*	Brazil nut	foods	globulin seed storage protein 11S
Bet v 1.0101	*Betula verrucosa*	*(Betula pendula)*	White birch tree	Bet v 1a
Beta v 2.0101	*Beta vulgaris*	Sugar beet	foods	Profilin, pollen
Bra n 1	*Brassica napus*	rapeseed	foods	2S albumin; Calcium-binding pollen allergen
Bra n 2	*Brassica napus*	rapeseed	foods	Polcalcin; ; Calcium-binding pollen allergen
Bra o 3	*Brassica oleracea*	Cabbage and others	foods	lipid transfer protein
Bra o 3.0101	*Brassica oleracea*	Cabbage and others	foods	lipid transfer protein
Cap a 1w	*Capsicum an nuum*	bell pepper	foods	osmotin-like protein PR5: Actinidin
Cap a 2	*Capsicum annuum*	bell pepper	foods	prof ilin
Car b 1	*Carpinus betulus*	hornbeam tree	Fagales	homolog: protein PR10
Car b 1.0101	*Carpinus betulus*	hornbeam tree	Fagales	Car b 1.1a
Car i 4	*Carya illinoinensis*	Pecan foods	foods	Legumin seed storage protein; Subunit of hexameric protein
Car p 1	*Carica papaya*	papaya	foods	papain
Cas s 1	*Castanea sativa*	chestnut tree	Fagales	homolog: pathogenesis related protein PR10
Cas s 5	*Castanea sativa*	chestnut tree	Fagales	chitinase
Cha o 2	*Chamaecyparis obtusa*	Japanese cypress tree	Pinales	Polygalacturonase
Cit r 3.0101	*Citrus reticulata*	Tangerine	foods	Non-specific lipid transfer protein
Cit s 1	*Citrus sinensis*	sweet orange	foods	germin-like protein
Cof a 1.0101	*Coffea arabica*	Arabian coffee	Foods	Class III chitinase
Cor a 13	*Corylus avellana*	hazelnut	foods	14-16 kDa oleosin
Cry j 1	*Cryptomeria japonica*	Japanese cedar, sugi tree	Pinales	pectate lyase; SBP/ Sugi basic protein
Cup a 4	*Cupressus arizonica*	cypress tree	Pinales	Pro-lcalcin
Dau c 1.0101	*Daucus carota*	carrot	foods	Ge a20
Dau c 1.0102	*Daucus carota*	carrot	foods	CR16
Fag s 1.0101	*Fagus sylvatica*	European beech tree	Fagales	PR-10 protein, Bet v 1 homologue
Fra a 3.0102	*Fragaria ananassa*	Strawberry foods	foods	Non-specific lipid transfer protein 1
Gly m 4	*Glycine max*	soybean	foods	SAM22, PR-10 protein
Gly m 5	*Glycine max*	soybean	foods	Beta-conglycinin (vicilin, 7S globulin)
n o 2	*Juniperus oxycedrus*	prickly juniper tree	Pinales pollen	Polcalcin; Calcium-binding
Jun o 4	*Juniperus oxycedrus*	prickly juniper tree	Pinales	homolog: calmodulin Calcium-binding pollen allergen
Jun v 3.010102	*Juniperus virginiana*	eastern red cedar tree	Pinales	Thaumatin-like protein
Lac s 1	*Lactuca sativa*	lettuce	foods	lipidid transfer protein
Len c 1.0101	*Lens culinaris*	lentil	foods	vicilin, Len c 3. 02
Lep w 1.0101	*Lepidorhombus whiffiagonis*	Megrim,	Whiff, Gallo foods	Beta-parvalbumin
Lyc e LAT52	*Lycopersicon esculentum*	tomato foods	anther specific	LAT52 protein
Mal d 4	*Malus domestica*	apple	foods	Profiling; GD4-1
Man e 5	*Manihot esculenta*	Cassava, manioc	foods	Glutamic acid rich protein
Mor n 3.0101	*Morus nigra*	Black Mulberry tree	Rosales	Nonspecific lipid transfer protein type 1
Mus a 4.0101	*Musa acuminate*	Banana	foods	Thaumatin-like protein
Ole e 1	*Olea europea*	olive tree	Lamiales Oleaceae	Pollen allergen
Ole e 11.0101	*Olea europea*	olive tree	Lamiales Oleaceae	Pectin methylesterase
Ole e 2	*Olea europea*	olive tree	Lamiales Oleaceae	profilin
Pers a 1	*Persea americana*	avocado foods	endochitinase	pathogenesis related protein PR3
Pha v 3.0201	*Phaseolus vulgaris*	French bean	foods	non-specific lipid transfer protein type 1
Pis v 2	*Pistacia vera*	Pistachio	foods	11S globulin subunit
Pru ar 1	*Prunus armeniaca*	apricot foods homolog:	Bet v 1; homolog:	pathogenesis related protein PR10
Pru du 4.0102	*Prunus dulcis*	Almond	foods	Profilin
Pru du 5	*Prunus dulcis*	Almond	foods	60s acidic ribosomal prot. P2
Pru p 4	*Prunus persica*	peach	foods	profilin
Pru p 4.0101	*Prunus persica*	peach	foods	profilin, Pru p 4.01
Pru p 4.0201	*Prunus persica*	peach	foods	profilin, Pru p 4.02
Rub i 3	*Rubus idaeus*	Red raspberry	foods	Nonspecific lipid transfer protein
Rub i 3.0101	*Rubus idaeus*	Red raspberry	foods	Nonspecific lipid transfer protein 1
Sec c 5.0101	*Secale cereale*	rye	foods	Group 5 grass pollen allergen
Ses i 1	*Sesamum indicum*	sesame	foods	2S albumin; Seed storage protein
Sin a 1	*Sinapis alba*	white mustard	foods	2S albumin
Sola t 4	*Solanum tuberosum*	potato	foods	aspartic protease inhibitor PIG; PIGEN1; STPIB; pF4
Zea m 12	*Zea mays* maize	corn	foods	Profilin
Zea m 14.0101	*Zea mays* maize	corn	foods	Nonspecific lipid-transfer protein
Zea m 25	*Zea mays* maize	corn	foods	thioredoxin
Ziz m 1	*Ziziphus mauritiana*	Chinese-date	foods	class III chitinase

Table 2: Showing major occupational allergens isolated from Natural Rubber-Latex

Allergen	Species scientific name	Trivial name	Function
Hev b 1	*Hevea brasiliensis*	rubber elongation factor	Rubber biosynthesis
Hev b 2	*Hevea brasiliensis*	beta-1,3-glucanases	defense-related protein
Hev b 3	*Hevea brasiliensis*	small rubber-particle protein	rubber biosynthesis
Hev b 4	*Hevea brasiliensis*	microhelix component	defense-related protein
Hev b 5	*Hevea brasiliensis*	acidic Latex protein	Allergen
Hevb6.01	*Heveabrasiliensis*prohevein, pre defense-related protein	hevein, preprotein	defense-related protein
Hev b 6.03	*Hevea brasiliensis*	prohevein	C-terminal fragment (latex coagulation)
Hevb13	*Heveabrasiliensis*	patatin	homologue from B-serum
Hevb7.02	*Heveabrasiliensis*	defense-related protein	inhibitor of rubber biosynthe
Hev b 8	*Hevea brasiliensis*	latex	profiling structural protein
Hev b 9	*Hevea brasiliensis*	latex enzyme	enolase glycolytic
Hev b 10	*Hevea brasiliensis*	Mn-superoxide	dismutase destruction of rad
Hev b 11	*Hevea brasiliensis*	class I endochitinase	defense-related protein
Hev b 12	*Hevea brasiliensis*	lipid transfer protein	defense-related protein
Hev b 13	*Hevea brasiliensis* latex	esterase	defense-related protein

Table 3: Clinical effects of aeroallergens and occupational non-plant materials act as allergic agents

Type of allergen	Source	Clinical effect
NRL rubber latex	Latex industry	Allergic cross reactivity and hyper sensitivity
Regweed pollens	Agriculture and Gardening	Allergic hypersensitivity and pollinosis
Donning powder	Medicare	Allergic and asthmatic
Marble stone dust	Stone cutting and processing	Allergic, asthmatic and bronchitis
Automobile dust	Automobile industry	Bronchitis, itching, headache and hypesenitivity
Grass pollens	Agriculture and Gardening	Allergic cross reactivity, pollinosis
Straw dust	Agriculture and Gardening	Sneezing, eczema and hypersensitivity
Insect venom	Hunting and rearing	Allergy, pain, swelling, toxicity, death
Animal venom	Pharmaceutical industry	Allergy, pain, swelling, toxicity, death
Bird feather dust	Zoo Keepers	Allergic hypersensitivity, bird flu, SARS
Insect wing dust	Animal collection	Allergic hypersensitivity, irritation
Animal fecal material and urine	Zoo and dairy industry	Sneezing and Allergic hypersensitivity
Tobacco dust	Cigarette industry	Sneezing, headache, vomiting, nausea, Tobacco smoke, Bad habits, Headache, vomiting, , bronchitis, lung cancer
Wood dust	Wood product industry	Bronchitis, Asthma
Fruit and latex	Floriculture	Oral Food Syndrome
Rice bran	Agriculture	Pollinosis type allergy
Paints and colours	Synthetic chemicals	Sneezing, headache and hypersensitivity
Suspended particulate matter	Automobiles transport	Bronchitis, asthma
Coal dust	Mining	Bronchitis, asthma, pleurisies
Cement	Cement industry	Bronchitis, asthma, pleurisies
Cat	Amino acids	sneezing, itchy swollen eyes
Cosmetics	Cosmetic industry	Inflammation, redness, [conjunctivitis, contact dermatitis, irritant contact dermatitis
Mold	Agriculture	congested feeling, joint aches, headaches, Respiratory problems such as iorritation fatigue
House dust mite	House hold exposure	Asthma
Nickel (nickel sulfate hexahydrate)	Industry	Allergic contact dermatitis
Gold (gold sodium thiosulfate)	Industry	Allergic contact dermatitis
Chromium	Industry	Allergic contact dermatitis, Cobalt chloride, Industry Allergic contact dermatitis
Formaldehyde	Industry	Allergic contact dermatitis
Photographic developers	Industry	Allergic contact dermatitis

More often, use of latex free fruits, no exposure to house pets and domestic animals, dust control by vacuum sucker, or avoidance of offending foods can reduce and check type –I allergic responses. But elimination of inhalant allergens such as pollens, petals, leaf particles, suspended dusts, pollutants is a physical impossibility; in such a condition high quality filtration mask is proved to be more helpful. For such patients immunotherapy by providing repetitive injections of an increasing dose of allergens become more helpful for some time to reduce the severity of type –I reactions. But repeated introduction of allergen by subcutaneous injections appears to cause a shift toward IgG production or to induce T cell mediated suppression that turns off the IgE response. The IgG antibody is used as blocking antibody because it competes with allergen and binds to it, and forms a complex that can be removed by phagocytosis. However, by doing this, allergen is not being made available to cross link the fixed IgE on the mast cell membrane and allergic symptoms decrease.

In addition, there is a problem in treating allergies that soluble antigens tend to induce a state of energy by activating T cells in the absence of the necessary co-stimulatory signal. When animals were injected with soluble antigens containing these T cell epitopes, the animals became anergic to the corresponding allergen. It is possible that a soluble antigen is internalized by endocytosis, processed and presented with class II MHC molecules on membrane surface, but it may fail to induce expression of the requisite co-stimulatory ligand on antigen presenting cells. Though the T-cell epitopes of ragweed pollen, cat, hair, and house dust mites have been recognized but there is no solution of multiple symptoms generated after allergen sensitization in most cases. Most IgE responses occur on mucous membrane surfaces and thus in response to allergens that enter the body either by inhalation or ingestion. Few important allergens which cause different types of clinical effects are listed in table 3.

References

[1] B.J. Meade, N. David. D. Weissman and H. Beezhold. (2000) Latex allergy: past and present. International Immunopharmacology, 2: 225 – 38.

[2] S.H. Nabavizadeh , A. Anushiravani and R. Amin . (2009). Natural rubber latex hypersensitivity with skin prick test in operating room personnel. Iranina Journal of Allergy Asthma and Immunology. 8(4) 219-20.

[3] R. Sutton, J.H. Skerritt, B.A. Baldo and C.W, Wrigley. 1984. The diversity of allergens involved in bakers' asthma. Clinical Allergy. 14: 93–107.

[4] J.M. Roll and R.E.O. Hehir. 2008. Latex allergy: amodel for therapy. Clinical and Experimental Allergy. 38: 898–912.

[5] M. Sugiura, R. Hayakawa, K. Sugiura, M. Shamoto, and T. Yagami. 2002. Latex protein induced delayed-type contact allergy. Environmental Dermatology. 9: 53-62.

[6] B. Añíbarro, F.J. Seoane, M.A. Perpińá and J. Carnés. 2010. Latex: a hidden occupational allergen. Annals of Allergy, Asthma and Immunology. 104(1) 94-5.

[7] S. Kitajima, K. Kamei, S. Taketani, M. Yamaguchi, F. Kawai, A. Komatsu and Y. Inukai. (2010). Two chitinase-like proteins abundantly accumulated in latex of mulberry show insecticidal activity. BMC Biochemistry. 11: 6-11.

[8] D.P. Souza, C.D. Freitas, D.A. Pereira, F.C. Nogueira, F.D. Silva, C.E. Salas and M.V. Ramos. (2011). Laticifer proteins play a defensive role against hemibiotrophic and necrotrophic phytopathogens. Planta. 234(1) 183-93.

[9] M. Larhsini, M. Bousad, H.B. Lazrek, M. Jana and H. Amarouch. (1997). Evaluation of antifungal and molluscicidal properties of extracts of *Calotropis procera*. Fitoterapia. 68: 371-373.

[10] A. Fernandez, Arche, M.T. Sanez, M. Arroya, R. Pureta de la. And M.D. Garcia (2010). Topical anti-inflammatory effect of tirucallol isolated from *Euphorbia lacteal* Latex. Phytomedicine. 17(2) 146-148.

[11] F. Pintus, D. Spanò, R. Medda, G. Floris. (2011). Calcium ions and a secreted peroxidase in *Euphorbia characias*latex are made for each other. The Protein Journal. 30(2) 115-23.

[12] L.C. Van-Loon, M. Rep and C.M. Pieterse. (2006). Significance of inducible defense-related proteins in infected plants. Annual Review of Phytopathology. 44: 135-62.

[13] N. Wasano, K. Konno, M. Nakamura, C. Hirayama, M. Hattori and K. Tateishi. (2009). A unique latex protein MLX56 defends mulberry trees from insects. Phytochemistry. 70: 880-888.

[14] A. Diaz-Perales, C. Collada, C. Blanco, R. Sanchez-Monge, T. Carrillo, C. Aragoncillo and G. Salcedo. (1998). Class I chitinases with hevein-like domain but not class II enzymes are relevant chestnut and avocado allergens. Journal of Allergy and Clinical Immunology, 102: 127-33.

[15] K. Konno, C. Hirayama, M. Nakamura, K. Tateishi, Y. Tamura, M. Hattori and K. Kohno.(2004). Papain protects papaya trees from herbivorous insects: role of cysteine proteases in latex. The Plant Journal. 37: 370-378.

[16] C. Hirayama, K. Konno, N. Wasano and M. Nakamura. (2007). Differential effects of sugar-mimic alkaloids in mulberry latex on sugar metabolism and disaccharidases of Eri and domesticated silkworms: enzymatic adaptation of *Bombyx mori* to mulberry defense. Insect Biochemistry and Molecular Biology. 37: 1348-1358.

[17] K. Konno, H. Ono, M. Nakamura, K. Tateishi, C. Hirayama, Y. Tamura, M. Hattori, A. Koyama, K. Kohno. (2006). Mulberry latex rich in anti-diabetic sugar-mimic alkaloids forces dieting on caterpillars. Proceedings of the National Academy of Sciences USA, 103: 1337-1341.

[18] D.E. Dussourd and T. Eisner. (1987). Vein-cutting behavior: insect counter play to the latex defense of plants. Science. 237: 898-901.

[19] K. Sekiya, K. Watai, M. Taniguchi, C. Mitsui, Y. Fukutomi, H. Tanimoto, N. Kawaura and K. Akiyama. (2011). Latex anaphylaxis caused by a Swan-Ganz catheter. Internal Medicine. 50(4) 355-357.

[20] S. Wagner, C. Radauer, C. Hafner, H. Fuchs, E. Jensen-Jarolim, B. Wuthrich, O. Scheiner and H. Breiteneder. (2004). Characterization of cross-reactive bell pepper allergens involved in the latex-fruit syndrome. Clinical and Exprimental Allergy 34: 1739–1746.

[21] A. Santos and R. V. Ree. (2011). Profilins: mimickers of allergy or relevant allergens. International Archives of Allergy Immunology. 155(3): 191-204.

[22] M. Wensing, J.H. Akkerdaas, W.A.V. Leeuwen, S.O. Stapel, C.A. Bruijnzeel-Koomen, R.C. Aalberse, B.J. Bast, A.C. Knulst and R.V. Ree,(2002), IgE to Bet v 1 and profilin: cross-reactivity patterns and clinical relevance. Journal of Allergy and Clinical Immunology. 110: 435–442.

[23] R. V. Ree. (2004). Clinical importance of cross-reactivity in food allergy.Curr.Opin.Allergy Clin.Immunol. 4, 235–240.

[24] M. Raulf-Heimsoth, S. Kespohl, J.F. Crespo, J. Rodriguez, A. Feliu, T. Bruning, H.P. Rihs. (2007). Natural rubber latex and chestnut allergy: cross-reactivity or cosensitization. Allergy. 62: 1277–1281.

[25] P. Karisola, A. Kotovuori, S. Poikonen, E. Niskanen, N. Kalkkinen, K. Turjanmaa, T. Palosuo, T Reunala, H. Alenius, M.S. Kulomaa. (2005). Isolated hevein-like domains, but not 31-kd endochitinases, are responsible for IgE-mediated in vitro and in vivo reactions in latex-fruit syndrome. Journal of Allergy and Clinical Immunology. 115: 598–605.

[26] K. Schlüter, B.M. Jockusch, and M. Rothkegel, (1997). Profilins as regulators of actin dynamics. Biochimica et Biophysica Acta.1359: 97–109.

[27] B.K. Haarer, A.S Petzold, and S.S. Brown, (1993). Mutational analysis of yeast profilin. Molecular Cellular Biology. 13: 7864–73.

[28] R.H. Sohn, J. Chen, K.S. Koblan, P.F. Bray, and P.J. Goldschmidt- Clermont. (1995). Localization of a binding site for phosphatidylinositol-4,5-bisphosphate on human profilin. The Journal of Biological Chemistry. 270: 21114–21120.

[29] K. Schlüter, M. Schleicher, and B.M. Jockusch, (1998). Effects of single amino acid substitutions in the actin-binding site on the biological activity of bovine profilin I. Journal of Cell Science. 111: 3261–3273.

[30] D.B. Ostrander, E.G. Ernst, T.B. Lavoie, and J.A. Gorman, (1999). Polyproline binding is an essential function of human profilingin yeast. European Journal of Biochemistry. 262: 26–35.

[31] R. Valenta, M. Duchêne, K. Pettenburger, C. Sillaber, P. Valent, P. Bettelheim, M. Breitenbach, H. Rumpold, D. Kraft, and O. Scheiner. (1991). Identification of profilin as a novel pollen allergen; IgE autoreactivity in sensitized individuals. Science. 253: 557–560.

[32] C.J. Staiger, B.C. Gibbon, D.R. Kovar, and L.E. Zonia, (1997). Profilin and actin depolymerizing factor: Modulators of actin organizationin plants. Trends Plant Science. 2: 275–81.

[33] N.C.A. De-Ruijter and A.M.C. Emons, (1999). Actin-binding proteinsin plant cells. Plant Biol. 1: 26–35.

[34] C.J. Staiger, D.V. Kovar and K.B. Drobak. (1993). Major profiling isoforms are functionally distinct. The Plant Cell. 12: 583–598.

[35] H.E.M. Christensen, S. Ramachandran, C.T. Tan, U. Surana, C.H. Dong, and N.H. Chua. (1996). *Arabidopsis* profilins arefunctionally similar to yeast profilins: Identification of a vascularbundle–specific profilin and a pollen-specific profilin. The Plant Journal 10: 269–279.

[36] B.C. Gibbon, L.E. Zonia, D.R. Kovar, P.J.Hussey and C.J.Staiger. (1998). Pollen profilin function depends on interaction withproline-rich motifs. The Plant Cell.10: 981–94.

[37] C.J. Staiger, D.R. Kovar and B.K. Drobak. (2000). Maize profiling isofprms are functionally distinct. The Plant Cell. 12: 583-598,

[38] Z. Chen, M. Düser, A. Flagge, S. Maryska, I. Sander, M. Raulf-Heimsoth and X. Baur. (2000). Identification and characterization of cross-reactive natural rubber latex and *Ficus benjamina* allergens. International Archives of Allergy and Immunology. 123: 291-98.

[39] P.C. Vlaicu, , L.C. Rusu, A. Ledesma, M. Vicente, M. Cuevas, M. Zamorano, D. Antolín, E. Álvarez and B. De-La-Hoz. (2011). Cucumber Anaphylaxis in a Latex-Sensitized Patient. Journal of Investigational Allergology and Clinical Immunology. 21(3) 236-239.

[40] T. Vieira , C. Lopes, A.M. Pereira, L. Araújo , A. Moreira and L. Delgado . (2012). Microarray based IgE detection in poly-sensitized allergic patients with suspected food allergy - an approach in four clinical cases. Allergologia et Immunopathologia (Madr). 40(3) 172-180.

[41] K. Sonofuchi , K. Watanabe, T. Onuma, T. Kaneko, H. Ohmizo, S. Furuta, K. Endo and T.A. Morota (2010). Case of anaphylactic shock by multiple causes. Masui. The Japanese journal of anesthesiology. 59(8) 1032-1035.

[42] T. Zuberbier, M. Balke , M. Worm, G. Edenharter and M. Maurer .(2010). Epidemiology of urticaria: a representative cross-sectional population survey. Clinical and Experimental Dermatology. 35(8) 869-873.

[43] B.K. Ballmer-Weber and K. Hoffmann-Sommergruber. (2011). Molecular diagnosis of fruit and vegetable allergy. Current Opinion in Allergy and Clinical Immunology.11(3) 229-235.

[44] T. Yagami. (1998). Plant defense-related proteins as latex allergens. Bulletin of National Institute of Health Sciences.116: 46-62.

[45] T. Yagami, H. Osuna, M. Kouno, Y. Haishima, A. Nakamura and Z.Ikezawa. (2002). Significance of carbohydrate epitopes in a latex allergen with beta-1,3-glucanase activity., International Archives of Allergy and Immunology. 129: 27-37.

[46] T. Yagami, M. Sato, and A. Nakamura. (1995). lant defense-related proteins eluting from latex gloves and ammoniated latex: Potential latex allergens. Journal Natural Rubber Research. 10: 100-107.

[47] M.H. Schmidt, M. Raulf-Heimsoth and A. Posch, (2002). Evaluation of patatin as a major cross-reactive allergen in latex-induced potato allergy. Annals of Allergy, Asthma and Immunology. 89: 613–18.

[48] S. Sowka, L.S. Hsieh, M. Krebitz, A. Akasawa, B.M. Martin, D. Starrett, C.K. Peterbauer, O. Scheiner and H. Breiteneder,(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*. The Jouranl of Biological Chemistry. 273: 28091–28097.

[49] D.I. Bernstein, R.E. Biagini, R. Karnani, R. Hamilton, K. Murphy, C. Bernstein, S.A. Arif, B. Berendts and H.Y. Yeang, (2003). In vivo sensitization to purified *Hevea brasiliensis* proteins in health care workers sensitized to natural rubber latex. Journal of Allergy and Clinical Immunology. 111: 610–616.

[50] M. Pedraza-Escalona, B. Becerril-Lujan, C. Agundis, L. Dominguez-Ramirez, A. Pereyra, L. Riano-Umbarila and A. Rodriguez-Romero. (2009). Analysis of B-cell epitopes from the allergen Hev b 6.02 revealed by using blocking antibodies. Mol. Immunol. 46, 668–676.

[51] O. Palomares, M. Villalba, J. Quiralte, F. Polo, R. Rodriguez. (2005). 1,3-Betaglucanases as candidates in latex-pollen-vegetable food cross-reactivity. Clinical and Experimental Allergy. 35. 345–51.

[52] C. Radauer, F. Adhami, I. Fürtler , S. Wagner, D. Allwardt, E. Scala, C. Ebner, C. Hafner, W. Hemmer, A. Mari and H. Breiteneder. (2011). Latex-allergic patients sensitized to the major allergen hevein and hevein-like domains of class I chitinases show no increased frequency of latex-associated plant food allergy. Molecular Immunology. 48(4), 600-609.

[53] R.T. Mayer, G.T. McCollum, R.P. Niedz, C.J. Hearn, R.E. McDonald, E. Berdis and H. Doostdar. (1996). Characterization of seven basic endochitinases isolated from cell cultures of *Citrus sinensis* (L.). Planta. 200: 289-295.

[54] Y. Fukuda, M. Ohme and H. Shinshi. (1991). Gene structure and expression of a tobacco endochitinase gene in suspension-cultured tobacco cells. Plant Moleculer Biology 16: 1-10.

[55] X. Ding, B. Gopalakrishnan, L.B. Johnson, F.F. White, X. Wang, T.D. Morgan, K.J. Kramer and S. Muthukrishnan (1998). Insect resistance of transgenic tobacco expressing an insect chitinase gene. Transgenic Research. 7: 77-84.

[56] A.S. Ponstein, S.A. Bres-Vloemans, M.B. Sela-Buurlage, P.J. Elzen van den, L.S. Melchers and B.J. Cornelissen. (1994). A novel pathogen- and wound-inducible tobacco (Nicotiana tabacum) protein with antifungal activity. Plant Physiology. 104: 109-118.

[57] D.H. Beezhold, V.L. Hickey, D.A. Kostyal, H. Puhl, L. Zuidmeer, R. Van-Ree and G.L. Sussman. (2003). Lipid transfer protein from Hevea brasiliensis (Hev b 12), a crossreactive latex protein. Annals of Allergy, Asthma and Immunology. 90: 439–445.

[58] L. Ylitalo, H. Alenius, K. Turjanmaa, T. Palosuo and T. Reunala. (1998). IgE antibodies to prohevein, hevein, and rubber elongation factor in children with latex allergy. Journal of Allergy and Clinical Immunology. 102: 659–64.

[59] M. Raulf-Heimsoth, S. Kespohl, J.F. Crespo, J. Rodriguez, A. Feliu, T. Bruning and H.P. Rihs. (2007). Natural rubber latex and chestnut allergy: cross-reactivity or cosensitization. Allergy. 62: 1277–281.

[60] F. Altmann. (2007). The role of protein glycosylation in allergy. International Archives of Allergy and Immunology. 142: 99–115.

[61] A. Barre, R. Culerrier, C. Granier, L. Selman, W.J. Peumans, E.J.V. Damme, F. Bienvenu, J. Bienvenu and P. Rouge, (2005). Mapping of IgE-binding epitopes on the major latex allergen Hev b 2 and the cross-reacting 1,3beta-glucanase fruit allergens as a molecular basis for the latex-fruit syndrome. Molecular Immunology. 46: 1595–604.

[62] Z. Chen, A. Posch, C. Lohaus, M. Raulf-Heimsoth, H.E. Meyer and X. Baur. (1997). Isolation and identification of hevein as a major IgE-binding polypeptide in Hevea latex. Journal of Allergy and Clinical Immunology. 99: 402–409.

[63] E. Ganglberger, C. Radauer, S. Wagner, G.O. Riordain, D.H. Beezhold, R. Brehler, B. Niggemann, O. Scheiner, E. Jensen-Jarolim and H. Breiteneder, (2001), Hev b 8, the *Hevea brasiliensis* latex profilin, is a cross-reactive allergen of latex, plant foods and pollen. International Archives of Allergy and Immunology.125: 216–27.

[64] D.H. Beezhold, V.L. Hickey, D.A. Kostyal, H. Puhl, L. Zuidmeer, R. Ree and G.L. Sussman. (2003). Lipid transfer protein from *Hevea brasiliensis* (Hev b 12), a crossreactive latex protein. Annals of Allergy, Asthma and Immunology. 90: 439–45.

[65] G.O. Riordain, C. Radauer, K. Hoffmann-Sommergruber, F. Adhami, C.K. Peterbauer, C. Blanco, J. Godnic-Cvar, O. Scheiner, C. Ebner and H. Breiteneder. (2002). Cloning and molecular characterization of the *Hevea brasiliensis* allergen Hev b 11, a class I chitinase. Clinical and Experimental Allergy. 32: 455–62.

[66] S. Sowka, S. Wagner, M. Krebitz, S. Arija-Mad-Arif, F Yusof, T. Kinaciyan, R. Brehler, O. Scheiner and H. Breiteneder. (1998). cDNA cloning of the 43-kDa latex allergen Hev b 7 with sequence similarity to patatins and its expression in the yeast

Pichia pastoris. European Journal of Biochemistry. 255: 213–219.

[67] A. Diaz-Perales, R. Sanchez-Monge, C. Blanco, M. Lombardero, T. Carillo and G. Salcedo. (2002). What is the role of the hevein-like domain of fruit class I chitinases in their allergenic capacity. Clinical and Experimental Allergy 32: 448–454.

[68] C. Blanco. (2003). Latex-fruit syndrome. Current Allergy and Asthma Reports. 3: 47-53.

[69] A. Diaz-Perales, C. Collada, C. Blanco, R. Sanchez-Monge, T. Carrillo, C. Aragoncillo, G. Salcedo. (1998). Class I chitinases with hevein-like domain but not class II enzymes are relevant chestnut and avocado allergens. Journal of Allergy and Clinical Immunology. 102: 127-33.

[70] R. Sutton, J.H. Skerritt, B.A. Baldo and C.W. Wrigley. (1984). The diversity of allergens involved in bakers' asthma. Clinical Allergy. 14: 93–107.

[71] S. Wagner and H. Breiteneder,(2002). The latex-fruit syndrome. Biochemical Society Transactions. 30: 935–940.

[72] R.D. Avino, M.L. Bernardi, M. Wallner, P. Palazzo, L. Camardella, L. Tuppo, C. Alessandri, H. Breiteneder , F. Ferreira , M.A. Ciardiello and A. Mari . (2011). Kiwifruit Act d 11 is the first member of the ripening-related protein family identified as an allergen. Allergy. 66(7) 870-877.

[73] S. Khan, S. Holding, P. Dore and C. Sewell. (2010). Pitfalls in the diagnosis of latex allergy. Allergology International. 59(3) 305-308.

[74] A.D. Amato, A. Bachi, E. Fasoli, E. Boschetti, G. Peltre, H. Sénéchal, J.P. Sutra, A. Citterio and P.G . Righetti. (2010). n-depth exploration of *Hevea brasiliensis* latex proteome and "hidden allergens" via combinatorial peptide ligand libraries. Journal of Proteomics.73(7) 1368-1380.

[75] W. Hemmer, M. Focke, G. Marzban, I. Swoboda, R. Jarisch and M. Laimer. (2010). Identification of Bet v 1-related allergens in fig and other Moraceae fruits. Clinical and Experimental Allergy. 40(4) 679-687.

[76] M. Egger, M. Hauser, A. Mari, F. Ferreira and G. Gadermaier. (2010). The role of lipid transfer proteins in allergic diseases. Current Allergy and Asthma Reports. 10(5). 326-335.

[77] A.R. Ibrahim, S. Kawamoto, M. Nishimura, S. Pak, T. Aki, A. Diaz-Perales, G. Salcedo, J.A. Asturias, T. Hayashi and K. Ono. (2010). A new lipid transfer protein homolog identified as an IgE-binding antigen from Japanese cedar pollen. Bioscience, Biotechnology and Biochemistry.74(3): 504-509.

[78] F. Altmann. (2007). The role of protein glycosylation in allergy. International Archives of Allergy and Immunology. 142: 99–115.

[79] N. Kohli and S. Habbal. (2010). Occupational allergic contact dermatitis due to thioureas. Dermatitis. 21(1) 5-6.

[80] N.A. Ismail. H.H. Anwar, S. Mehtar (1997). Latex allergy in health care workers: prevalence and knowledge at a tertiary teaching hospital in a developing country. International Journal of Infection Control. 6(1) 1-6.

[81] B.C. Carlsen, M. Meldgaard, D. Hamann, Q. Hamann, C. Hamann, J.P. Thyssen, D.M. Meyer, S.E. Gruninger and C. Hamann. (2011). Latex allergy and filaggrin null mutations. Journal of Dentistry. 39(2) 128-132.

[82] H. Allmers, J. Schmengler and C. Skudlik. (2002). Primary prevention of natural rubber latex allergy in the German health care system through education and intervention. Journal of Allergy and Clinical Immunology.110(2), 318-323.

[83] J.M. Lima, F.J. Freitas, R.N. Amorim, A.C. Câmara, J.S. Batista and B. Soto-Blanco (2011). Clinical and pathological effects of *Calotropis procera* exposure in sheep and rats.Toxicon. 57(1) 183-185.

[84] S. Liengprayoon, K. Sriroth, E. Dubreucq, L. Vaysse. (2011). Glycolipid composition of *Hevea brasiliensis*latex. Phytochemistry 72(14-15) 1902-1913.

[85] S. Swiderska-Kiełbik, A. Krakowiak, M. Wiszniewska, W. Dudek, J. Walusiak-Skorupa, P. Krawczyk-Szulc, A. Michowicz and C. Pałczyński.(2010), Health hazards associated with occupational exposure to birds. Medycyna Pracy. 61(2) 213-222.

[86] P.D. Siegel, B.F. Law, J.F. Fowler and L.M. Fowler.(2010). Disproportionated rosin dehydroabietic acid in neoprene surgical gloves. Dermatitis. 21(3) 157-159.

[87] F.J. Carballada, R. González-Quintela, L. Núñez-Orjales, M. Vizcaino and M. Boquete. (2010). Double (Honeybee and Wasp)Immunoglobulin E Reactivity in PatientsAllergic to Hymenoptera Venom: The Role of Cross-reactive Carbohydrates and Alcohol Consumption. Journal of Investigational Allergology and Clinical Immunology. 20(6) 484-489.

[88] H.Y. Yeang, R.G. Hamilton, D.I. Bernstein, S.A. Arif, K.S. Chow, Y.H. Loke, M. Raulf-Heimsoth, S. Wagner, H. Breiteneder and R.E. Biagini. (2006). Allergen concentration in natural rubber latex. Clinical and Experimental Allergy. 36: 1078–1086.

[89] L. Yip, V. Hickey, B. Wagner, G. Liss, J. Slater, H. Breiteneder, G. Sussman and D. Beezhold. (2000). Skin prick test reactivity to recombinant latex allergens. International Archives of Allergy and Immunology.121, 292–99.

[90] D.H. Beezhold, D.A. Kostyal and G.L. Sussman. (1997). IgE epitope analysis of the hevein preprotein: a major latex allergen. Clinical and Experimental Immunology. 108: 114–121.

[91] C.A. Reyes-Lopez, A. Hernandez-Santoyo, M. Pedraza-Escalona, G. Mendoza, A. Hernandez-Arana and A. Rodriguez-Romero. (2004). Insights into a conformational epitope of Hev b 6.02 (hevein). Biochem. Biophys. Res. Commun. 314: 123–130.

[92] B. Banerjee, X. Wang, K.J. Kelly, J.N. Fink, G.L. Sussman, V.P. Kurup. (1997). IgE from latex-allergic patients binds to cloned and expressed B

cell epitopes of prohevein. The Journal of Immunology 159: 5724–5732.

[93] Z. Chen, A. Posch, R. Cremer, M. Raulf-Heimsoth and X. Baur, (1998). Identification of hevein (Hev b 6.02) in Hevea latex as a major cross-reacting allergen with avocado fruit in patients with latex allergy. Journal of Allergy and Clinical Immunology.102: 476–481.

[94] D.G. Ebo, M.M. Hagendorens, K.J. De-Knop, M.M. Verweij, C.H. Bridts, L.S. De Clerck and W.J. Stevens. (2010). Component-resolved diagnosis from latex allergy by microarray. Clinical and Experimental Allergy. 40: 348–358.

[95] A. Armentia, J. Castrodeza, P. Ruiz-Muñoz, J. Martínez-Quesada, I. Postigo, M. Herrero, M. Gonzalez-Sagrado, D. Luis, B. Martín-Armentia and J.A. Guisantes. (2011), Allergic hypersensitivity to cannabis in patients with allergy and illicit drug users. Allergoligia et Immunopathologia. (Madr). 39(5) 271-279.

[96] C. Radauer, F. Adhami, I. Fürtler, S. Wagner, D. Allwardt, E. Scala, C. Ebner, C. Hafner, W. Hemmer, A. Mari and H. Breiteneder. (2011). Latex-allergic patients sensitized to the major allergen hevein and hevein-like domains of class I chitinases show no increased frequency of latex-associated plant food allergy. Molecular Immunology. 48(4) 600-609.

[97] M.L. Sanz, M.C. Garcia-Aviles, A.I. Tabar, M .Anda, B.E. Garcia, D. Barber, G. Salcedo, H.P. Rihs and M. Raulf-Heimsoth, (2006). Basophil Activation Test and specific IgE measurements using a panel of recombinant natural rubber latex allergensto determine the latex allergen sensitization profile in children. Pediatric Allergy and Immunology. 17: 148–156.

[98] V. Kampen, M. Raulf-Heimsoth, I. Sander, R. Merget and S. 1-Gruppe. (2010). Diagnostics of occupational type I allergies--comparison of skin prick test solutions from different manufacturers for selected occupational allergens. Pneumologie. 64(5) 271-277.

[99] S.N. Bains, R.G. Hamilton, S. Abouhassan, D. Lang, Y. Han and F.H. Hsieh. (2010). Identification of clinically relevant cross-sensitization between *Soliadgo virgaurea* (goldenrod) and Hevea brasiliensis (natural rubber latex). Journal of Investigational Allergology and Clinical Immunology. 20(4) 331-339.

[100] S.M. Walker, S.R. Durham, S. J. Till, G. Roberts, C.J. Corrigan, S.C. Leech, M. T. Krishna, R.K. Rajakulasingham, A. Williams, J. Chantrell, L. Dixon, A.J. Frew and SM. Nasser (2011). Immunotherapy for allergic rhinitis. Clinical and Experimental Allergy. 41(9) 1177–1200.

[101] W.G. Shreffler.(2011). Microarrayed recombinant allergens for diagnostic testing. Journal of Allergy Clinical Immunology. 127(4) 843-849.

[102] C. Sontimuang, R. Suedee, B. Canyuk, N. Phadoongsombut and F.L. Dickert. (2011). Development of a rubber elongation factor, surface-imprinted polymer-quartz crystal microbalance sensor, for quantitative determination of Hev b1 rubber latex allergens present in natural rubber latex products. Analytica Chimica Acta. 687(2) 184-192.

[103] A. Sano, A. Yagami, Y. Inaba, T. Yamakita, K. Suzuki and K. Matsunaga. (2011). Sensitization profiles of a case of pollen-food allergy syndrome. Allergology International. 60(1) 97-101.

[104] R.I. Siles, F.H. Hsieh. (2011). Allergy blood testing: A practical guide for clinicians. Cleveland Clinical Journal of Medicine. 78(9) 585-92.

[105] M. Chelminska, M. Niedoszytko and E. Jassem .(2011). Clinical value of conjunctival allergen challenge in diagnosing allergic conjunctivitis related to latex. International Archives of Allergy Immunology. 154(2) 149-54.

[106] C.L. Monitto, R.G. Hamilton, E. Levey, A.E. Jedlicka, A. Dziedzic, J.P. Gearhart, S.A. Boyadjiev and R.H. Brown.(2010), Genetic predisposition to natural rubber latex allergy differs between health care workers and high-risk patients.Anesth Analg.110(5),1310-1317.

[107] M.J. Abramson, R.M. Puy and J.M. Weiner. (2010). Injection allergen immunotherapy for asthma. Cochrane Database Systematic Reviews. 4(8) CD001186.

[108] S. Buyukozturk, A. Gelincik, F. Ozşeker, B. Colakoğlu and M. Dal. (2010). Latex sublingual immunotherapy: can its safety be predicted. Annals of Allergy, Asthma and Immunology. 104(4) 339-42.

[109] V. Pecora, A. Aruanno, A. Buonuomo, T. D. Pasquale, A. Colagiovanni , V. Sabato, A. Rizzi, L. Pascolini, A.G. Ricci, G. Patriarca, E. Nucera and D. Schiavino. (2010). Sublingual immunotherapy with natural rubber latex: a case report with 8-year follow-up. Contact Dermatitis. 63(1) 53-54.

[110] L. Terracciano, E.Calcinai, S.Avitabile, E.Galli.(2009).Age and indications to SLIT. Int J Immunopathol Pharmacol. 22(4), 5-8.

[111] B. Niggemann. (2010). IgE-mediated latex allergy--an exciting and instructive piece of allergy history. Pediatric Allergy and Immunology. 21(7) 997-1001.

[112] A. Nienhaus, K. Kromark, M. Raulf-Heimsoth, V. Kampen, R. Merget, (2008). Outcome of occupational latex allergy—work ability and quality of life. PLOS ONE. 3: e3459.

[113] R. Merget, V. Kampen, K. Sucker, E. Heinze, D. Taeger, N. Goldscheid, M.G. Haufs, M. Raulf-Heimsoth, K. Kromark, A. Nienhaus and T.Bruening. (2010).The German experience 10 years after the latex allergy epidemic: need for further preventive measures in healthcare employees with latex allergy. International Archives of Occupational and Environmental Health. 83(8) 895-903.

[114] T. Palosuo, I. Antoniadou, F. Gottrup and P. Phillips. (2011). Latex Medical Gloves: Time for a Reappraisal. International Archives of Allergy Immunology. 156(3) 234-246.

[115] M.J. Bendewald, S.A. Farmer and M.D. Davis. (2010). Patch testing with natural rubber latex: the Mayo Clinic experience. Dermatitis. 21(6) 311-316.

[116] K. Blumchen, P. Bayer, D. Buck, T. Michael, R. Cremer, C. Fricke, T. Henne, H. Peters, U. Hofmann, T. Keil, M. Schlaud, U. Wahn and B. Niggemann. (2010). Effects of latex avoidance on latex sensitization, atopy and allergic diseases in patients with spina bifida. Allergy. 65(12) 1585-1593.