EDITORIAL

Ficus benjamina, a new source of household environmental allergens

Non-pollinating ornamental plants have been achieving increasing importance over the last few years as sources of allergens capable of inducing both occupational[1-9] and non-occupational[10-12] respiratory allergy. Among such plants, the species *Ficus benjamina* (also known as "weeping fig") is one of the foremost.

BOTANICAL CHARACTERISTIC OF *FICUS*

The genus *Ficus* belongs to the order *Urticales*, family *Moraceae*, and has about 1000 species. Most of these species are trees and many of them achieve great sizes in the tropical regions where they mostly originate; however, when cultivated in our temperate latitudes, their proportions are more modest. In their original environment, the crown of some species attains very considerable extension. There is for instance one *Ficus* in the Andhara valley in India, the crown of which has a perimeter of over 600 meters and is supported by over 300 aerial roots. The emission of such aerial roots is arguably the most noteworthy characteristic of this botanical genus. They originate from the branches and grow downwards to the soil, which they penetrate like any other root; they thus serve as a support for the crown, which may therefore grow and attain the already stated dimensions. This does not occur in our climate, and the emission of aerial roots is rather scarce and restricted to some trees of rather advanced age, although this phenomenon can be clearly observed in the climate of the Canary Islands.

Beyond this curious characteristic, the *Ficus* share other particular features: the presence of a milky sap (latex); having rigid, often large sized leaves, and a characteristic fruit termed sycone or "fig", which is actually not a fruit but an infrutescence comprising a large number of very small fruitlets enclosed in a fleshy receptacle.

The best-known *Ficus* species is the "common fig tree" or *Ficus carica*, cultivated because of its fruits since long before the time of Jesus Christ and today quite widely distributed. Among the *Ficus* species grown only for ornamental purposes, there are some which are used as indoors decorative plants, such as *Ficus benjamina, Ficus cyathistipula, Ficus deltoidea, Ficus elastica, Ficus lyrata, Ficus microcarpa (F. nitida), Ficus parcellii, Ficus pumila, Ficus rubiginosa (F. australis)* and *Ficus sagittata (F. radicans)*.

Other *Ficus* species are commonly used in Spain as decorative outdoor plants in gardens and/or promenades in areas where the climate allow it, such as the Levant, Andalusia and the Canary Islands; the commonest among these are *Ficus altissima, Ficus benghalensis, Ficus macrophylla* and *Ficus religiosa*.

Among the indoor *Ficus* species, one of the most widely used is *Ficus benjamina*. This is a shrub or small tree, which may attain 1.5 - 2 metres, with drooping branches and some 1800 small, oval, pointed and hanging leaves. Its area of origin is India and Malaysia, and since some years ago it has become one of the most used indoor plants both in households and in offices, due to the fact that it requires almost no care[13].

OCCUPATIONAL RHINITIS AND ASTHMA DUE TO *FICUS BENJAMINA*

The first scientific report on the allergenicity of *Ficus* species was published by the Swedish physician G. Axelsson, who in 1985 described two patients, one of them with asthma and the other with allergic rhinitis. Both patients were occupied in the care of indoor plants, and in both of them the symptoms were clearly triggered when they energetically shook *Ficus benjamina* in order to get rid of the dust deposited on their leaves. Both patients evidenced positive skin tests and RAST with an extract of leaves and an extract of stems of *Ficus benjamina*[14].

Companies dedicated to gardening and plant care services for offices, including rental and maintenance of plants, have become increasingly

important in Stockholm in recent times. In 1985, about 100 people were already employed in the daily cleaning of office *Ficus* (plant caretakers). Axelsson and co-workers were able to study 52 such plant caretakers and found that 30% of them evidenced IgE mediated sensitization to *Ficus benjamina*, which caused occupational rhinoconjunctivitis in 100% of the cases and added occupational asthma in 37%. 87% of the sensitized workers also suffered localized contact urticaria upon contact with latex from *F. benjamina*. Atopy did not appear to be a predisposing factor, as 61% of these cases were not atopic. The degree of exposure, however, was indeed a predisposing factor, as the prevalence of *Ficus* sensitization among 16 workers (commercial agents, florists and executives from these companies) who only on occasion worked with this plant was as low as 11%[1].

According to these investigators, the mechanism probably involved in the sensitization is as follows: the allergens emanate from the latex of the plant, and it is the water diffusing from the plant interior to the surface (a diffusion phenomenon favoured by the hot and dry air in office environments) which osmotically carries the latex allergens to the exterior of the leaves. This solution soaks the dust particles present on the leaves, and these particles, when dry, become aerosolised into the air and behave as pneumoallergens. Several data lend support to this possible mechanism: (A) The skin tests and RAST were more strongly positive with the latex extract than with those from leaves, stems or dust deposited on the leaves. (B) Some patients had positive skin tests and RAST to the extract of dust deposited on the leaves, but not to the extract of leaves. (C) The lack of humidity in the environment appears to be crucial, as the workers from greenhouses with high exposure to *Ficus benjamina* but with high relative humidity are seldom sensitized (the high humidity in the air decreases both the diffusion of water to the surface of the leaves and the evaporation of water from the dust particles, causing a much lesser degree of aerosolisation)[1].

PERENNIAL RHINITIS AND ASTHMA DUE TO *FICUS BENJAMINA*

Axelsson, in 1985, carried out a study on 395 consecutive patients attending his Allergy service in order to assess the importance of this allergen in persons not occupationally exposed to it. 56% of his cases were atopics, 62% of them had *Ficus benjamina* as ornamental plants in their households and/or offices, and 3% evidenced positive skin tests and RAST to this *Ficus* species. All but one of the sensitized patients had this plant in their households; all of them evidenced sensitisations to other pneumoallergens, and all of them had rhinitis and/or bronchial asthma. The sensitization to *Ficus* was considered to be clinically relevant in approximately one half of the cases, as their symptoms of rhinitis and/or asthma improved upon removing the *Ficus* from the household environment. The authors concluded that 6% of the atopic population (in Stockholm) evidence sensitization to *Ficus benjamina*, and 3% develop respiratory symptoms because of this sensitization[10].

Some years later, the group of Wüthrich reported the case of a 32-year-old non-atopic male with moderately severe rhinoconjunctivitis and bronchial asthma of one year's evolution, who became asymptomatic three months after removing one *Ficus benjamina* from his bedroom. This patient evidenced positive skin tests and RAST to the latex of *Ficus benjamina*, but not to other pneumoallergens. This study clearly demonstrated that also non-atopic individuals (with non-occupational exposure) might develop perennial rhinitis and asthma due to *Ficus* sensitization. A little later, Axelsson confirmed this fact with the report of four non-atopic women with perennial rhinoconjunctivitis due to monosensitization to *Ficus benjamina*[15].

Bircher *et al*., using RAST inhibition studies, found *Ficus benjamina* allergens in the household floor dust in four out of five households of *Ficus*-allergic patients who had this indoor plant in their homes, suggesting that direct manipulation of the plant is not a prerequisite to experiencing symptoms. In one of these households the allergens were still present in the dust despite having removed the *Ficus* six months earlier; this might explain the persistence of the symptoms and stresses the need for energetic cleaning measures after the plant has been removed from the environment[16].

In the present issue of *Alergología e Inmunología Clínica*, Gaig and co-workers report a 6% prevalence of sensitization to *Ficus benjamina* among a group of 347 consecutive patients studied in their Allergy service. This prevalence doubles that observed by Axelsson (3%), although the

exposure to *Ficus* among the Spanish patients is only about one-half that among the Swedish ones (29% vs 62%). However, this difference may be due to the greater percentage of atopic in the Spanish group (78% vs 56%); this results in a final 8% prevalence of *Ficus benjamina* sensitization among the atopic Spanish population, which is almost the same as the 6% one observed among the atopic Swedish population.

FICUS BENJAMINA ALLERGENS

Axelsson and co-workers again studied *Ficus benjamina* in order to ascertain the allergenic composition of a raw extract of its latex, using SDS-PAGE and immunodetermination techniques. They used to this purpose the sera from 20 exposed patients with positive RAST to *Ficus benjamina* (11 plant caretakers, 7 of whom were non-atopics, and 9 atopic patients). They identified 11 allergenic components, three of which were major ones (identified by >50% of the sera); these three components were thermolabile (60-90ºC) and had molecular weights of 29, 28 and 25 kDa[17].

Gaig and co-workers report that they have evidenced in the leaf and stem extracts a pattern of IgE-linking protein bands which is similar to that observed in the latex extract by Axelsson *et al*., again pointing to the latex of *Ficus benjamina* as the original source of its allergens.

CROSS REACTIVITY BETWEEN *FICUS BENJAMINA* AND OTHER ORNAMENTAL *FICUS SPECIES*

The Swedish group carried out a cross reactivity study applying RAST inhibition with latex extracts from eight types of ornamental *Ficus*, using the sera from 24 patients with positive RAST to *Ficus benjamina* (12 atopic subjects and 12 plant caretakers). The greatest RAST positivity was observed for *Ficus benjamina* and particularly for its "starlight" variety (24/24), followed by *F. nitida, F. westland* and *F. australis* (22/24), *Ficus lyrata* (20/24), *Ficus cyathistipula* (16/24) and *F. elastica* (5/24), the latter thus being the least allergenic species[18].

The RAST to the six last species could be completely inhibited with a *Ficus benjamina* extract, but not inversely (the inhibition was in this last case only partial). These data suggest the presence of a primary sensitization to *Ficus benjamina* and hence a secondary sensitization to the remaining *Ficus* species due to cross reactivity. The greater sensitization to *F. benjamina* might be explained by a greater exposure to this particular species, but this does not explain the low sensitization observed wit *Ficus elastica*, which is also a widely encountered indoor *Ficus* species. The authors suggest that the difference might be due to the size of the leaves, small and numerous in the case of *F. benjamina* and larger but fewer in number in *F. elastica*, which would condition a lesser degree of dust deposition on the latter species and hence a lesser degree of allergen aerosolisation[18].

CROSS REACTIVITY BETWEEN THE LATEX OF *FICUS BENJAMINA* AND THE FRUIT OF *FICUS CARICA*, THE "COMMON FIG TREE"

A case has been reported in France of a 77-year-old non-atopic woman who suffered an anaphylactic reaction (disseminated urticaria, facial angioedema, vomiting and diarrhoea) immediately after the ingestion of a fresh fig. Three days earlier she had experienced similar but milder symptoms three hours after the ingestion of another fig. The patient had earlier had one *Ficus benjamina* in her home, which had had to be removed some 18 months earlier not because of inducing symptoms but because of having grown too large. The patient had high levels of specific serum IgE to common edible fig *(F. carica)* and weeping fig *(F. benjamina)*. The fig extract was able to inhibit the CAP to *F. benjamina* by 49%[19]. Díez-Gómez and co-workers have also observed this cross reactivity, in a 36-year-old male with perennial asthma of three years' evolution due to *Ficus benjamina* sensitization, who in two occasions developed vomiting and oropharyngeal and lingual angioedema minutes after the ingestion of an edible fig. Similar to the French group, these investigators found that the common fig extract caused only partial inhibition (33%) of the CAP to *F. benjamina*, while the *F. benjamina* extract inhibited 99% of the CAP to common fig, thus again pointing to *F. benjamina* as the primary sensitizing agent[20].

In the study of Gaig and co-workers, among 22 patients sensitized to *F. benjamina* eight were also sensitized to the common fig *(F. carica)* (36%);

this sensitization was considered to be clinically relevant in one half of these cases (three patients).

The presence of cross reactivity between different parts of a same plant, or between taxonomically close plants is not infrequent. This may be sometimes observed between the grains of cereals and the pollens of *Gramineae*, between the seeds of *Plantago ovata* (Metamucil®) and the pollen of *Plantago lanceolata*, or, in the present case, between the fruit of *Ficus carica* and the latex of *Ficus benjamina* (both of them belonging to the same *Moraceae* family)[21,22]. The fact that only some patients, but not all of them, evidence this cross reactivity simply indicates that not all become sensitized to the same epitopes. In any case, it appears to be prudent to routinely investigate common edible fig sensitization in patients allergic to *F. benjamina*.

CROSS REACTIVITY BETWEEN THE LATEX OF *FICUS BENJAMINA* AND NON-RELATED ALLERGENS

a) Papain, kiwi

Cross reactivity between allergens with no taxonomic proximity is coming to be the rule rather than the exception[24-26], and *Ficus benjamina* is by far not an exception to this. In this context, Díez-Gómez *et al*. reported that their already-mentioned patient also evidenced sensitization to papain and to kiwi fruit *(Actinidia chinensis*, family *Actinidiaceae)*, and had presented with the latter symptoms similar to those elicited by the common fig[20]. The extract of *F. benjamina* was able to inhibit the CAP to papain by 57%. This observation is highly interesting, as cross reactivity between papain and *F. benjamina* might in some cases explain the sensitization to kiwi fruit observed in these patients[23]. Nevertheless, in the study by Gaig and co-workers, although seven out of twenty-two patients sensitised to *Ficus benjamina* were also sensitized to kiwi (32%), only one of them was sensitized to papain.

b) *Hevea brasiliensis* latex

In the previously commented study by Axelsson *et al*.[17], three out of the 22 sera of the patients allergic to *F. benjamina* yielded a positive RAST to *Hevea brasiliensis* latex (family *Euphorbiaceae*). Precisely in these three sera, the immunodetermination studies on the extract of *F. benjamina* were able to detect three additional bands, suggesting that these might be the expression of cross reactivity to the latex of *Hevea brasiliensis*.

Delbourg *et al*. published two patients, one of them with rhinitis and the other one with asthma due to allergy to the latex of *F. benjamina*, who also evidenced sensitization to the latex of *Hevea brasiliensis*. With the help of the RAST inhibition studies, these investigators found in the sera of both patients an important cross reactivity between the two latexes. As one of the patients had never had contact with the latex of *H. brasiliensis*, the authors suggested that the sensitization to this latex might have been secondary to that to *Ficus benjamina*[27].

Brehler and coworkers[28] found 21% vs 6% incidences of *Ficus benjamina* latex sensitization among patients with (n = 151) and without (n = 346) allergy to latex of *Hevea brasiliensis*. Among these 497 patients, 48 (9.7%) evidenced positive specific IgE to both latexes *(F. benjamina and H. brasiliensis)*. Using five of these 48 sera, these investigators found that the *H. brasiliensis* extract completely inhibited the CAP to *Ficus benjamina* in all cases. However, *Ficus benjamina* inhibited the CAP to *H. brasiliensis* with less intensity (21 to 100%, mean 57%). The authors concluded that cross reactivity between these two latexes is often found in the sera of atopics, and that patients allergic to the latex of *H. brasiliensis* should be routinely investigated as to a possible allergy to *F. benjamina*[28].

Gaig and co-workers report that, out of their 22 patients sensitized to *Ficus benjamina*, only two were also sensitized to *H. brasiliensis* (9%); furthermore, one of these two sensitizations was a subclinical one. This prevalence of sensitization to latex of *H. brasiliensis* among patients with *Ficus benjamina* sensitization does not differ from that observed among blood donors (6-8%)[29,30]. The joint consideration of these studies suggests the interpretation that although sensitization to the latex of *Hevea brasiliensis* might indeed be a predisposing factor for a secondary sensitization to *Ficus*, the inverse situation of primary sensitization to the latter does not appear to generally influence a secondary sensitization to the latex of *H. brasiliensis*.

CONCLUSION

Ficus benjamina is a relatively common indoor household allergen, with a prevalence of sensitization similar to that observed for moulds. Many

cases of perennial extrinsic rhinitis and asthma caused by *Ficus benjamina* remain undetected, probably because these patients are typically also sensitized to other pneumoallergens (mites, epithelia, pollens), and the possible contribution of *Ficus benjamina* to their symptoms has not been studied. The growing use and presence of this indoor decorative plant and its cross reactivity to the latex of *Hevea brasiliensis* lead to supposing that its allergenic importance may well be on the rise. For diagnostic purposes, the prick test with latex of *Ficus benjamina* is more sensitive than the CAP or RAST. Atopic individuals with sensitization to the latex of *Hevea brasiliensis* should not have *Ficus benjamina* in their household environments. The study by Gaig and co-workers which is published in the present issue of *Alergología e Inmunología Clínica* is an important work which clarifies may aspects related to this new indoor household allergen.

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