

The allergen of *Ficus benjamina* in house dust

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Summary

Ficus benjamina, a member of the *Moraceae* family, is a tropical, non-flowering green plant which is widely used for ornamental purposes. It is an occupational allergen in plant keepers but sensitization is also increasingly found in non-occupationally exposed atopic and non-atopic patients. The allergen of *Ficus benjamina* is located in the plant sap, a so-called latex. By radioallergosorbent test-(RAST)-inhibition studies allergen could also be demonstrated in the dust collected from the leaf surface and in dust samples from the floor of rooms where the plant was placed. These findings could result in more extensive preventive measures in patients sensitized to *Ficus benjamina*. In addition there is some evidence that possibly a crossreactivity between latex of *Ficus benjamina* and latex from the rubber tree *Hevea brasiliensis*, a member of the *Euphorbiaceae* family, may exist.

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Introduction

Ficus benjamina (Fb) is a popular, non-flowering green plant that belongs to the *Moracea* family. For ornamental purposes it has become very popular and it is widely present in private and public buildings including offices and hospitals. It has been first identified in 1985 as occupational allergen in two plant keepers [1]. In a larger study involving 78 plant keepers and gardeners, 23% were found to be sensitized [2]. Later on in routinely tested atopic patients referred for allergological investigation and in atopic patients with exposure to Fb at home or at the workplace, sensitization in 4–6% [3] and 7.5% respectively [4] was found. In approximately half of these atopic patients the sensitization was considered to be clinically relevant [3,5]. Symptoms included rhinoconjunctivitis, asthma, eye lid oedema, and contact urticaria [2,5].

The allergens of Fb are located in the milky plant sap, a so-called latex (Fb-latex), contained in the leaves and in the twigs. When cutting or cleaning the plant one may become directly exposed to the Fb-latex, as it is typical in

occupational exposure. On the other hand, it has been postulated that particularly in dry, heated environments, water-soluble antigens may accumulate by diffusion on the leaf surface and bind to dust particles [3]. Close contact with the plant and airborne dust particles may then induce sensitization and elicit allergic symptoms.

The aim of the present study was to investigate if allergen of Fb is present in dust from the surface of Fb leaves and also in house dust from rooms where Fb plants are placed. Furthermore, a possible crossreactivity between the Fb-latex and latex (Hb-latex) from the rubber tree *Hevea brasiliensis* was examined.

Materials and methods

Patients

Patients who were investigated for the presence of atopy because of respiratory symptoms, were routinely tested with a series of common respiratory allergens, a leaf and wood extract from Fb, and Hb-latex.

Skin tests

Skin-prick tests were performed with standard respiratory allergens (Allergopharma, Reinbeck, Germany) and

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Fb-prick test solutions (5000 PNU/ml) which were prepared from Fb wood and Fb leaves (special preparation, Allergopharma, Germany). Skin-prick tests with Hb-latex were performed with a commercially available test solution (1/100 w/v, Stallergènes Laboratoires, France). A skin-prick reaction equivalent to or greater than the histamine reaction (1 mg/ml) was considered as positive.

Specific IgE

Sera from patients with a positive skin-prick test to Fb were taken. Specific IgE were measured by the CAP method (Pharmacia, Sweden) and by a RAST technique (Allergopharma, Germany) according to the guidelines of the manufacturers. For CAP measurements the CAP allergen k81 (mix of Fb and *Ficus elastica decorativa*) was used, for the RAST determinations allergen disks (k81, Allergopharma) were prepared from Fb wood extract. Specific IgE in 15 sera were measured by both techniques. As negative control for the RAST a pooled serum from non-allergic individuals ($n = 6$) was used.

In nine sera (eight positive, one negative to Fb) specific IgE to Hb-latex were determined. Hb-latex allergen disks made from natural Hb-latex called Neotex FA Film (k82, Allergopharma) were used [6].

RAST inhibition

Dust samples were collected from leaves of Fb and from the carpeted floor where the plant was standing. Dust from leaves was obtained by gently cleaning the leaf surface with a brush. For the floor samples a dust collecting device with a dust filter (ALK, Denmark) was used. Patients were instructed to collect dust according to the guidelines of the manufacturer (ALK, Denmark). Dry secretion droplets which are sometimes excreted at Fb leaf stems were collected with tweezers from two plants.

Extracts were prepared by stirring the materials in Coca's solution (5 g NaCl/l and 2.5 g NaHCO₃) at 6°C over night. The extracts were then centrifuged and, if necessary, filtered (filter 0.45 µm). The non-dialysed extracts were measured by RAST-inhibition [7,8]. For RAST-inhibition a pooled serum of two high titrated Fb-allergic patient sera (1:3 diluted) and Fb allergen disks were used. As positive controls Fb-prick test solutions (5000 PNU/ml) were taken which were prepared from leaves (standard A) and wood (standard B). As tracer for specific IgE ¹²⁵I-anti-human-IgE (Allergopharma) was used. Three extract concentrations (undiluted, 1:500, 1:5000) were tested. The results were expressed as total %-RAST-inhibition values.

SDS-PAGE

For the determination of the protein pattern of the extract used for the preparation of the allergen disks sodium dodecylsulfate-polyacrylamide gel electrophoresis (SDS-PAGE) was performed according to the guidelines of the manufacturer (Pharmacia, Sweden). Marker proteins were obtained from Pharmacia. They were stained with Coomassie brilliant blue (E. Merck, Germany).

Results

Patients and skin tests

The prevalence of positive Fb skin tests varies between 5 and 7.5% in our clinic [4]. Fifteen patients (eight male, age range 18–48 years) with perennial symptoms who had a positive skin test to Fb were identified (Table 1), five of these patients (patients 4, 6, 9, 11, 12) have been found during an earlier study [5]. With one exception the patients were atopic with sensitization to pollen, animal danders or house dust mites. Among seven skin-prick tested with Hb-latex, only one had a positive test reaction.

Specific IgE

Specific IgE to Fb were found with the CAP in 10, and with the RAST technique in nine sera (Table 1). The pool serum of non-allergic controls was negative with RAST, indicating that the positive results are due to specific binding of IgE. In five out of eight sera with specific IgE to Fb also specific IgE to Hb-latex were found. The other four sera including one negative to Fb were negative to Hb-latex (Table 1). However, in four patients positive to Hb-latex *in vitro*, who were also skin tested with Hb-latex, only one had a positive skin test.

RAST-inhibition

In Figs 1 and 2 the total %RAST-inhibition values measured with the different extracts are shown. The background value of the method is ≤10%. The highest values (86%, 89%) were obtained with the skin-prick test solutions (standards A, B). The dust from leaves showed inhibition values from 12 to 41%, whereas secretion droplets from the leaf stems showed none or only marginal inhibition (Fig. 1). However, in five of six floor dust samples inhibition values from 22 to 61% were found (Fig. 2).

Table 1. Results of allergological investigations in patients sensitized to *Ficus benjamina*

No	Initials	Sex	Age (years)	Symptoms	Exposure to Fb	Skin-test to Fb	CAP (class/kU/l)	RAST (class)	Skin-test Hb-latex	RAST Hb-latex	Sensitization to other inhalant allergens
1	MM	M	30	RC	LR, OF	Pos	3/7.32	2.1	Neg	0	mites, pollen, animals
2	MS	M	25	R	∅	Pos	0/<0.35	0	ND	ND	pollen, cat
3	PC	M	30	RCA	LR	Pos	0/<0.35	0	ND	ND	pollen, animals
4	HI	F	19	RCA	LR, OF	Pos	3/5.3	3.2	Pos	4	mites, pollen, cat
5	ST	F	18	RC	∅	Pos	0/<0.35	0	Neg	0	mites, pollen, cat
6	TH	M	48	A	LR	Pos	2/1.19	1.6	ND	2.1	mites, pollen, cat
7	BS	F	34	RC	LR	Pos	5/50.6	4.0	Neg	0	pollen, cat
8	SF	M	38	A	∅	Pos	1/0.51	2.1	Neg	1.7	mites, pollen
9	SM	F	36	RC, CU	BR, LR	Pos	4/21.3	3.1	ND	0	—
10	GB	F	31	A	∅	Pos	2/0.9	1.2	Neg	2.0	pollen
11	LS	F	32	RCA	LR, OF	Pos	0/<0.35	0	ND	ND	pollen, animals
12	SP	M	35	RC, CU	LR, OF	Pos	2/0.75	0	ND	ND	pollen
13	AC	M	30	R	LR	Pos	ND	0	ND	ND	pollen
14	SH	M	38	RC	LR, OF	Pos	3/6.46	3.7	ND	ND	mites
15	WC	F	44	RC	LR	Pos	6/>100	4.0	Neg	1.1	pollen, animals

R. Rhinitis. C. Conjunctivitis. A. Asthma. CU. Contact urticaria. LR. Living room. BR. Bedroom. OF. Office. ND. Not done. Fb. *Ficus benjamina*. Hb. *Hevea brasiliensis*. Pos. Positive. Neg. Negative.

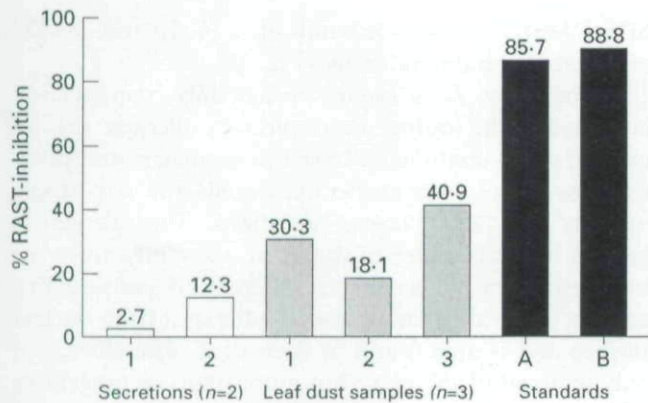


Fig. 1. Total % RAST-inhibition by leaf stem secretion and leaf dust samples from *Ficus benjamina* (positive $\geq 10\%$). Standard A. Leaf extract. Standard B. Wood extract.

SDS-PAGE

In the SDS-PAGE most of the proteins showed molecular weights of ≤ 14.4 kDa. But also between 14.4 and 20.1 and at approximately 28 kDa protein bands of varying staining intensity could be seen (Fig. 3).

Discussion

The degree of sensitization in a population depends on the extent of exposure to a particular allergen and its potency. For Fb it has been shown that all sensitized subjects with low-grade exposure are atopic [3,5]. In high grade exposure as it is present in occupational settings [2], in repeated cutting of a Fb Bonsai [5] or long-lasting bedside exposure [9] also non-atopic individuals may become sensitized.

In our investigation considerable amounts of FB allergen were demonstrated in dust extracts from the leaf surface by RAST-inhibition. This is in accordance

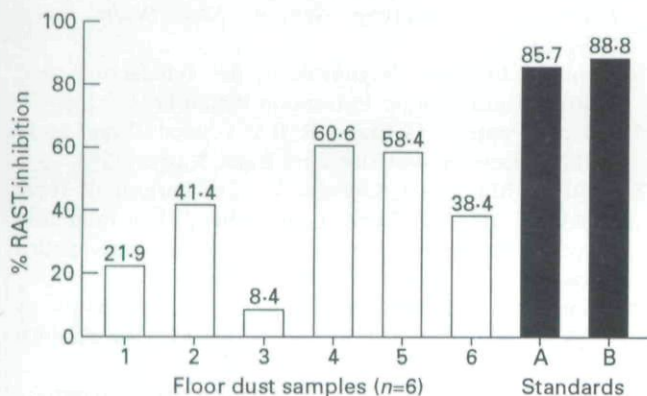


Fig. 2. Total % RAST-inhibition by floor dust samples collected at *Ficus benjamina* locations (positive $\geq 10\%$). Standard A. Leaf extract. Standard B. Wood extract.

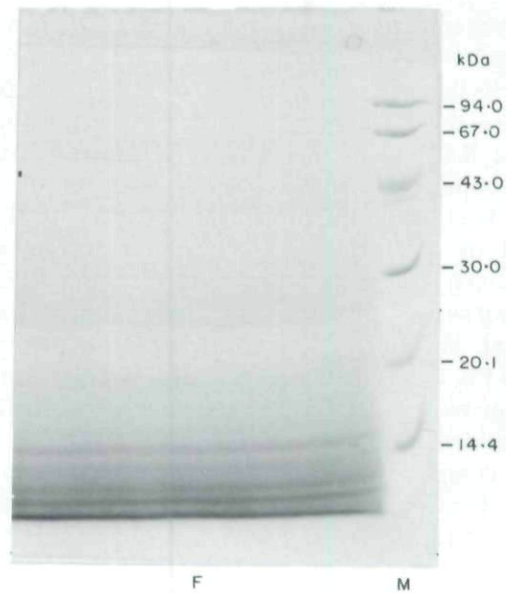


Fig. 3. SDS-PAGE using extract from *Ficus benjamina* wood. F. *Ficus* extract. M. Marker proteins, kDa. Kilodaltons.

with the hypothesis that water-soluble antigens accumulate by diffusion on the leaf surface and bind to dust particles. That Fb-allergen is present in leaf dust has been shown in patients sensitized to Fb in whom skin tests with test solutions made from Fb leaf dust were positive in 17 out of 18 patients [2]. On the other hand it has been found, that the major allergenic components of Fb are present in the Fb-latex of the plant [10]. Therefore, skin tests with Fb-latex extracts were more reliable in identifying clinically relevant sensitization to Fb than the ones with leaf extracts [3]. Fb plants secrete small sticky particles underneath the leaf at the stem. In these particles we could not identify Fb-allergen by RAST-inhibition. This may be due to the small amount of material available for investigation or that water-soluble antigens may have already evaporated. Based on these limited results these particles seem not to contain Fb-latex allergen.

In the majority of the dust samples collected from the floor a high RAST-inhibition was found indicating the presence of Fb allergen. This is not surprising for the dust from the leaves will eventually fall to the floor and the allergens will then accumulate in the house dust. This is well documented for other perennial allergens such as the house dust mites and animal danders [11]. This finding has some clinical implications. Patients may be exposed to Fb allergens through airborne dust without having direct contact with the plant. Two observations support the relevance of Fb allergen in floor dust. The floor sample with the lowest RAST-inhibition value of

21% was collected at a site of a Fb plant which had been removed to another apartment 6 months earlier. This indicates that allergen may persist for longer time periods in house dust. The patient whose dust sample had the highest RAST-inhibition value of 62%, suffered from rhinoconjunctivitis whenever he was lying on the carpet in his living room. Although he was additionally sensitized to other dust allergens the reduction of his symptoms after removal of the plant and thorough cleaning suggest that Fb allergens were at least partially relevant. Therefore, in individuals who are highly sensitive to Fb, the removal of the plant may not be sufficient to attain relief of symptoms but further measures have to be considered.

The comparative measurement of specific IgE to Fb by the CAP technique and a RAST method showed a good correlation, there was but one discordant CAP-positive RAST-negative result (Table 1). Most of the CAP results showed higher classes, however, a direct comparison can not be made since different allergen preparations are used and different unit systems are applied to express the results (classes) of the two methods.

Hb-latex is an important and frequent allergen particularly in occupationally exposed medical personnel [12,13]. Its allergen has been chemically and recently also been immunologically characterized [13,14]. Fb and Hb do not belong to the same plant family (*Moraceae* and *Euphorbiaceae* respectively), but both contain milky saps commonly referred to as latex and latex from *Ficus* species has also been used to produce rubber [5,10]. Therefore, crossreactivity between the two latexes has been suggested [10]. In immunoblot studies three patients with positive RAST to Hb-latex had additional bands at 34 kDa which were distinct from bands typical for Fb [10]. We found specific IgE to Hb-latex in five out of eight sera with specific IgE to Fb. On the other hand skin tests with a Hb-latex extract from another manufacturer was positive in only one patient and there was no distinct history of allergic symptoms to Hb-latex in the Hb-latex-positive patients. The difference between *in vivo* and *in vitro* data may be due to different raw material used for the preparation of skin-test solutions and allergen carriers for specific IgE *in vitro*. Despite these inconsistencies it is possible that at least *in vitro* crossreactivity between the two latexes may exist. Recently, crossreactive antigens between Fb- and Hb-latex have been demonstrated by inhibition studies [15,16]. The results suggest a considerable similarity of allergen epitopes between the two plants.

The molecular weights of the protein components of Fb-latex have been determined by SDS-PAGE and immunoblot studies [10]. Bands at approximately 14, 25, 28 and 29 kDa were observed. The results of our

SDS-PAGE demonstrate bands at ≤ 14 , 20 and 28 kDa of different staining intensity (Fig. 3).

In summary, *Ficus benjamina* has only been recently identified as the source of a respiratory allergen. It is an important occupational allergen in gardeners and plant keepers, but exposed atopic individuals and non-atopic patients may also become sensitized. The allergen is located in the Fb-latex of the plant, secretions from the leaf stem seem not to contain allergen. A considerable amount of Fb allergen is present in the dust from the leaf surface and is also found in floor dust. Therefore, not only removal of the plant but more rigorous preventive measures may be necessary in the management of sensitized patients. In addition, there is emerging evidence that crossreactivity between Fb-latex and Hb-latex may exist which could be also of major clinical importance.

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References

- 1 Axelsson IGK, Skedinger M, Zetterström O. Allergy to weeping fig — a new occupational disease. *Allergy* 1985; 40:461–4.
- 2 Axelsson IGK, Johansson SGO, Zetterström O. Occupational allergy to weeping fig in plant keepers. *Allergy* 1987; 42:161–7.
- 3 Axelsson IGK, Johansson SGO, Zetterström O. A new indoor allergen from a common non-flowering plant. *Allergy* 1987; 42:604–11.
- 4 Bircher AJ, Levy F, Hirsbrunner P. *Ficus benjamina*, an ubiquitous allergen of considerable clinical relevance. *Allergy* 1993; 48:179.
- 5 Bircher AJ, Wüthrich B, Langauer S, Schmid P. *Ficus benjamina*, ein perenniales Inhalationsallergen von zunehmender Bedeutung. *Schweiz Med Wschr* 1993; 123:1153–9.
- 6 Wahl R. In vitro Diagnostik in der Inhalations- und Nahrungsmittelallergie. *Prävention Rehab* 1993; 5:156–62.
- 7 Yman L, Ponterius G, Brandt R. RAST-based allergen assay methods. *Develop Biol Standard*. Basel: Karger, 1975.
- 8 Wahl R, Maasch H, Geissler W. Comparison of three variations of the Radioallergosorbent Test-Inhibition assay for measuring allergenic activity of grass pollen extracts. *Analyt Biochem* 1983; 134:189–94.
- 9 Schmid P, Stöger P, Wüthrich B. Severe monovalent allergy to *Ficus benjamina* after bedroom exposure. *Allergy* 1993; 48:466–7.
- 10 Axelsson IGK, Johansson SGO, Larsson PH, Zetterström O. Characterization of allergenic components in sap extract from the weeping fig (*Ficus benjamina*). *Int Arch Allergy Appl Immunol* 1990; 91:130–5.

- 11 Wahl R, Oliver JD, Hauck PR, Roig J. (Radio) rocket immunoelectrophoresis is a useful screening method for house dust extracts. *Ann Allergy* 1989; 63:137-41.
- 12 Fuchs Th, Wahl R. Immediate reactions to rubber products. *Allergy Proc* 1992; 13:61-6.
- 13 Levy DA, Charpin D, Pecquet C, Leynadier F, Vervloet D. Allergy to latex. *Allergy* 1992; 47:579-87.
- 14 Czuppon AB, Chen Z, Rennert S et al. The rubber elongation factor of rubber trees (*Hevea brasiliensis*) is the major allergen in latex. *J Allergy Clin Immunol* 1993; 92:690-7.
- 15 Alroth M, Alenius H, Turjanmaa K, Palosuo T. Cross-reacting allergens in latex and in several other plant allergens. *ACI News* 1994, Suppl. 2:93 (Abstr 331).
- 16 Delbourg MF, Guilloux L, Ville G, Moneret-Vautrin DA. Crossreactivity between *Hevea brasiliensis* and *Ficus benjamina* latex allergens. *ACI News* 1994, Suppl. 2:467 (Abstr 1704).

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