ORIGINAL ARTICLE

Identification of Clinically Relevant Cross-Sensitization Between *Soliadgo virgaurea* (Goldenrod) and *Hevea brasiliensis* (Natural Rubber Latex).

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Abstract

Background: Solidago virgaurea (goldenrod) is a perennial weed from which no allergens have been identified. A high latex content in its leaves has been reported. Although not an airborne allergen, it may be an important occupational sensitizer.
Objective: To identify allergenic proteins in goldenrod and to determine whether they cross-react with *Hevea brasiliensis* latex.
Methods: Potential cross-reactive allergens in latex and goldenrod were investigated by immunoblot inhibition and ImmunoCAP inhibition analyses using serum from patients with clinically evident goldenrod and/or latex allergy. Cross reactivity between latex allergens and goldenrod proteins was studied using recombinant Hev b 1, 3, 4, 5, 6.01, 6.02, 8, 9, or 11 in ImmunoCAP inhibition analyses.
Results: Immunoglobulin (Ig) E antibodies from individuals with goldenrod allergy bound extracted goldenrod proteins ranging from 20 kDa to 130 kDa in Western blots. Evidence for latex and goldenrod cross reactivity was identified by ImmunoCAP and immunoblot inhibition experiments using serum from patients with strongly positive concomitant latex and goldenrod-specific IgE antibody responses. Observed latex-goldenrod cross reactivity could not be ascribed to any of the recombinant major latex allergens evaluated.
Conclusions: H brasiliensis latex and goldenrod contain cross-reactive and unique allergenic proteins. Exposure to goldenrod may sensitize patients to latex and vice versa.

Key words: Cross-reactivity. *Hevea brasiliensis* natural rubber latex. IgE. Occupational allergy. *Solidago virgaurea* (goldenrod).

Resumen

Antecedentes: Solidago virgaurea (vara de oro) es una herbácea perenne de la que todavía no se ha identificado ningún alérgeno. Se ha notificado un alto contenido de látex en sus hojas. Aunque no se trata de un alérgeno transportado por el aire, puede ser un importante sensibilizador en el lugar de trabajo.
Objetivo: Identificar las proteínas alergénicas de la vara de oro y determinar si presentan reactividad cruzada con el látex de *Hevea brasiliensis*.
Métodos: Se investigaron los posibles alérgenos de reactividad cruzada del látex y la vara de oro mediante análisis de inhibición de inmunotransferencia e inhibición ImmunoCAP con suero de pacientes con alergia clínicamente manifiesta a la vara de oro y/o al látex. La reactividad cruzada entre los alérgenos del látex y las proteínas de la vara de oro se estudió mediante Hev b 1, 3, 4, 5, 6.01, 6.02, 8, 9 u 11 recombinante en análisis de inhibición ImmunoCAP.
Resultados: Los anticuerpos anti-inmunoglobulina (Ig) E de pacientes con rinitis alérgica inducida por vara de oro se unieron a proteínas de vara de oro extraídas con un peso molecular de entre 20 kDa y 130 kDa en transferencias Western. Las evidencias de la reactividad cruzada del látex y la vara de oro se identificaron mediante análisis de inhibición ImmunoCAP e inhibición de inmunotransferencia con suero de pacientes con respuestas concomitantes altamente positivas de anticuerpos IgE específicos frente a la vara de oro y el látex. La reactividad cruzada observada del látex y la vara de oro no se pudo atribuir a ninguno de los principales alérgenos recombinantes del látex evaluados.
Conclusiones: El látex de *H. brasiliensis* y la vara de oro contienen proteínas alergénicas únicas y con reactividad cruzada. La exposición a la vara de oro puede sensibilizar a los pacientes al látex y viceversa.

Palabras clave: Reactividad cruzada. Látex de caucho natural de *Hevea brasiliensis.* IgE. Alergia en el trabajo. *Solidago virgaurea* (vara de oro).

Introduction

Goldenrod (*Solidago virgaurea*) is a perennial weed of the *Asteraceae* family with bright yellow flowers that bloom in late summer. It is commonly encountered by gardeners and florists, who use it in floral arrangements. Goldenrod is mainly insect-pollinated, although anemophily may also occur [1]. Although goldenrod is not considered an important source of airborne allergens, exposure can trigger symptoms of allergic rhinoconjunctivitis, asthma, and contact urticaria. It is thus an occupational sensitizer [2,3]. Allergic contact dermatitis after systemic exposure to goldenrod has also been reported [4]. No allergenic components have yet been identified in extracts of *S virgaurea*.

Several species of goldenrod, such as *Solidago gigantea*, may contain significant concentrations of latex [5]. Goldenrod has been investigated as a source of natural rubber latex, although yields are low and the derived rubber of inferior quality [6]. Goldenrod is known to have varying degrees of cross-reactivity with other members of the Asteraceae family including *Ambrosia* (ragweed), *Chrysanthemum, Matricaria chamomilla* (chamomile), *Artemisia vulgaris* (mugwort), and *Helianthus annuus* (sunflower) [7-9].

Immunoglobulin (Ig) E–mediated reactions to natural rubber latex produced from *Hevea brasiliensis* have been frequently observed in professions involving health care and gardening, where occupational exposure to latex products occurs [10-12]. The prevalence of latex sensitization is estimated to be approximately 1% in the general population and between 1% and 9% in atopic individuals [13]. Latex allergens include both water-soluble proteins (eg, Hev b 5 and 6.02) and glycoproteins that are associated with the *H brasiliensis* rubber particle (Hev b 1 and 3) [14,15]. Latex allergen exposure can trigger a spectrum of allergic reactions including asthma and anaphylaxis [16]. There has been a downward trend in the prevalence of latex-induced occupational asthma since the mid-1990s, and this is temporally associated with decreasing use of powdered natural rubber latex gloves [17]. Nevertheless, workers who use allergenic gloves continue to be at risk for sensitization and latex-induced allergic reactions.

Although investigators have studied cross-reactivity between latex and various fruits (eg, banana, kiwi), limited information is available concerning cross-reactivity between latex and pollens [18]. Latex allergens may cross-react with grass, mugwort, and ragweed [19]. However, the extent and immunochemical basis of cross-reactivity, if any, between goldenrod and natural rubber latex is unknown.

In the current study we evaluated florists and healthcare workers with immediate hypersensitivity reactions to both latex and goldenrod with the objective of exploring possible cross-reactivity between *Hevea* latex and goldenrod antigens. We identified a number of latex-allergic individuals with evidence of goldenrod sensitization and present evidence that latex and goldenrod share both cross-reactive and non–cross-reactive allergenic proteins. Our data suggest that none of the known relevant latex allergens (Hev b 1, 3, 4, 5, 6.01, 6.02, 8, 9, or 11) cross-react with goldenrod allergens.

Methods

Patient Selection

Forty-one individuals were selected for the study (Table 1). The cases consisted of 3 patients with a history of goldenrod allergy (P1, P2, P3 [study group 1]); 2 of these patients also had latex allergy (P1, P3). Several control groups were also enrolled, including 2 participants with no latex or goldenrod allergy (P4, P5 [study group 2]), sera from 4 patients with primary latex allergy (L2, L6, L8, L10 [study group 3]), sera

Table 1. Study Groups and Characteristics

	Cases	Controls			
Study Group	1	2	3	4	5
Designation	P1, P2, P3	P4, P5	L2, L6, L8, L10	A1-12	HCW 1-20
No. of patients	3	2	4	12	20
Selection criteria	Cases with GR allergy	Absence of sensitization to GR and latex	Latex-sensitized subjects	Non–latex-sensitized subjects	Latex-sensitized subjects
Clinical history available	Yes	Yes	No	No	Yes
GR allergy	All	None	Unknown	Unknown	Unknown
Latex allergy	P1, P3	None	Unknown	Unknown	All
GR sensitized	All	None	L6, L10	Unknown	HCW 6, 15, 19
Latex sensitized	P1, P3	None	All	None	All

Abbreviation: GR, goldenrod; HCW, health care worker.

from 12 non–latex-allergic participants (A1-12 [study group 5]), and 20 latex-allergic patients (health care workers 1-20 [study group 5]). Serum was collected from these patients after obtaining informed consent and institutional review board approval.

Extracts

Goldenrod pollen extract 1:20 w/v (Greer Laboratories, Lenoir, North Carolina, USA) was used for diagnostic testing and in vitro experiments. Investigational high and low ammoniated *H brasiliensis* latex (Greer Laboratories) was used for diagnostic skin testing as previously described [20,21]. Prick/puncture testing through a piece of sterile powdered latex glove was also performed [22]. Lyophilized *Hevea* latex extract consisting of the dialyzed C-serum fraction of nonammoniated latex sap was donated by Greer Laboratories and used for in vitro research purposes only. Total protein content was assessed using the Bradford assay (BioRad, Hercules, California, USA).

Diagnostic Skin Tests

Percutaneous skin testing was performed using a bifurcated needle (Precision Medical Products, Denver, Pennsylvania, USA) with a positive histamine control (10 mg/mL) and negative saline control applied in parallel [23]. The immediate reaction (wheal and flare diameter) was read at 15 minutes, and a 3-mm wheal with the presence of a flare was considered positive.

Western Blot Analysis

Goldenrod extract was separated using sodium dodecyl sulfate–polyacrylamide gel electrophoresis (SDS-PAGE) under reducing conditions with 50 µg of protein per lane. The separated proteins were transferred to an Immobilon-P membrane (Millipore, Billerica, Massachusetts, USA) and incubated overnight in 2 mL of 1:1 to 1:40 diluted patient serum at 4˚C. After washing, the blots were probed with goat antihuman IgE-horseradish peroxidase (HRP) (Sigma, St. Louis, Missouri, USA) at a 1:4000 dilution. IgE was detected by chemiluminescence (Amersham, Little Chalfont, UK). Serum from patients with no evidence of latex and/or goldenrod allergy was used as a negative control. The HRP-conjugated goat antihuman IgE did not recognize any proteins in the absence of patient serum (data not shown).

Immunoblot and ImmunoCAP Inhibition Studies

Two milliliters of 1:1 to 1:40 diluted patient or control serum was preincubated with up to 200 µg of *H brasiliensis* latex protein (Greer Laboratories) overnight at 4˚C. These sera were then blotted against goldenrod protein separated by SDS-PAGE. The IgE bound to the blot strips was detected as described above. IgE binding to goldenrod was not inhibited by preincubation with an unrelated allergen (dog extract 1:20 w/v, Greer Laboratories).

IgE competitive inhibition analyses were performed as follows. Sera from latex-allergic participants were preincubated with goldenrod extract 1:20 w/v (Greer Laboratories) or Phadia negative diluent (negative control). Each was then separately analyzed in the ImmunoCAP 250 autoanalyzer (Phadia, Portage, Michigan, USA) for IgE antibodies specific for goldenrod (W12) and Hev b 5–enriched *H brasiliensis* latex (RK82). Sera from 3 participants with evidence of goldenrod and latex cross reactivity were also analyzed in the ImmunoCAP 250 autoanalyzer (Phadia) for IgE antibodies specific for Hev b 1 (RK215), Hev b 3 (RK217), Hev b 5 (RK218), Hev b 6.01 (RK 219), Hev b 6.02 (RK220), Hev b 8 (RK 221), Hev b 9 (RK 222), and Hev b 11 (RK224). The codes indicate the specificity of the ImmunoCAP allergosorbent used in the analysis. The minimum detectable concentration of the ImmunoCAP 250 was 0.1 kU_A/L. Reported IgE antibody levels (kU_A/L) were corrected for dilution and the percentage inhibition was computed as [(uninhibited – inhibited)/ uninhibited] × 100.

Results

Study Population

Study groups 1 and 2: Patient 1 (P1) (Table I) was a 53-year-old atopic florist who experienced rhinorrhea, sneezing, ocular irritation, and contact urticaria with dyspnea, wheezing and chest tightness within 30 minutes of handling a large shipment of goldenrod. She also reported a pruritic rash after wearing powdered latex gloves on several occasions. Specific IgE to both goldenrod and natural rubber latex was confirmed by skin testing and serologic analysis. Patient 2 (P2) was a 50-year-old atopic, asthmatic florist who developed rhinorrhea, wheezing, dyspnea, cough, and contact urticaria triggered by exposure to goldenrod at work. She also reported a rash after wearing powdered latex gloves. Skin and serologic testing revealed presence of IgE to goldenrod only. Patient 3 (P3) was a 51-year-old health care worker with chronic urticaria reportedly exacerbated by sleeping on a latex mattress. She also described exacerbations of urticaria when gardening. ImmunoCAP was strongly positive to both latex and goldenrod. Skin testing was not performed, because the patient could not suspend antihistamine treatment due to chronic urticaria. Two patients (P4 and P5) with no adverse reactions to latex or goldenrod were recruited as negative controls. Absence of allergy was confirmed by skin and serologic testing.

Study groups 3 and 4: Serum was collected from 4 patients (L2, L6, L8, and L10) who had a positive ImmunoCAP to latex as defined by IgE antibody >0.35 kU_A/L (Tables 1 and 2). No additional demographic or clinical information could be collected for these patients. ImmunoCAP to goldenrod could not be performed on L2 due to insufficient quantity of serum sample. L6 and L10 had a positive ImmunoCAP result to goldenrod (>0.35 kU_A/L) whereas L8 did not. Serum was also collected from 12 participants with negative ImmunoCAP results to latex (A1-12).

Study group 5: Sera were collected from 20 health care workers (HCW 1-20) employed at Johns Hopkins University School of Medicine. They all had a positive history of latex allergy involving rhinitis and conjunctivitis following exposure to powdered *Hevea* latex gloves, which was supported by

Table 2. Serologic Characterization and ImmunoCAP Inhibition Studies Demonstrating Cross-reactivity Between Goldenrod and Latex

Participant	GR ImmunoCAP kU_A/L	Heve Latex kU_A/L	Total Serum ng/mL	*Hevea* Latex InmunoCAP After Princubation With Goldenrod Extract kU_A/L	Inhibition, %
P3	81.90	84.90	188	9.24	89.1[a]
L6	16.00	12.06	403	0.28	97.7[a]
HCW15	11.50	12.40	2017	2.62	78.9[a]
P2	7.27	0.17	175	ND	ND[b]
HCW6	2.56	32.20	792	27.00	16.1[c]
HCW19	2.04	35.40	3316	30.80	13.0[c]
P1	1.72	0.25	291	ND	ND[b]
L10	0.63	3.06	324	2.70	11.8[c]
HCW12	0.21	39.40	1387	30.80	21.8[c]
HCW3	0.19	32.60	183	25.20	22.7[c]
HCW11	0.17	25.40	2295	23.40	7.9[c]
HCW5	0.11	2.16	147	1.98	8.3[c]
HCW1	<0.1	12.12	96	10.40	14.2[c]
HCW2	<0.1	22.20	344	20.20	9.0[c]
HCW4	<0.1	11.62	205	10.38	10.7[c]
HCW7	<0.1	13.30	209	11.16	16.1[c]
HCW8	<0.1	7.58	211	6.20	18.2[c]
HCW9	<0.1	10.00	83	9.88	1.2[c]
HCW10	<0.1	11.76	354	9.90	15.8[c]
HCW13	<0.1	22.40	239	20.20	9.8[c]
HCW14	<0.1	4.06	168	3.42	15.8[c]
HCW16	<0.1	11.38	328	10.60	6.9[c]
HCW17	<0.1	10.80	224	7.90	26.9[c]
HCW18	<0.1	5.42	80	4.68	13.7[c]
HCW20	<0.1	31.40	276	29.90	4.8[c]
P4	<0.1	<0.1	ND	ND	ND[b]
P5	<0.1	<0.1	ND	ND	ND[b]
L2	ND	0.71	ND	ND	ND[b]
L8	<0.1	1.6	ND	ND	ND[b]

Abbreviations: GR, goldenrod; ND, not done.
[a] Represents significant inhibition of latex-specific IgE binding to Hev b 5–enriched *Hevea* latex allergosorbent by preincubation of sera with goldenrod.
[b] ImmunoCAP inhibition studies could not be performed since the concentration of anti-*Hevea* latex IgE in these sera was too low.
[c] Represents background (nonspecific) inhibition of latex-specific IgE binding to Hev b 5–enriched *Hevea* latex allergosorbent by preincubation of sera with goldenrod.

a positive latex-specific IgE result. Three of these patients (HCW 6, 15, and 19) had serologic evidence of sensitization to goldenrod (Tables 1 and 2).

IgE Reactivity Profile to Goldenrod

IgE immunoblotting was performed on the 3 patients (P1-P3) with primary goldenrod allergy. Patient serum IgE recognized several goldenrod proteins (Figure 1) ranging from 20 kDa to 130 kDa. P1 serum IgE recognized a 42-50–kDa and a 70-kDa protein. P2 and P3 serum IgE recognized several proteins ranging from 20 kDa to 130 kDa. However, serum IgE from negative controls P4 and P5 recognized several proteins ranging from 25 kDa to 100 kDa. Thus, some proteins within this range bound patient serum IgE in both sensitized and nonsensitized participants, and this likely represents nonspecific binding, whereas proteins of 20, 42-50, 110, and 130 kDa in size may represent clinically relevant goldenrod allergens associated with IgE-mediated symptoms. A 42-50–kDa protein was identified in all sensitized individuals, suggesting it may be a principal allergen in goldenrod. IgE binding was not affected by treatment of goldenrod protein after SDS-PAGE with 10 mM sodium m-periodate; therefore, the IgE was not recognizing a carbohydrate antigen (data not shown).

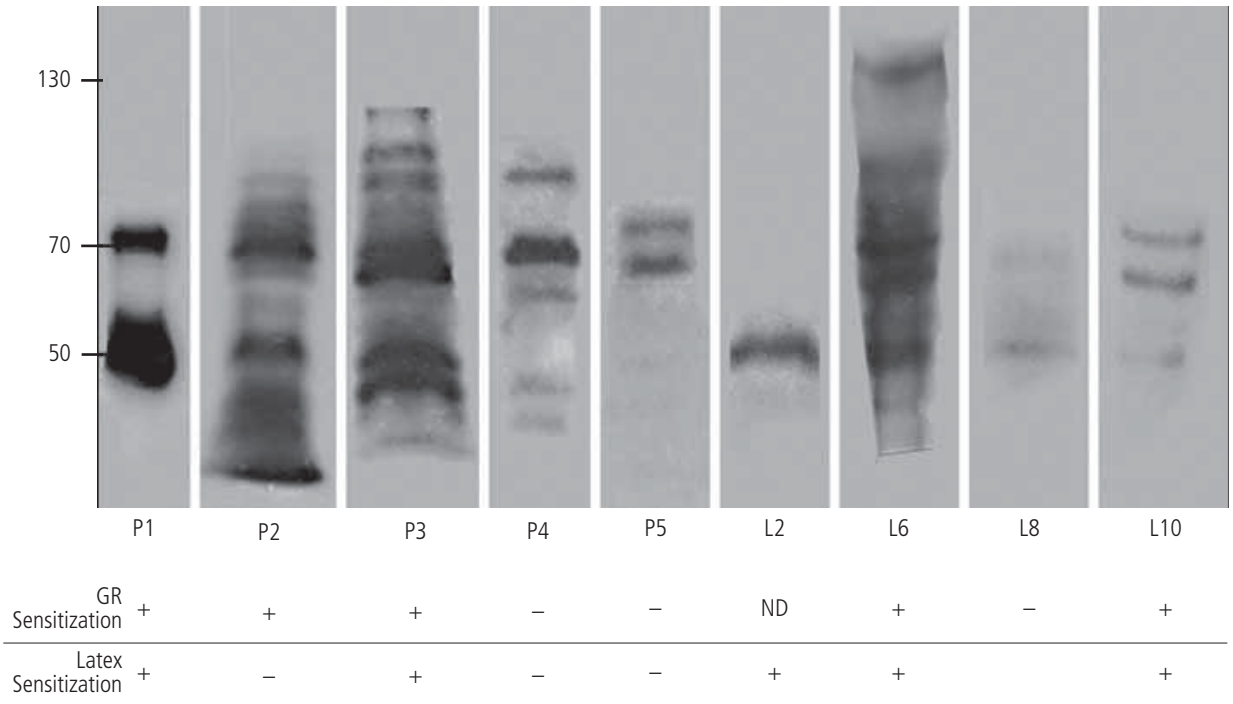

Figure 1. IgE-Immunoblot analysis of goldenrod extract. Goldenrod (GR) proteins were separated by 10% SDS-PAGE and blotted with serum from patients with goldenrod and/or latex allergy. Ig indicates immunoglobulin; SDS-PAGE, sodium dodecyl sulfate–polyacrylamide gel electrophoresis.

The IgE binding profiles of participants with primary latex sensitization (L2, L6, L8, and L10) are presented in Figure 1. L6 serum IgE bound several proteins in goldenrod ranging from 30 kDa to 130 kDa. L2 serum IgE recognized a 40-50–kDa goldenrod protein. L8 serum IgE recognized a 50-kDa and 80-kDa protein. L10 serum IgE recognized 3 proteins (50, 70, and 95 kDa). Thus, serum IgE from latex-sensitized individuals (participants L2, L6, L8, and L10) recognized goldenrod proteins, such as the 50-kDa protein also identified by serum IgE in goldenrod-sensitized subjects P1-P3. In HCW 1-20 with primary latex allergy, sera from 3 participants (HCW 6, 15, and 19) contained IgE antibodies that reacted with goldenrod proteins by ImmunoCAP (Table 2).

Patients with negative IgE anti-*Hevea* latex (A1-12) were used as negative controls, although their goldenrod allergy status was unknown. Of the 12 participants tested, serum IgE from 6 (A1, A5, A6, A7, A8, and A11) did not recognize any goldenrod proteins. Serum IgE from 6 other negative controls (A2, A3, A4, A9, A10, and A12) bound various goldenrod proteins in the Western blot nonspecifically from 20 kDa to 100 kDa (data not shown).

Cross-reactive Latex and Goldenrod Allergens

ImmunoCAP inhibition using serum from 3 patients sensitized to both latex and goldenrod (P3, L6, and HCW 15) displayed 79%-98% (essentially complete) inhibition of their latex specific IgE binding to the Hev b 5–enriched *Hevea* latex allergosorbent (rk82) following preincubation of their sera with goldenrod extract (Tables 2 and 3). Immunoblot inhibition experiments demonstrated that IgE binding to proteins in goldenrod extract was also completely inhibited by preincubation with latex in the case of patient P3, and strongly inhibited in the case of L6 (Figure 2). Immunoblot inhibition experiments were not performed with the serum of participant HCW 15. These results indicate that cross-reactive allergens in *Hevea* latex inhibit IgE binding to goldenrod proteins.

ImmunoCAP inhibition analyses based on serum from 7 participants with primary latex allergy (HCW 5, 11, 3, 12, 19, 6, and L10) demonstrated <25% inhibition of latex-specific IgE binding to the Hev b 5–enriched *Hevea* latex allergosorbent (rk82) following preincubation with goldenrod extract (Table 2). Sera from 13 participants with primary *Hevea* allergy (HCW 1, 2, 4, 7, 8, 9, 10, 13, 14, 16, 17, 18, and 20) had no detectable antigoldenrod IgE. In these sera, the extent of inhibition of IgE anti-*Hevea* binding to *Hevea* allergosorbent following preincubation with goldenrod extract was variable and generally low (27% or less) (Table 2).

We next investigated if any of the commercially available recombinant latex allergens were cross-reactive with goldenrod. ImmunoCAP inhibition experiments revealed that for participants HCW 6 and 19, goldenrod was not cross-reactive with the known major *Hevea* allergens (Hev b 1, 3, 4, 5, 6.01, 6.02, 9, and 11), which were available in recombinant form for testing (Table 4). Serum from patient P3 contained antilatex IgE that inhibited >90% following preincubation with goldenrod. However, because the initial titer for IgE specific for recombinant Hev b proteins was low (1.33-2.51 kU_A/L), no definitive conclusion can be drawn about cross-reactivity

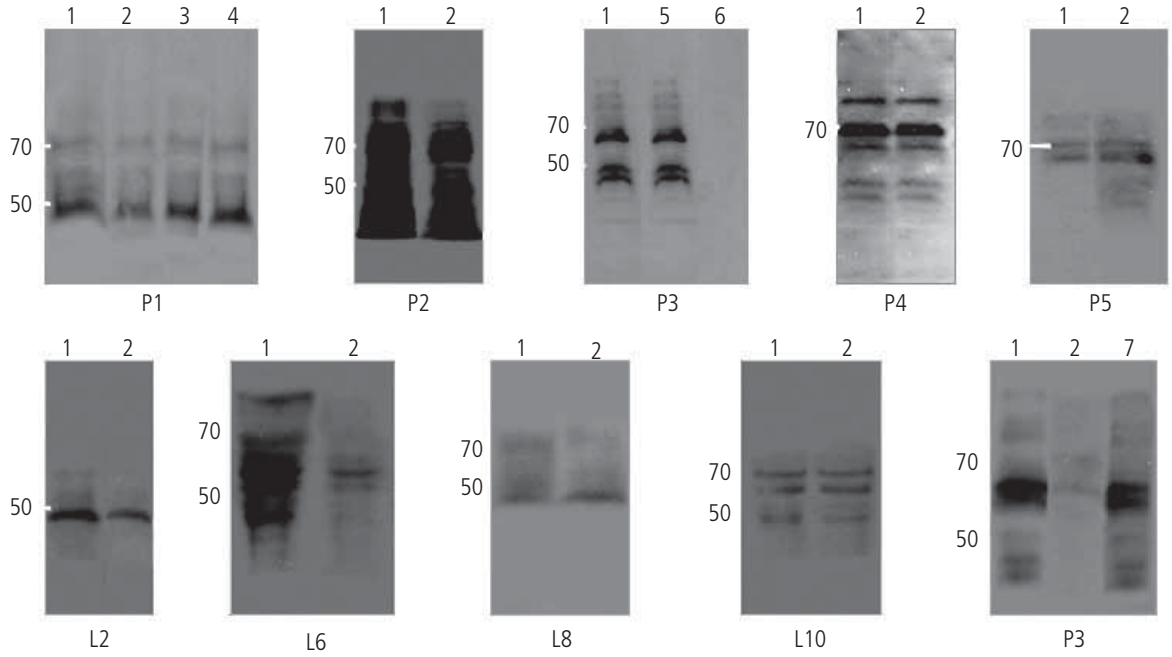

Figure 2. Immunoblot-inhibition determination of cross-reactivity between goldenrod and latex allergens. Goldenrod extracts were blotted against patient sera containing no latex (lane 1) and sera preincubated with increasing amounts of latex protein as follows: lane 2, 50 μg latex; lane 3, 100 μg latex; lane 4, 200 μg latex. IgE binding to goldenrod was completely inhibited by preincubation in the case of P3 (lane 2, lower panel) and L6 (lane 2, lower panel). Nonspecific inhibition of binding was ruled out by preincubation with 50 μg dog extract, lane 7 (lower panel). To demonstrate that inhibition of IgE binding occurred in a dose-dependent manner, P3 serum was preincubated in 0.05 μg latex (lane 5) and 2.5 μg latex (lane 6). There was no inhibition of IgE binding to goldenrod after preincubation with up to 200 μg latex (lane 4) in the case of P1, P2, P4, P5, L2, L8, and L10. Thus, latex and goldenrod contain both cross-reactive and unique allergens.

Table 3. Comparison of IgE-Immunoblot Inhibition and ImmunoCAP Inhibition Results

Patients	IgE Antigoldenrod		IgE Antilatex	Cross-reactivity	
	ImmunoCAP (kU_A/L)	Immunoblot	ImmunoCAP (kU_A/L)	Immunoblot Inhibition	ImmunoCAP Inhibition
P1	1.72	42, 70 kDa	0.25	None	ND[a]
P2	7.27	>8 proteins 20-80 kDa	0.17	None	ND[a]
P3	81.9	>8 proteins 20-80 kDa	84.9	Complete	89%
L2	ND	50 kDa	0.71	None	ND
L6	16	6-7 proteins 30-130 kDa	12.06	Strong	98%
L8	<0.1	50 and 80 kDa	1.6	None	ND
L10	0.63	55, 70, 95 kDa	3.06	None	12%
HCW15	11.5	ND	12.4	ND	78.9%

Abbreviation: ND, not done
[a]Not done because ImmunoCAP titer was <0.35 kU_A/L

to goldenrod with the individual Hev b allergens. Based on our results, it appears that the cross-reactive antigen in goldenrod is not well-represented in *Hevea* latex–sensitized individuals and is thus likely not a major allergen in *Hevea*-containing products.

Non–cross-reactive Latex and Goldenrod Allergens

Seven participants (P1, P2, P4, P5, L2, L8 and L10) had no IgE antibodies that recognized both latex and goldenrod allergen (Figure 2), as demonstrated by immunoblot-inhibition

in all cases, and by ImmunoCAP inhibition for L10 (Figure 2, Tables 2 and 3). ImmunoCAP-inhibition studies could not be performed using sera from participants P1, P2, P4, or P5, since their concentration of anti-*Hevea* latex IgE was too low.

Discussion

We studied the IgE reactivity profile of 3 participants (P1-P3) with documented goldenrod allergy. Serum IgE recognized up to 8 proteins—ranging from 20 kDa to 130 kDa—in the goldenrod extract by Western blot (Figure 1). Considerable variability in the proteins recognized by serum IgE from goldenrod-sensitive individuals is consistent with previous reports investigating IgE binding profiles in patients with pollen allergy. Loria et al [24] demonstrated that IgE from oak-sensitive sera identified 23 proteins ranging from 13.2 kDa to 106 kDa. Likewise, sera from 26 patients with ragweed allergy demonstrated IgE reactivity against various ragweed proteins [25]. IgE from control patients (P4 and P5) with no evidence of goldenrod sensitivity recognized a select number of goldenrod proteins (Figure 1), either due to nonspecific binding or possibly sensitization to other weeds such as ragweed and mugwort, which may share allergenic epitopes with goldenrod [8,9].

Evidence for latex and goldenrod cross-reactive allergens was demonstrated by immunoblot and ImmunoCAP inhibition experiments (Figure 2, Tables 2 and 3) in patients with strongly positive ImmunoCAP to both latex and goldenrod. For L6 and P3, essentially complete inhibition of IgE immunoblot binding to goldenrod was achieved by preincubation with latex (Figure 2). Furthermore, ImmunoCAP inhibition experiments confirmed almost complete inhibition of IgE binding to *Hevea* latex by preincubation with goldenrod in the case of L6, P3, and HCW 15 (Tables 2 and 3). We have therefore demonstrated for the first time that goldenrod pollen and latex may contain cross-reactive allergens.

None of the commercially available latex allergens (Hev b 1, 3, 4, 5, 6.01, 6.02, 9, or 11), including profilin (Hev b 8), were cross reactive with goldenrod as assayed by a latex-goldenrod ImmunoCAP inhibition analysis (Table 4). Reindle et al [26] demonstrated cross-reactivity between birch pollen profilin Bet v 2 and latex profilin Hev b 8, suggesting that profilin may be an important mediator of latex-pollen cross-reactivity. However, when Radauer et al [27] investigated cross-reactivity between timothy, mugwort, birch, and latex profilins by IgE inhibition experiments, up to 60% of IgE binding reacted with species-specific epitopes. This indicates that profilins derived from latex and from other pollens may have both shared and unique epitopes, and provides a plausible explanation for the absence of cross-reactivity between latex profilin and goldenrod. Other recombinant latex proteins including Hev b 7, 10, and 12 were not available for study. Further studies will be required to address this question.

We also observed that some participants were allergic exclusively to either latex or goldenrod. This is consistent with previous observations demonstrating that not all patients with latex sensitization develop birch pollen allergy, possibly only those with IgE to anti–Hev b 8, which cross-reacts with birch Bet v 2 [27]. Participant L8 had a positive result for IgE antilatex serology and a negative IgE antigoldenrod serology. Participant P2 had the reverse pattern. Participant P1 had

Table 4. Absence of Cross-reactivity Between Goldenrod and Known Major Latex Allergens

	P3			HCW 6			HCW 19		
	CAP kIU/L	CAP after pre-incubation with GR kU_A/L	% Inhibition	CAP kIU/L	CAP after pre-incubation with GR kU_A/L	% Inhibition	CAP kIU/L	CAP after pre-incubation with GR kU_A/L	% Inhibition
Goldenrod	71.93	7.14	90.1%	4.53	0.27	94.1%	2.85	0.85	70.1%
H brasiliensis Latex	74.21	5.02	93.2%	36	38.67	-7.4%	42.67	45.33	-6.3%
Hev b 1	1.33	0.1	92.5%	<0.1	<0.1	ND	12.47	11.95	4.2%
Hev b 3	2.51	0.1	96%	<0.1	<0.1	ND	12.29	12.4	-0.9%
Hev b 5	1.46	0.1	93.1%	22	22.8	-3.6%	12.8	12.56	1.9%
Hev b 6.01	2.28	0.1	95.6%	8.09	9.03	-11.5%	14.4	14.4	0.0%
Hev b 6.02	1.67	0.1	94%	6.23	5.76	7.5%	13.73	12.99	5.4%
Hev b 8	2.37	0.1	95.8%	<0.1	<0.1	ND	<0.1	<0.1	ND
Hev b 9	2.04	0.1	95.1%	<0.1	<0.1	ND	0.27	0.24	10%
Hev b 11	1.77	0.1	94.4%	0.2	<0.1	ND	0.68	0.52	23.5%

a positive ImmunoCAP result to goldenrod and a weakly positive ImmunoCAP result to latex, whereas participant L10 demonstrated the reverse pattern. Immunoblot and ImmunoCAP inhibition experiments demonstrated that these participants' sera did not contain cross-reactive latex or goldenrod allergens (Figure 2, Tables 2 and 3).

Our data suggest that latex sensitization may also sensitize to goldenrod, as 5 of 24 (21%) patients with primary latex sensitivity had serologic evidence for goldenrod-specific IgE (participants HCW 6, HCW 15, HCW 19, L6, and L10) -(Tables 2 and 3). However, both latex and goldenrod may cross-react with ragweed and mugwort [8,9,19]. Thus, sensitization to ragweed or mugwort in the latex-allergic population may account for sensitization to goldenrod. However, no clinical data were available for review regarding ragweed and mugwort sensitization in these individuals, and further studies with larger numbers of patients will be required to test this hypothesis.

In conclusion, our findings indicate that goldenrod and latex contain both non–cross-reactive and cross-reactive allergens that may be of clinical significance. Exposure to goldenrod may sensitize patients to latex and vice versa. Future studies with a larger sample size are needed to more fully define the clinical significance for patients with natural rubber latex allergy who are exposed to goldenrod. It may be prudent for individuals with occupational exposure to goldenrod to limit their exposure to natural rubber latex products.

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