

ORIGINAL ARTICLE**Hipersensitivity to *Ficus benjamina***

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Background: *Ficus benjamina* is a plant belonging to the *Moraceae* family; although it does not bloom, it may be a source of indoor allergens. The aim of the present study was to assess the prevalence of exposure and sensitization to *Ficus benjamina* in our environment, the clinical expression of such sensitization, and the possible cross reactivity with other allergens.

Patients and methods: a total of 347 patients attending the Allergy Unit of a general hospital were studied. Extracts prepared from the leaves and stems of *Ficus benjamina* were used for skin tests, for specific IgE quantitation (enzyme immunoassay) and SDS-PAGE immunoblotting. The serum specific IgE concentrations were also measured using the Pharmacia CAP-system. In those patients who were hypersensitive to *Ficus benjamina*, skin tests to common edible fig, kiwi, bromelain, papain, latex and mulberry tree pollen were also performed.

Results: Exposure to *Ficus benjamina* or other *Ficus* species was documented in 101 (29%) patients. Twenty-two of them were sensitized to *Ficus benjamina*, but only four had symptoms when immediately exposed to the plant. The specific IgE was positive in four out of ten patients by enzyme immunoassay, and in two out of nineteen by the CAP-system. SDS-PAGE immunoblotting demonstrated the presence of IgE-fixing proteins with molecular weights ranging between 8 and 42 kDa. Out of the 22 patients with hypersensitivity to *Ficus benjamina*, eight evidenced hypersensitivity to common edible fig (three of them with associated symptoms), seven to kiwi (three with symptoms) and two to latex (one with symptoms).

Conclusions: both the prevalence of exposure and sensitization to *Ficus benjamina* and the presence of allergic manifestations in some patients lend support to the consideration of this plant as an indoor allergen which may also have implications in food allergy.

KEY WORDS: *Ficus benjamina* / Fig / Hypersensitivity / Latex.**Hipersensibilidad a *Ficus benjamina***

Fundamento: *Ficus benjamina* es una planta de la familia de las *Moraceae* que, aunque no florece, puede actuar como fuente de alérgenos de interior. El objetivo del estudio fue determinar la prevalencia de exposición y sensibilización al *Ficus benjamina* en nuestro medio, su trascendencia clínica y la posible reactividad cruzada con otros alérgenos.

Métodos: Se estudiaron 347 pacientes consecutivos remitidos a una consulta de alergia de un hospital general. Se prepararon extractos de hojas y de tallos de *Ficus benjamina* que se utilizaron para las pruebas cutáneas, IgE específica (enzimoinmunoanálisis) y SDS-PAGE *immunoblotting*. Se determinó también la IgE específica mediante Pharmacia CAP System. En los pacientes sensibles a *Ficus benjamina* se practicaron, además, pruebas cutáneas frente a higo, kiwi, bromelina, papaína, látex y polen de morera.

Resultados: Ciento un pacientes (29 %) referían exposición a *Ficus benjamina* o a otras especies de *Ficus*. Veintidós pacientes (6,3 %) estaban sensibilizados a *Ficus benjamina* pero sólo cuatro tenían sintomatología relacionada con su cercanía. La Ig E específica fue positiva en 4 de 10 pacientes (enzimoinmunoanálisis) y en 2 de 19 (CAP-System). El SDS-PAGE *immunoblotting* mostró la presencia de proteínas fijadoras de Ig E con masas moleculares entre 8 y 42 kDa. De los 22 pacientes sensibles a *Ficus benjamina*, ocho estaban sensibilizados a higo (tres con síntomas asociados), siete a kiwi (tres con síntomas) y dos a látex (uno con síntomas).

Conclusiones: La prevalencia de exposición y sensibilización a *Ficus benjamina* y la presencia de sintomatología alérgica en algunos pacientes hacen que deba considerarse a esta planta como un alérgeno de interior, con implicaciones en alergia alimentaria.

PALABRAS CLAVE: *Ficus benjamina* / Higo / Hipersensibilidad / Látex.

Ficus benjamina is a plant belonging to the family *Moraceae* that has been experiencing increasing use as an indoor decorative plant. Similar to many other such decorative plants, *Ficus benjamina* (Fig. 1) has a tropical origin. It has abundant foliage and requires little care, and these features facilitate its use as a decorative plant both in public premises and in households¹.

The first description of its allergenic properties was the report by Axelsson *et al.* in 1985², who characterised it as an occupational allergen; these authors attributed this allergenicity to proteins in the plant's sap or latex³. Later on patients were reported who were sensitized to *Ficus benjamina* and evidenced perennial symptoms in relation to domestic environmental exposure^{1,4}.

To this date three major allergens of *Ficus benjamina* have been described (proteins with molecular weights of 25, 28 and 29 kDa) as well as eight minor allergens with molecular masses ranging between 13 and 56 kDa^{5,6}. Some investigators have suggested the existence of cross reactivity between *Ficus benjamina* and other species of the genus *Ficus*⁷, as well as with the latex of *Hevea brasiliensis*⁶, the common edible fig⁸, kiwi⁹, and papain¹⁰.

The aim of the present study was to assess the prevalence of exposure and sensitization to *Ficus benjamina* in our environment, as well as to assess the clinical relevance of this sensitization and the possible cross reactivity to other allergens.

PATIENTS AND METHODS

The study population comprised 347 consecutive patients referred to the allergy outpatient clinic of a general hospital in the coastal area of Catalonia (Spain). Two extracts were prepared for the skin tests and immunological assays, one of them from leaves and the other one from stems of *Ficus benjamina*. The two samples (leaves and stems) were cut up separately into small pieces and macerated for 24 hours in 50 mM phosphate buffer, pH 7.5, NaCl 150 mM, at 4°C after centrifugation of the macerates, the supernatants were filtered through 0.22 µm pore size nitrocellulose ester filters (Millipore Corporation, Bedford, MA, USA); they were then exhaustively dialysed against distilled water for 24 h at 4°C (with seve-



Fig. 1. *Ficus benjamina*.

ral changes of the distilled water) and lyophilised in a Cryodos-45 lyophiliser (Telstar SA, Terrassa, Spain) at a temperature of -49°C and a pressure of 3.7×10^{-2} mB. The extracts thus obtained were used for performing skin tests (prick tests with a protein concentration of 20 mg/ml), for the quantitation of specific IgE (enzymimmunoanalysis, Bial-Arístegui, Bilbao, Spain) and for SDS-PAGE immunoblotting.

The specific IgE was quantitated using two procedures: the Pharmacia CAP System and an enzymimmunoanalysis with the allergen coupled to BrCN-activated paper discs (2 mg/disc) (Bial-Arístegui); values equal to or greater than 0.70 PRU/ml were considered positive.

Sodium dodecylsulphate-polyacrylamide gel electrophoresis (SDS-PAGE) was carried out following the discontinuous method described by Laemmli¹¹ in 12.5% polyacrylamide gel, with para-

lled application of a reference standard of proteins with known molecular masses. Coomassie blue R-250 or a silver stain were used as required for staining the gels. Aliquots of 10 μ l/lane of the standard or of the samples were applied, containing 20 μ g protein (measured as described by Bradford¹²) when the Coomassie blue stain was used, and 1 μ g protein when the silver stain was used. For the preparation of the sample 0.125 M HCl-Tris buffer was used (pH 6.8, 0.1% SDS, 5% β -mercaptoethanol under reducing circumstances, and the same buffer without β -mercaptoethanol for electrophoresis under non-reducing circumstances).

For the SDS-PAGE immunoblotting, the proteins separated in the SDS-PAGE were electrotransferred to PVDF membranes (Immobilon-P) and incubated with the patients' sera. The IgE-fixing bands were detected with the help of an enzymatic system using an anti-IgE-peroxidase conjugate which is developed with 4-chloro-1-naphthol or with luminol (chemoluminescence detection) as best convenient. The molecular mass standard was identified with amido black.

Skin tests were performed with a panel of pneumoallergens containing the main allergens prevalent in our environment (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Lepidoglyphus destructor*, *Alternaria tenuis*, *Cladosporium herbarum*, *Aspergillus* spp., *Penicillium* spp., cat and dog epithelia, latex, and the pollen of *Phleum pratense*, *Cynodon dactylon*, *Phragmites communis*, *Olea europaea*, *Cupressus arizonica*, *Corylus avellana*, *Platanus acerifolia*, *Parietaria judaica*, *Artemisia vulgaris*, *Plantago lanceolata*, *Chenopodium album* and *Salsola kali*). In the patients sensitive to *Ficus benjamina*, skin tests were also performed with common edible fig (*Ficus carica*), kiwi, papain, bromelin, latex and mulberry pollen (commercially acquired extracts) and, in the cases positive with the fig extract, also with the fresh food (prick by prick). The criterion of positivity for these tests was the presence of wheals greater than 3 mm in diameter in the presence of negative control tests.

RESULTS

Out of the 347 patients studied, 272 (78.4%) were atopic and 101 (29.1%) reported exposure to *Ficus benjamina* or to other *Ficus* species.

Positive skin prick tests to *Ficus benjamina* were observed in 22 patients (6.3% of the overall sample and 8.1% of the atopic population). The tests were positive to the leaf extract in 21 cases, and to the extract prepared from the stems in only five. Thirteen out of the 22 sensitized patients (59.1%) acknowledged exposure to *Ficus benjamina*, but only four of them had clinical symptoms (rhinoconjunctivitis in two cases, conjunctivitis in one and contact urticaria in one) in relation to the presence of *Ficus benjamina* in their household environments; the symptoms disappeared in all four cases after removing the plant from the premises. All these four patients were women, they were all sensitized to other airborne allergens and none of them had spontaneously related the presence of symptoms with the exposure to the plant. Re-exposure to *Ficus benjamina* in one of these patients triggered the reappearance of the symptomatology (conjunctivitis) within 24 hours.

The specific IgE levels were quantitated by ELISA (Bial-Aristegui) in ten patients sensitive to *Ficus benjamina* and with continued exposure to the plant (with positive results in four of them), and with the Pharmacia CAP System in 19 patients (with positive results in only two). The SDS-PAGE immunoblotting of the extracts of leaves and stems of *Ficus benjamina* incubated with the sera of the ten patients revealed the presence in both extracts of IgE-fixing proteins of varying molecular masses: under reducing conditions, bands of $\approx$ 30-35 kDa and of $\approx$ 26-27 kDa, and under non-reducing conditions, bands of $\approx$ 8-14 kDa, $\approx$ 32 kDa and $\approx$ 42 kDa (Figs. 2a and 2b).

Among all the 22 patients sensitized to *Ficus benjamina*, eight had positive skin tests to common edible fig (three of them with urticaria, oral syndrome and conjunctivitis, which were later demonstrated with challenge tests), seven had positive tests to kiwi (three of them with allergic symptomatology, but no challenge tests were performed), two had positive tests with latex (one of them with symptoms), one with papain and one with mulberry pollen (the latter two with no apparent clinical relevance).

DISCUSSION

Indoor ornamental plants may be the source of

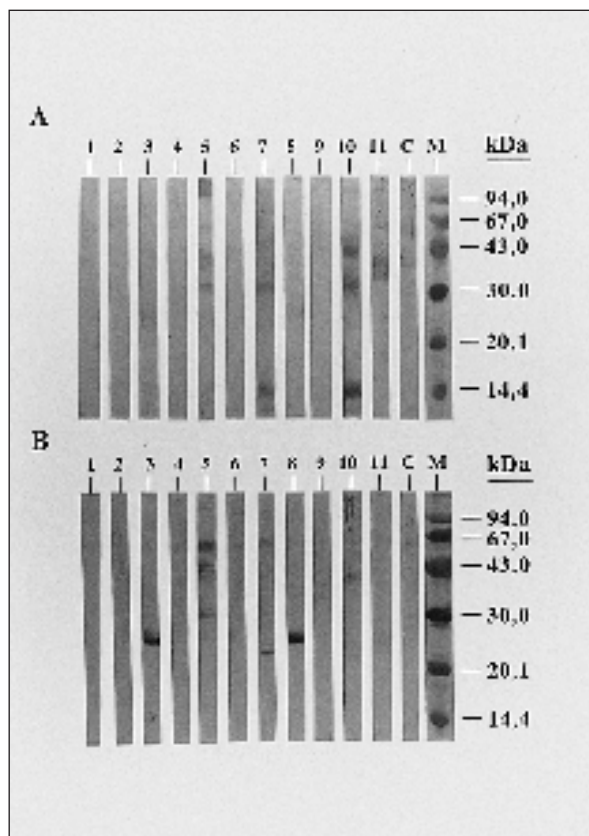


Fig. 2.a. SDS-PAGE immunoblotting of the extract from leaves of *Ficus benjamina*. A) Sample under non-reducing conditions. B) Sample under reducing conditions (with β -mercaptoethanol). The numbered lanes correspond to the patients' sera, lane C contains a pool of sera from non-allergic subjects, and lane M the molecular mass standard.

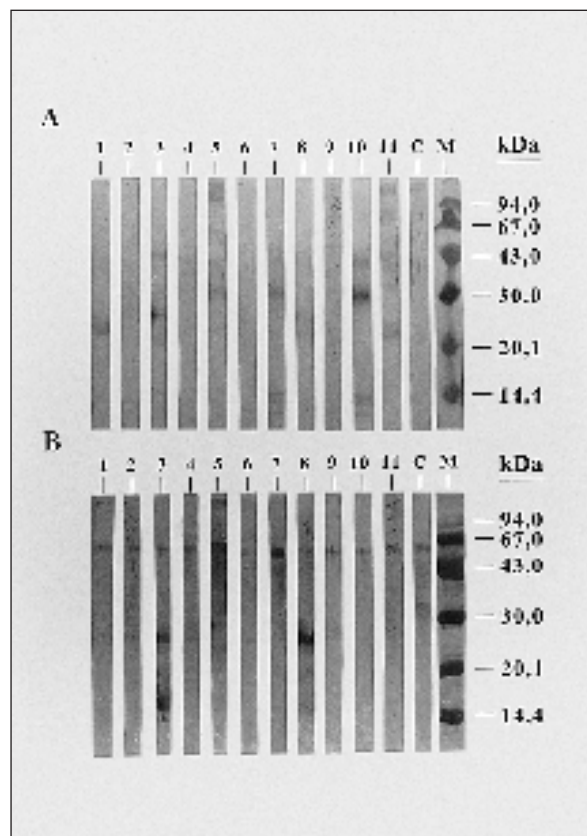


Fig. 2.b. SDS-PAGE immunoblotting of the extract from stems of *Ficus benjamina*. A) Sample under non-reducing conditions. B) Sample under reducing conditions (with β -mercaptoethanol). The numbered lanes correspond to the patients' sera, lane C contains a pool of sera from non-allergic subjects, and lane M the molecular mass standard.

various allergens, such as pollen, proteins from the leaves or sap, moulds, and parasites^{13,14}. *Ficus benjamina* is a plant that is being increasingly used as a decorative element in public premises, offices and households, and allergenic proteins from its latex have been detected in the household dust even up to six months after having removed it from the premises. *Ficus benjamina* may thus be considered to be a perennial indoors allergenic source⁴.

Ficus benjamina, which is a non-blooming plant, may be a source of airborne proteins through the evaporation of water from the plant's sap or latex; this evaporation osmotically carries with it soluble allergens which are deposited on

the surfaces of the leaves and which then adhere to dust particles, facilitating their airborne transportation and diffusion¹. The usual placement of these ornamental plants in dry and warm environments facilitates their transpiration, a phenomenon that does not occur in the tropical countries where it originates and where the high environmental humidity prevents the release of allergenic proteins¹.

The prevalence of sensitization observed in the studied population (6.3%) is similar to that reported by other authors¹. However, the exposure rate of our population to *Ficus* spp. (29%) is quite lower than the 62% one in the population studied by Axelsson *et al.*¹. The four patients evidencing clini-

cal symptomatology attributable to the exposure to *Ficus benjamina* acknowledged that exposure and observed the remission of their symptoms upon removing the plant from their environments. This stresses and highlights the relevance of the aetiological diagnosis in these patients, as the implementation of the opportune environmental measures was resolute for their symptoms.

The sensitivity of the leaf extract was higher than that of the stem extract. The difference in sensitivity observed in the quantitation of the specific *Ficus benjamina* IgE should also be stressed: while the Bial-Arístegui ELISA performed with *Ficus benjamina* extract detected four of the ten patients with positive skin tests, the CAP System from Pharmacia, which uses a mixture of *Ficus benjamina* and *Ficus elastica*, detected only two out of nineteen patients. As the cross reactivity between the two *Ficus* species is only partial, the lesser sensitivity achieved by the CAP System might probably be due to a lesser concentration of the *Ficus benjamina* extract in the solid phase of this assay^{4,7}.

The results of the SDS-PAGE immunoblotting disclosed a pattern of IgE-fixing protein bands which was similar in both extracts (leaves and stems), both under reducing and under non-reducing conditions; these IgE-fixing proteins had molecular masses ranging between 13 and 56 kDa, similar to those previously described^{5,6}. The presence of β -mercaptoethanol modifies the pattern of IgE-fixing bands: it leads to loss of recognition for some of them (the 8-13 kDa bands disappear) and changes the mobility of yet others. All this is coincident with the reports by other authors⁵ regarding the role of disulphide bridges in maintaining the protein structures of some of the allergens present in this type of extracts.

On the other hand, in this group of patients a high prevalence of positive skin tests to the common edible fig (the fruit of *Ficus carica*) and to kiwi was observed; the yield of the skin tests to fig was greater when using the fresh fruit than with the commercially acquired extract. Approximately one half of the patients sensitive to *Ficus benjamina* and to these fruits evidenced or developed clinical symptoms after the ingestion of fig or kiwi, a correlation already reported by other authors^{8-10,15}. The high level of association observed between the latex of *Ficus benjamina* and these fruits, which was also confirmed by the *in vitro*

techniques^{8,10}, might warrant the recommendation that the ingestion of those fruits be avoided by patients sensitive to *Ficus benjamina*. In the case of the latex of *Hevea brasiliensis* this association was less evident, as only two patients had positive skin tests to both of them, in one case with clinical symptomatology (anaphylaxis) in association to the exposure to latex. Although there are studies which confirm the existence of cross reactivity between *Ficus benjamina* and *Hevea brasiliensis*, and a 33 kDa protein shared by both has been described⁶, other authors have not observed such cross reactivity using CAP inhibition tests¹⁰. Only one of our patients evidenced coincident sensitization to *Ficus benjamina* and papain, which has already been reported by other authors¹⁰, and a further one had coincident sensitivity to *Ficus benjamina* and mulberry pollen.

The prevalence of exposure and of sensitization to *Ficus benjamina* and the presence of allergic symptomatology in some patients should lead to *Ficus benjamina* being considered a potential indoor allergen which also has implications in food allergy.

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