

Parietaria pollinosis: a review

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Species of the genus *Parietaria* (pellitory) are a prevalent cause of allergy in the Mediterranean area and the most important in some European regions such as southern Italy and coastal Spain (14, 26, 27, 29, 30, 31, 36, 59, 69). Up to now, however, *Parietaria* has received little attention in northern Europe and the US because of its limited regional distribution. Therefore, less is known about *Parietaria* allergy than about other inhalant allergens such as those of grasses, ragweed, and mites.

During the last 5 years, only 31 reports on *Parietaria* allergy have appeared in the literature, as compared with 37 papers on birch pollen. This ratio may appear unbalanced, considering that millions of people suffer from pollinosis caused by *Parietaria*, while a much smaller number have rhinitis and/or asthma caused by birch pollen.

The increasing movement of people throughout Europe and to and from the US is reason to broaden our knowledge of patterns of inhalant allergy in each geographic area, especially where tourism and immigration are high.

This paper briefly reviews available data and personal studies on the botanical, aerobiological, immunochemical, and clinical features of *Parietaria* allergy.

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Parietaria officinalis and *P. judaica* are the most common species within the genus *Parietaria*. Others are *P. lusitanica*, *P. mauritanica*, and *P. cretica* (62). These highly productive, anemophilous species are characterized by numerous, grouped, individually small and drab, scentless florets (Fig. 1). *P. judaica* is thermophilic and heliophilic; consequently, it commonly grows in coastal Mediterranean countries, such as Spain, southern France, Italy, the former Yugoslavia, Albania, and Greece (13, 14, 16, 30, 31, 32, 34, 35, 42, 57, 59) (Fig. 2). *Parietaria* spp. also occur outside the Mediterranean area. *Parietaria* is said to have been introduced from the Mediterranean area to the southern coast of England by monks during the Middle Ages. The common British name of *Parietaria judaica* is pellitory of the wall (16, 46) since it readily grows on buildings. *Parietaria* spp. have recently been identified in the US (12, 48) and in Australia (6, 41). *P. officinalis*'s habitat is hilly or mountainous areas (under 1000 m altitude) in Spain, France, northern Italy, Austria, Bulgaria, Czechoslovakia, Romania, and southwestern regions of the former USSR (13, 14, 30, 34, 35, 36, 57, 59) (Fig. 2).

Aerobiology

Parietaria pollen grains (Fig. 3) are small (mean diameter 12–16 µm), light, and spheroidal. These characteristics favor wind pollination. A large number of triplicate pollen grains can be spread by propulsion (spring release) from the anther's flexible filaments.

Factors influencing the pollen output include temperature, humidity, and light intensity. The anthers of *Parietaria* open during favorable weather, particularly when it is warm and dry. They tend to open during daylight hours, from early morning to late afternoon. Pollination can also be triggered by rapid declines in solar radiation, as with passing clouds.

Parietaria anther dehiscence is favored by water withdrawal from the anther endothelium, which causes splitting and release of pollen in clouds.

The pollination periods of *Parietaria* and *Urtica dioica* overlap. In addition, it is not possible to distinguish the pollen grains by means of microscopic analysis, despite slight differences in size. Therefore it is preferable to quote as "Urticaceae" (the family including *Parietaria* as well as the genus *Urtica* [nettles]) the counts of atmospheric pollen without at-



Fig. 1. *Parietaria judaica*.

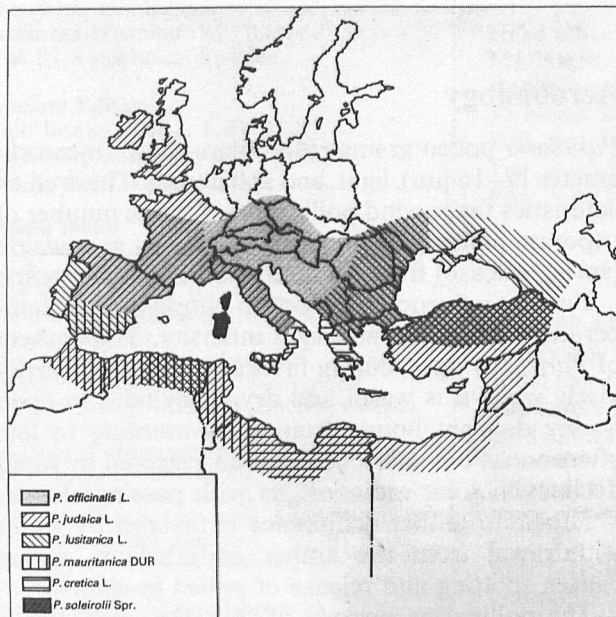


Fig. 2. Distribution of *Parietaria* species in Europe and North Africa.

tempting to discriminate between genera or species (26, 35).

The duration of *Parietaria*'s pollen season varies

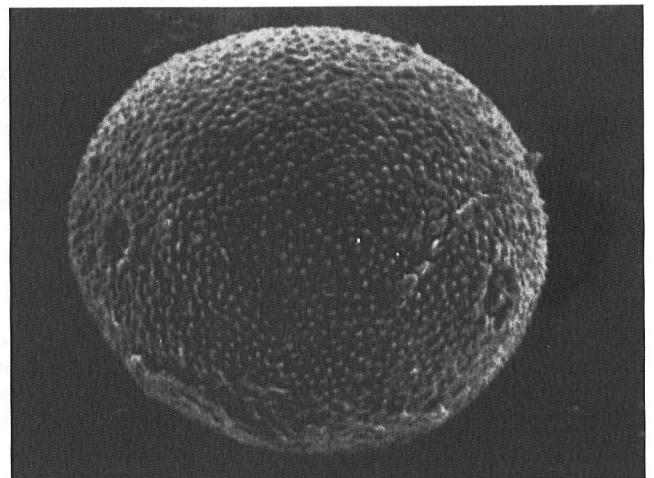


Fig. 3. Pollen grain of *P. judaica* shown by scanning microscopy (original magnification $\times 4000$). The grain is spheroidal, triporate, and very small (diameter of 12–16 μm).

with the climate. In southern Italy it can persist from February to December (30, 32, 33, 35), resulting in almost perennial symptoms, whereas in northern Italy and southern France and on the Mediterranean coast of Spain, pollination occurs on average from April to September (9, 13, 14, 31, 57, 69). The flowering season in the British Isles lasts from June to

September (46) and in San Francisco (US) from late February through December (1, 48, 73).

The main *Parietaria* cycle of flowering in southern Italy, particularly in the Naples area, begins in March and continues until July (29, 30). Peak pollination occurs in May and June. In September and October a lower peak is detectable (Fig. 4).

A prodigious output of pollen ensures the reproductive success of the plant. The mean pollen counts from the end of April to the end of June vary from 100 to 500 pollen grains/m³ of air, sometimes reaching peaks of 700–800/m³ of air. This depends on climate and on yearly variations in pollen production. It has been estimated that at the peak of the *Parietaria* pollen season in Naples a person can inhale more than 150 pollen grains with the tidal volume (35).

Pollen allergens

The pollen extracts of *P. officinalis* and *P. judaica* contain allergens recognized by IgE and IgG serum antibodies in patients with *Parietaria* allergy. Such

allergens are, to a large extent, immunologically cross-reactive (9, 11, 20, 22).

Pollen extracts of either species have been fractionated by several different methods (4, 7, 9, 18, 19, 20, 21, 23, 39, 41, 44, 52, 55, 57): the reported numbers of IgE-binding components are nine (*P. judaica*) and eight (*P. officinalis*) (Table 1). Individual differences in the array of IgE antibody specificities for allergens fractionated by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS–PAGE) have been assessed by comparing immunoblot patterns of individual sera (23, 41). *P. officinalis* and *P. judaica* pollen extracts contained a 10–15-kDa band on electrophoresis. This corresponded to a major allergen, since it was present in each individual pattern; from one to eight additional bands (18–90 kDa) appeared sporadically (in approximately 50% of the patterns).

The major allergens of *P. judaica* and *P. officinalis* have been purified from pollen extracts (2, 17, 21, 51, 54, 60, 61, 64). *Par o* I (54) and *Par j* I are glycoproteins: the first has an apparent mol. wt of 14.5 kDa. Reports on the mol. wt of the second are contradictory: there is general agreement on a mol. wt of 10–15 kDa by SDS–PAGE in reducing conditions (2, 17, 45, 61), while by size-exclusion high-performance liquid chromatography (HPLC) analysis (nonreducing conditions) the reported mol. wt varies from 13 to 26 kDa (2, 17, 45).

The sequence of 12 NH₂-terminal amino-acid residues of *Par o* I has been determined (54).

It is often impossible to purify allergens from pollen extracts as single molecular species: it has been suggested that this microheterogeneity, which is a serious limit to studies on structure/function relationship, may reflect events at the genetic level (allelic, isotypic, species variability) and/or the epigenetic (post-translational modifications of proteins, such as addition of carbohydrate chains) (51). Purified *Par j* I and *Par o* I preparations contain closely related molecular species different for charge and electrophoretic mobility (53, 54, 61). Polo et al. (61) report that charge heterogeneity of *Par j* I is decreased by deglycosylation.

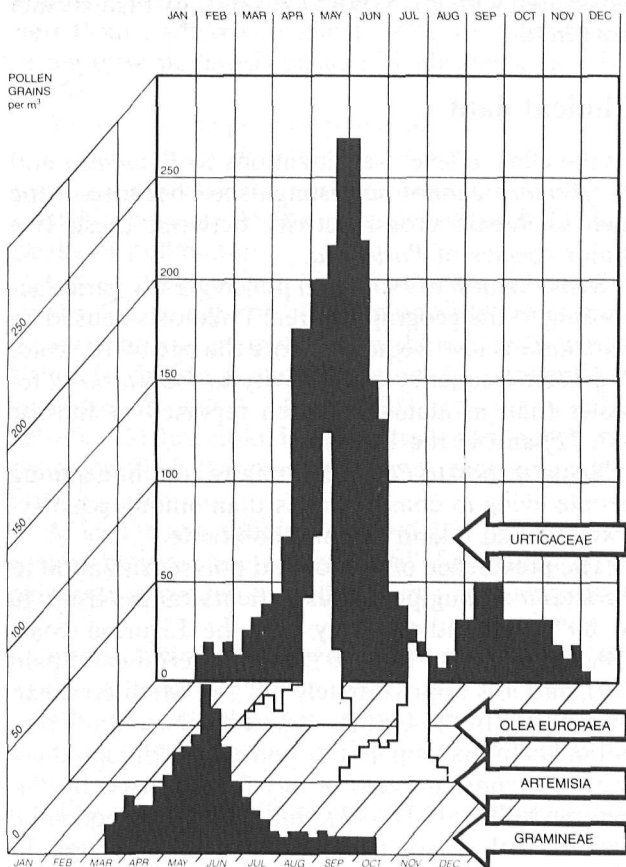


Fig. 4. Behavior of most important allergenic pollen grains in atmosphere of Naples (weekly mean values from daily pollen counts (pollen grains per m, air) in various years from 1 January 1980 to 31 December 1990). *Parietaria* pollen is included under Urticaceae family.

Table 1. Identification of allergens in the pollen extracts

Method of fractionation	IgE-binding components
<i>P. judaica</i>	
CRIE (18)	2 arcs (serum pool)
CRIE (43)	9 arcs (serum pool)
SDS–PAGE (immunoblotting) (41)	9 bands (10–80 kDa) (52 sera)
<i>P. officinalis</i>	
CRIE (55)	4 arcs (serum pool)
SDS–PAGE (immunoblotting) (23)	8 bands (8–90 kDa) (serum pool, 30 sera)

High-performance ion-exchange chromatography and immunoaffinity chromatography suggest that *Par j* I is a very unstable molecule which tends to fragment in solution. Several fragments obtained from *Par j* I have shown positivity toward an anti-*Par j* I monoclonal antibody, suggesting that they retain the structure of the allergenic determinant (5).

Recently, cDNA technology has been used to define the physicochemical and immunochemical structure of pollen allergens (11, 15, 49, 58, 63, 70, 71). Preliminary reports suggest that the recombinant allergens are individual members of families of proteins that are represented in the mixture of isoforms composing the natural allergen (58, 63).

Preliminary experiments to clone the cDNA genes specifying the major *P. judaica* allergen have been performed by Scotto d'Abusco et al. (68). A cDNA expression library constructed in the vector lambda gt 11 (66, 68) has been immunoscreened with rabbit *Par j* I antisera and with sera of allergic patients to identify clones with inserts encoding epitopes of the major allergen. A short cDNA insert expressing a fusion protein with *Par o* I/*Par j* I crossreactive epitope(s) for human and rabbit antibodies has been characterized.

The relationship between the physicochemical structure of *Par j* I and its IgE-binding ability has been studied by Polo et al. (61): their findings strongly suggest that the epitopes for the human IgE antibody are located mostly in the protein moiety and are conformational, as the IgE-binding activity was maintained after deglycosylation, but abolished by reduction and alkylation of the native allergen.

IgE-binding proteins from partially purified fractionation of the pollen extracts include three *P. judaica* polypeptides (20, 30, and 40 kDa by SDS-PAGE) crossreactive with *Par j* I. These were isolated by affinity chromatography with a mouse monoclonal antibody. Low molecular weight IgE-binding components were separated by gel filtration of *P. judaica* and *P. officinalis* pollen extracts (40, 65).

Leaves and stems of *P. judaica* have also been found to have allergenic quality (28).

Di Felice et al. (37) have reported the ability of *P. judaica* pollen extract to induce antigen-specific proliferation of peripheral blood mononuclear cells (BPMC) in *Parietaria* allergic and nonallergic subjects.

Allergenic crossreactivity

The genus *Parietaria* belongs to the family Urticaceae, which also comprises the genus *Urtica* (nettles), a genus which has no allergenic relevance. Despite their close taxonomic relationship, no antigenic crossreactivity exists between the two genera (9, 20, 22).

A common 10-kDa allergenic polypeptide in the pollen of four different *Parietaria* species has been reported. *Urtica dioica* pollen has revealed weak allergenic crossreactivity with them.

Crossreactivity analyses of pollen extracts suggest extensive homology between the allergens of the two main species of *Parietaria*, *P. judaica* and *P. officinalis* (20, 22).

Morus alba, a plant of the Moraceae family, belongs, like *P. judaica*, to the order Urticales. Some common allergenic determinants have been identified in *M. alba* and *P. judaica* extracts by RAST inhibition, crossed-radio immunoelectrophoresis (CRIE), and immunoblotting techniques (3).

Genetics

Several studies have shown that the antibody response of allergic patients to specific minor pollen allergens of *Lolium* and *Ambrosia* is strictly associated with particular HLA-D haplotypes (50). According to a preliminary survey of 43 HLA-D typed allergic subjects, high levels of IgE antibody response to the major allergen *Par o* I were positively associated with HLA-DR5 ($P = 0.02$ by Fisher exact test) (67).

Clinical data

At the clinical level, sensitizations to *P. judaica* and *P. officinalis* cannot be distinguished because of the high allergenic crossreactivity between these two major species of *Parietaria*.

Sensitization to *Parietaria* pollen greatly varies according to the geographic area. Pollinosis caused by *Parietaria* is less frequent before the age of 10 years. A greater frequency of reactivity to *Parietaria* in females than in males has been reported in Europe (32, 72) and in the US (48).

Sensitization to *Parietaria* is more common among people living in coastal towns than among country-dwellers and inland urban inhabitants.

The prevalence of mono- and polysensitization to *Parietaria* among pollinosis patients ranges from 40 to 80% in southern Italy and the Ligurian coast (30, 33), and from 10 to 60% in Mediterranean Spain (59), and it is approximately 25% in Mediterranean France (9). In the US, *Parietaria* has been known to botanists for as long as 180 years (1), although there were no reported cases of hay fever caused by *Parietaria* before 1971 (73). In 1988, 100 sequential patients with seasonal respiratory allergy were prick-tested with *P. judaica* and *P. officinalis* (48). Eight percent reacted, raising the question of whether these patients represent single cases or indicate a large unrecognized population sensitive to *Parietaria*.

Up to now, there have been no reports of *Pari-*

etaria pollen counts in the US. Moreover, in states such as Florida, where the sp. *P. floridiana* is found, no diagnostic extract has been obtainable (47).

In 1988, 13% of patients with respiratory allergy in the Southampton area (UK) were reported to be skin-positive to *Parietaria* (46). It may be that the *Parietaria* allergy has existed for years in the UK prior to the 1980s, as illustrated by the fact that many British *Parietaria*-positive patients had never traveled to the Mediterranean.

The extraordinarily long persistence in the atmosphere of *Parietaria* pollen in the Mediterranean area is responsible for a multiseasonal symptomatology. This can be almost perennial in some areas for some subjects. Even in areas where the pollination period is shorter, late asthmatic reaction (LAR) may challenge patients both in summer and in winter (24).

The clinical and immunological reactivity of patients allergic to multiple-pollen spp. such as *Parietaria* has not been sufficiently investigated up to now (10, 25).

Bronchial asthma, almost always associated with rhinoconjunctivitis, is present in 52% of the monosensitized *Parietaria* patients in central and southern Italy, reaching a peak of 60% in Naples and Rome, whereas it affects 40% of patients suffering from pollinosis caused by Gramineae (30–33, 38).

Because of the poor response of specific hyposensitization therapy, *Parietaria* hay fever is often a frustrating experience for both patients and clinicians, possibly because of the long period and the high peaks of pollination.

Up to now, only a few double-blind, placebo-controlled studies on the immunotherapy of *Parietaria* rhinoconjunctivitis and asthma have been published (8, 56). In one investigation (56), a significant increase in nasal ($P=0.029$) and conjunctival ($P=0.003$) threshold doses was recorded with a partially purified *Parietaria* pollen extract conjugated with alginate.

A significant difference ($P<0.01$) in symptom scores between the placebo and the treated group has been recorded in a short-term immunotherapy trial (7).

In conclusion, the very effective sensitizing properties of *Parietaria* pollen, which acts for long periods of time over the year on sensitized patients, are due not only to irritant pollutants present in urban areas, but also to the following factors:

- 1) The plant is distributed widely and abundantly in urban areas.
- 2) The pollen grains are small (12–16 μm), light, and spherical, qualities that favor wind pollination.
- 3) The pollen is produced in large quantities and its concentration in the air may reach high levels.

- 4) The pollen is sufficiently buoyant.
- 5) Impurities are present that cause irritation of the respiratory mucosa.

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