

Inhalant Allergens in Portugal

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Keywords

Aeroallergens · Allergen exposure · Allergen sensitization · Allergy · Portugal

Abstract

This review aims to present in a simple manner the work performed in Portugal regarding the identification of the most prevalent aeroallergens in the country and the sensitization levels in Portuguese patients. Much of the data was summarized in tables and illustrated on maps, enabling the community of clinicians, researchers, and patient organizations to access the knowledge about the research performed. This study provides an overview about the distribution of aeroallergens in Portugal, signaling regions and critical periods of exposure of the sensitized population. The illustrated data can help the community of allergy specialists to view the temporal and spatial distribution of aeroallergens across the country. In addition, this information can guide clinicians to select the most appropriate allergens for allergy diagnostic testing, treatment, and allergen avoidance.

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Introduction

The allergens represent an important component of air quality and may have a detrimental impact on health, particularly on respiratory allergic diseases [1]. Allergic

rhinitis is an example of allergic disease commonly associated with exposure to aeroallergens, where the sensitization level and the resulting symptoms are correlated with exposure [2]. Among the known allergens, house dust mites are the most common, followed by fungi, pollens and animal epithelia. The occurrence frequency of those allergens in a given region and the sensitization degree of the population exposed depend on geoclimatic conditions, vegetation and the urban or rural environment [3].

Aerobiological studies conducted in several countries have revealed the pollen and fungal spore content in the atmosphere and the seasonal patterns of these common bioaerosols. Their regular monitoring is of major importance due to their detrimental effects as human allergens. Knowledge of pollen and spore dispersion trends combined with clinical data represents an important tool for the prevention of respiratory allergic diseases, improving diagnostics and treatment [4].

Allergen sensitization also influences significantly disease development and severity and should be considered during a treatment. Increased allergen exposure can lead to sensitization in genetically susceptible individuals, which might increase the risk of asthma and the development of other allergic diseases [5]. Sensitization can occur at any stage of life, and the likelihood of its occurrence is dependent on different factors besides genetic susceptibility [6]. There is evidence of early sensitization to inhalant allergens during pregnancy, not necessarily linked to

the clinical history of the family concerning type I allergy [7, 8]. The aeroallergen sensitization prevalence changes from region to region and reflects differences in exposure to several risk factors [9]. The European Community Respiratory Health Survey study showed that the aeroallergen sensitization prevalence, common in young adults, was greater in developed countries [10, 11]. Similar patterns in 8- to 12-year-old children were observed in the International Study of Asthma and Allergies in Childhood [12].

The type of allergic sensitization is also crucial for respiratory allergic disease diagnostics and treatment [13]. Nowadays, allergy testing comprises several methods such as skin prick tests (SPTs) and blood tests for allergen-specific IgE. They are usually based on the use of extracts from allergens to which the population is normally exposed. Skin prick testing in particular is the recommended standard technique for detecting type I sensitization against inhalant allergens, providing a feasible method in epidemiological studies as it determines trends in sensitization rates or regional differences [14, 15]. Allergen extracts, however, represent a heterogeneous mixture of allergenic and nonallergenic components from a given allergenic source. Furthermore, standardization which ensures consistency among extract composition is difficult to achieve, especially for fungal [16] and house dust mite allergen extracts [17].

Presently, the allergen extracts are being gradually replaced by molecule-based products and implemented in clinical practice. Molecular diagnosis using well-characterized purified allergen components from a natural source or produced as recombinant molecules allows clinicians to obtain more accurate sensitization profiles of each atopic patient and to identify the allergens or epitopes responsible for symptoms [18, 19]. The recent methodological approaches have also involved aerobiology. Currently, a molecular approach to improve the detection and characterization of aeroallergens is being developed and improved. Although the direct measurement of allergens is nowadays possible, it is however expensive, and it has not been applied in practice yet [20]. Considering all the above constraints, current aerobiological monitoring systems based on sampling and identification techniques of pollen and fungal spores are still quite remarkable from a clinical point of view.

Taking into account the investigation carried out in Portugal regarding the identification of aeroallergens and sensitization rates, mostly published in Portuguese, this review aims to present the results of these works in a simplified form to the scientific community.

Materials and Methods

This review presents the results from studies conducted in Portugal, published in national and international journals between the years 1991 and 2015. Articles were searched through the electronic databases Online Knowledge Library (B-On), Scientific Electronic Library Online (SciELO) and Vésila – Digital Library (Biblioteca Digital, <http://biblioteca.versila.com/>). Some works published in the *Portuguese Journal of Immunoallergy* (*Revista Portuguesa de Imunoalergologia*) before the year 2000 were not accessible in digital format and for that reason were consulted in a paper form. The following terms (in Portuguese and English) were used separately and in combinations for search: aeroallergens; allergen exposure; sensitization; skin tests; molecular allergy; molecular diagnostics; Portugal. Peer-reviewed and non-peer-reviewed articles were considered. The Portuguese Aerobiology Network website was also consulted. The information given by master theses, doctoral theses, and conference presentations compiled in abstract books were also included. Digital dissertations and theses were found in the Scientific Repository of Open Access from Portugal and in the Digital Deposit of Theses and Dissertations (<http://dited.bn.pt/>).

Pollen Data

In order to provide a simple and concise information, pollen aeroallergens were organized according to López [3] and Pablos et al. [21] with modifications, which finally resulted in the following allergen categorization:

- (a) trees (pollinating mostly in late winter and early spring);
- (b) trees (pollinating mostly in late spring and summer);
- (c) grasses (pollinating mostly in spring and early summer);
- (d) weeds (pollinating mostly in spring and early summer);
- (e) weeds (beginning pollination in spring and extending throughout the summer and early autumn).

Data are broken down by season and city or region (for details on botanical definitions, consult the online suppl. material; see www.karger.com/doi/10.1159/000458150 for all online suppl. material).

Sensitization Data

The majority of analyzed aeroallergens in this review are currently used in SPTs at a national level. However, only those reported in the Portuguese surveys were considered in the present work.

The SPTs are still considered the gold method for the allergy diagnostics and include the following allergen set: trees: long-leaved wattle (*Acacia longifolia*), birch (*Betula verrucosa*), chestnut (*Castanea sativa*), Arizona cypress (*Cupressus arizonica*), walnut (*Juglans regia*), London plane tree (*Platanus acerifolia*), pine (*Pinus* sp.), olive (*Olea europaea*), oak (*Quercus robur*), willow (*Salix* sp.); grass mixture: orchard grass (*Dactylis glomerata*), meadow fescue (*Festuca pratensis*), meadow soft grass (*Holcus lanatus*), perennial rye grass (*Lolium perenne*), timothy grass (*Phleum pratense*), smooth meadow grass (*Poa pratensis*); weeds: mugwort (*Artemisia vulgaris*), goosefoot (*Chenopodium album*), pellitory (*Parietaria judaica*), wall pellitory (*Parietaria officinalis*), English plantain (*Plantago lanceolata*), Russian thistle (*Salsola kali*); fungi: *Alternaria alternata*, *Aspergillus fumigatus*, *Candida albicans*, *Cladosporium herbarum*, *Penicillium notatum*; house dust mites: *Acarus siro*, *Blomia tropicalis*, *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, *Euroglyphus maynei*, *Glycyphagus domesticus*, *Lepi-*

doglyphus destructor, *Tyrophagus putrescentiae*; insects (cockroach): *Blatta orientalis*, *Blatella germanica*; animal epithelium: cat and dog. Aeroallergen sensitization data were also obtained from studies performed in Portugal. It is assumed that there is a direct relationship between the allergen exposure and sensitization development to a particular allergen. The inclusion criteria were elaborated on the basis of allergen sensitization prevalence rates by region and/or by age group and the use of SPTs. In turn, the exclusion criteria were based on case studies and lack of information about aeroallergen sensitization rates by region and/or by age groups.

Statistical Analysis

The relationship between the annual pollen and fungal spores' concentrations observed in Portugal and the sensitization prevalences was analyzed. The nonnormality of the variables, tested with the Shapiro-Wilk test, implied the use of the Spearman rank correlation test. Statistical analysis was carried out using IBM SPSS Statistics 20 software.

Results

The distribution of pollen allergens, fungi, and house dust mites in various regions of the country is shown in Figures 1 and 2. The maps show the occurrence of different aeroallergens in the Portuguese districts or regions (north, center, or south) according to the research group descriptions (for more details regarding the vegetation landscape and bioclimatic characteristics of the Portuguese territory, consult the online suppl. material).

Tables 1 and 2 summarize data relating to the pollen and fungal spore indices by region and the relative distribution of the most common aeroallergens. They also show the sensitization rates determined by several research groups and the allergic pathologies manifested by the sensitized populations.

Trees (Pollinating in Late Winter and Early Spring)

Cypress

During the winter months, cypress pollen prevails throughout the country. The cypress belongs to the Cupressaceae family which comprises the genus *Cupressus*, widely spread in the Mediterranean area [22]. The sensitization rates to this pollen type in Portugal reached 5.1% [15]. Cupressaceae pollen allergy has increased in the Mediterranean region in recent decades [23, 24] and constitutes one of the few causes of respiratory allergy of winter. The increasing epidemiological impact of pollinosis induced by Cupressaceae plants is related to the increasing use of these plants for gardening and reforestation [25].

Betulaceae sp. (Betulaceae Family), *Fagales sp. (Fagaceae Family)*, and *Pinus (Pinaceae Family)*

Betulaceae pollen was detected in Porto from January to February, extending its occurrence until April [26]. From late winter to early spring, the *Corylus* (hazel) pollen type was observed in Funchal, Madeira [27]. In spring, *Fagaceae* and *Pinaceae* pollen types are dominant in mainland Portugal.

In northern, central, and eastern Europe, tree pollen including members of the *Betulaceae* and *Fagaceae* families are important sources of allergens [28]. *Betula* and *Quercus* spp. are representative of the temperate Eurosiberian region [29]. *Betula* sp. represents one of the most important allergenic pollen types that causes hay fever and asthma in the spring. Birch pollen typically peaks in May in northern Europe, whereas in southern Europe the birch pollen concentration generally peaks in April [30]. The peak time of birch pollen was observed earlier in North Portugal (January–February).

Corylus sp. (hazel) pollen is also considered as an important aeroallergen in early spring in central Europe. The onset of the hazel pollen season was related to the mean maximum temperature during late December [31]. Other authors reported that the flowering season of *Corylus* sp. lasted from late January to early March, with the full bloom occurring in February [32].

As regards the *Pinaceae* family which includes the genus *Pinus*, it is found from the Arctic to the southern hemisphere. Owing to their pollen size and weight, the pines are only occasionally implicated in allergy [33].

Plane Tree (Platanus)

Between March and April *Platanus* sp. normally records its highest counts in Portugal [26, 34–36]. Species of the *Platanus* genus such as *Platanus hispanica* have been used for ornamental purposes, also in the Portuguese territory [37]. However, this pollen type has been detected as an important cause of pollinosis in several cities of the Iberian Peninsula [38–40]. The elicitation of seasonal asthmatic symptomatology to plane tree pollen occurs during its flowering period that occurs mainly during the spring months [41].

Trees (Pollinating in Late Spring and Summer)

Fagales sp. (Fagaceae Family) and *Olive (Oleaceae Family)*

During this entire period *Oleaceae* and *Castanea* (chestnut) pollen types were found in the northern and

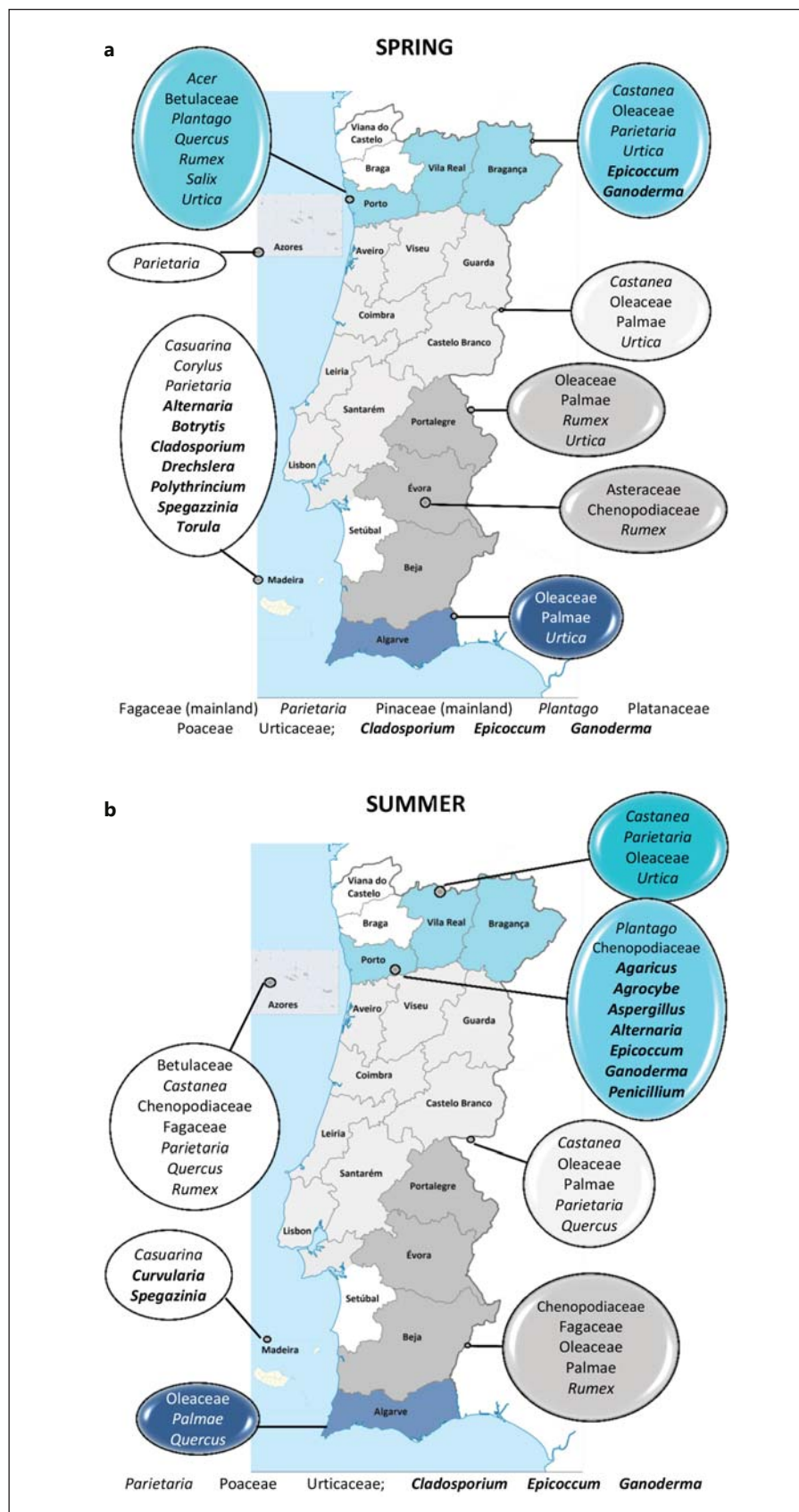


Fig. 1. a–d Distribution of pollen and fungal aeroallergens in Portugal, by season of the year. The most frequent aeroallergens that occur throughout the Portuguese territory are indicated below each map. The genera of fungal spores are in bold.

(Figure continued on next page.)

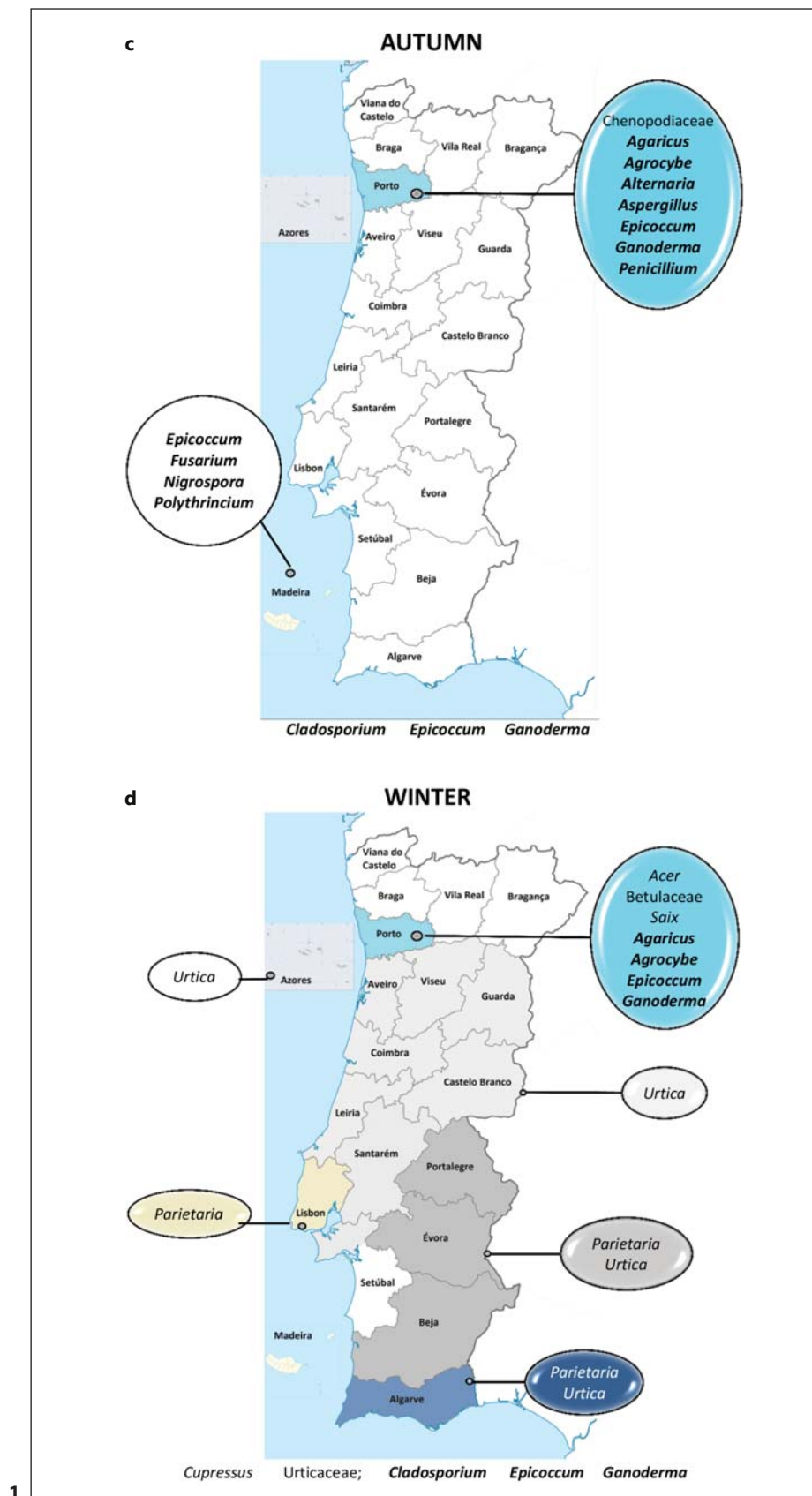
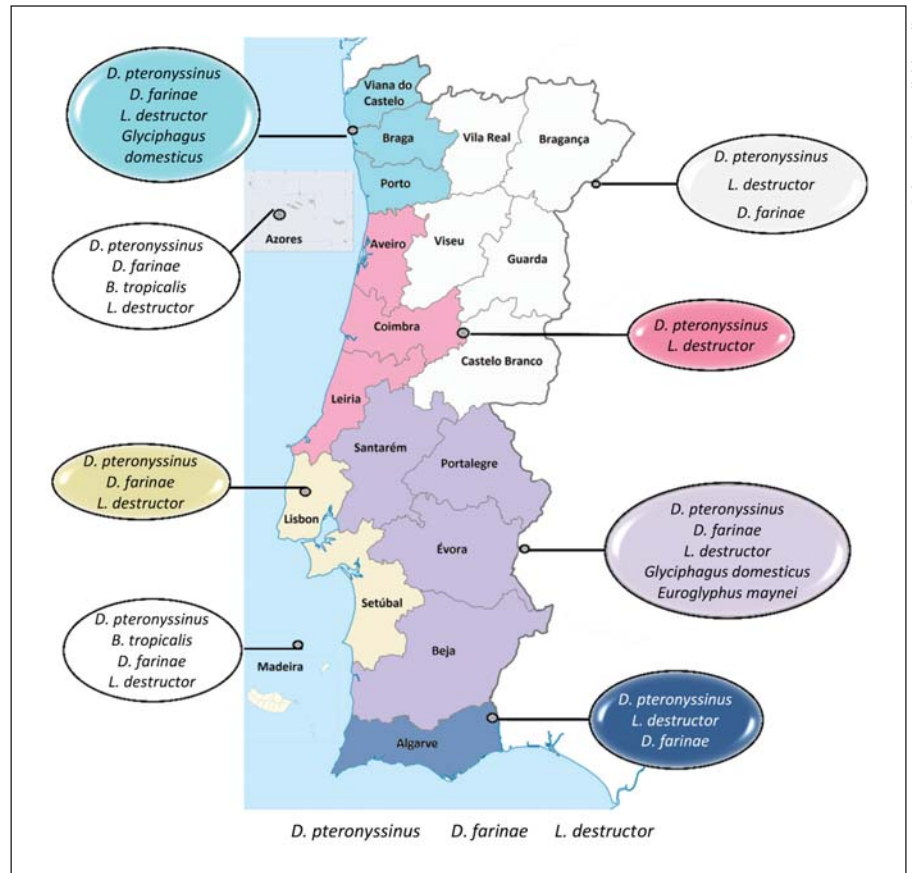


Fig. 2. Distribution of the most prevalent house dust mite allergens in Portugal. The most frequent aeroallergens that occur throughout the Portuguese territory are indicated below the map.



central regions of Portugal. The pollen of Oleaceae also appears in southern regions. The palm tree (family Palmae) is another taxon detectable in central and southern regions [26, 34, 35, 42–44].

During the summer *Quercus* (oak) pollen appeared mostly in Portimão (Algarve) and Ponta Delgada (Azores) cities. This pollen type occurs earlier (April) in Porto [26]. Further, Fagaceae and Oleaceae pollen prevailed in the Beja region (Baixo Alentejo) [35]. Fagaceae, Betulaceae and *Castanea* sp. are dominant pollen types in summer in Ponta Delgada city, while Australian pine tree (*Casuarina*) pollen prevailed in Funchal, Madeira [27].

In springtime, tree pollen grains of the Fagales order, which includes the *Quercus* genus, is a main allergen source in the temperate zone of the northern hemisphere [45]. Several other genera of the Fagaceae family pollinate during the spring and also during early summer in some European sites [45].

In the Oleaceae family, the most allergenic pollen is produced by *Olea europaea*, the olive tree, which in the Mediterranean area has been recognized as being one of

the most important causes of seasonal respiratory allergy [45]. Ladeira et al. [46] found that the content of the major allergens of olive (Ole e 1) in Évora atmosphere was directly correlated with the pollen counts of Oleaceae. The olive pollination season lasts from April to the end of July and can cause severe symptoms (rhinoconjunctivitis and/or bronchial asthma) [47].

The flowering of chestnut (*Castanea*) usually lasts about 6 weeks. *Castanea* begins flowering in late April–May and finishes flowering in late September [32].

Sensitization Rates to Tree Pollen Aeroallergens Betulaceae Species and Olive (Oleaceae Family)

Sensitization to Oleaceae reached 64.7% ($n = 34$) in the population of patients from Lisbon and southern regions. Lower positive levels were obtained for birch pollen with 29.4% ($n = 34$) [48]. In Coimbra the monosensitization to birch pollen reached 6.8% ($n = 275$) [9]. In the case of birch, it was found that Bet v 2 and Bet v 4 molecular allergens were involved in the sensitization [48]. The *Olea europaea* pollen sensitization level reached 27.5% ($n =$

Table 1. Average pollen indices in the Portuguese regions, relative distribution of the most frequent allergenic pollen types and sensitization rates

Region	Average pollen concentrations		Allergenic pollen		Sensitization		Ref.	
	pollen/m ³ air/year	comments	Ref.	most frequent types	%	prevalence, %		
North								
Entre Douro e Minho	13,678	Data from 2003 to 2013	43	Urticaceae	21	English plantain/ <i>Plantago lanceolata</i> (35%; n = 472)	Urticaria and/or angioedema (38% female; average age = 34.8 years)	64
				Poaceae	15.1			
				<i>Quercus</i>	13.8			
				Pinaceae	10.7			
				<i>Urtica membranacea</i>	10.5			
				<i>Parietaria</i>	10.2			
				Cupressaceae	7			
				<i>Platanus hispanica</i>	5			
				Betulaceae	5			
				<i>Olea europaea</i>	4			
				<i>Plantago</i>	3.2			
				<i>Castanea sativa</i>	3			
				Myrtaceae	3			
<i>Rumex</i>	3							
Amaranthaceae	2							
		1						
Porto	9,500	Data from 2003 to 2006	35	Urticaceae	17.2	Pellitory/ <i>Parietaria</i> (34.2%; n = 415)	Sensitization to pollen (no information regarding gender or age)	62
	10,315	obtained during the spring	54	Pinaceae	15 ^a	Pellitory/ <i>P. judaica</i> (84.5%; n = 120)		
	12,802	Data from 2005 to 2007	42	Poaceae	16.7	Pellitory/ <i>P. officinalis</i> (8.5%; n = 120)		
		Data from 2006 to 2009		<i>Quercus</i>	16.6			
				<i>Olea europaea</i>	16.4			
			<i>Platanus hispanica</i>	6.4				
				6.0				
Center								
Coimbra	7,841	Data from 2003 to 2006	35	Urticaceae	30 ^b	Timothy grass (18.6%; n = 275)	65.1% female; average age = 46 years	9
	15,935	obtained during the spring	42	<i>Olea europaea</i>	12.1	Grasses (18.2%; n = 275)		
		Data from 2006 to 2009		Pinaceae	22.7	Pellitory/ <i>Parietaria</i> (9.6%; n = 275)		
				Poaceae	21.8	Olive/ <i>Olea</i> (9.6%; n = 275)		
				Cupressaceae	12.6	Mugwort/ <i>Artemisia</i> (9.6%; n = 275)		
				<i>Quercus</i>	8	Birch/ <i>Betula</i> (6.8%; n = 275)		
					7.6			
Cova da Beira (Castelo Branco)	-	-	-	-	-	Grasses (64.7%; n = 686) ^c	Rhinitis and nonallergic rhinitis, some patients revealed asthma, sinusitis, pharyngitis, urticaria and drug allergy; ^c (66% female; average age = 33 years) Patients observed for suspected allergic symptoms ^{d, f} (€15 years old) ^d (59.4% female; average age = 26.5 years) ^f Asthma symptoms (elderly with average age = 72 years; young adults with average age = 29 years) ^e	57 ^c 49 ^d 63 ^e 58 ^f
						Grasses (44.9%; n = 1,096) ^d		
						<i>P. judaica</i> (70.8%; n = 24) (in young adults) ^e		
						<i>P. judaica</i> (41.2%; n = 17) (in elderly) ^c		
						Olive/ <i>Olea europaea</i> (27.5%; n = 1,096) ^d		
						<i>P. judaica</i> (23.4%; n = 1,096) ^d		
						Olive/ <i>Olea europaea</i> (23.3–30.2%; n = 1,096) ^f		
						Mugwort/ <i>Artemisia</i> (17.6%; n = 1,096) ^d		
						Pellitory/ <i>P. judaica</i> (14–29.4%; n = 1,096) ^f		
						Plane/ <i>Platanus acerifolia</i> (11.4%; n = 1,096) ^d		
					English plantain/ <i>Plantago</i> (10.6%; n = 1,096) ^d			

Table 1 (continued)

Region	Average pollen concentrations		Allergenic pollen		Sensitization		Ref.
	pollen/m ³ air/year	comments	Ref.	most frequent types	%	prevalence, %	
Lisbon	40,765	Data from 2003 to 2006 obtained during the spring	35	Urticaceae	30 ^g	Grasses (97%; n = 34)	Allergic rhinitis and/or bronchial asthma (56% female; 4–50 years old) 48
				<i>Urtica membranacea</i>	30	Olive/Oleaceae (64.7%; n = 34)	
				Cupressaceae	20.1	Plane/ <i>Platanus</i> (52.9%; n = 34)	
	40,749	Data from 2002 to 2013	114	<i>Olea europaea</i>	12.5	Russian thistle/ <i>Salsola</i> (52.9%; n = 34)	
	44,035	Data from 2006 to 2009	42	<i>Quercus</i>	12	Birch/ <i>Betula</i> (29.4%; n = 34)	
				<i>Parietaria</i>	11.3		
				Poaceae	10.2		
				<i>Platanus hispanica</i>	9.4		
				Pinaceae	6.0		
				Myrtaceae	2		
South	54,366	Data from 2003 to 2006 obtained during the spring	35	<i>Quercus</i> sp.	27.9	Orchard grass/ <i>Dactylis</i> (94%) ^j	Rhinitis or rhinitis and asthma (71.42% female; 1–50 years old) ⁱ 50 ⁱ
				Poaceae	26.2	Grasses/Poaceae (85.71%; n = 27) ⁱ	
				<i>Olea europaea</i>	11.2	Barley/ <i>Hordeum</i> (75%) ^j	
				Urticaceae	9.2	Timothy grass/ <i>Phleum</i> (72%) ^j	
					9 ^h	Meadow grass/ <i>Poa</i> (69%) ^j	
				<i>P. hispanica</i>	9.1	Oat/ <i>Avena</i> (66%) ^j	
				Cupressaceae	4.2	Meadow fescue/ <i>Festuca</i> (63%) ^j	
						Wheat/ <i>Triticum</i> (59%) ^j	
						Rye/ <i>Secale</i> (53%) ^j	
						Perennial rye grass/ <i>Lolium</i> (50%) ^j	
Beja	76,232	Data from 2006 to 2009	42		–	Olive/Oleaceae (39.2%; n = 27) ⁱ	Allergic rhinitis, conjunctivitis, asthma and rhinitis (32 children 18 years old; average age = 5.3±1.44 years) ^j 59 ^j
	12,722	Data from 2005 to 2011 only for grass (Poaceae)	115		–	Grasses/Poaceae (38%; n = 32) ⁱ	
					–	Maize/ <i>Zea</i> (31%) ^j	
					–	English plantain/ <i>Plantago</i> (21.42%; n = 27) ⁱ	
					–	Goosefoot/ <i>Chenopodium</i> (14.28%; n = 27) ⁱ	
					–	Plane/ <i>Platanus</i> (14.28%; n = 27) ^j	
	40,119	Data from January 2003 to January 2005	36	Poaceae	40		
				<i>Olea europaea</i>	16.8		
				<i>Quercus</i>	15.8		
				Cupressaceae	5.2		
Algarve	38,887	Data from 2002 to 2013 obtained from Portimão station	44	<i>Olea europaea</i>	35.7		–
				<i>Quercus</i>	12.6		
				Poaceae	12.3		
				Urticaceae	10		
				<i>Urtica membranacea</i>	8.6		
				Cupressaceae	5		
				<i>Plantago</i>	4		
				Areaceae; Amaranthaceae	3		
				Pinaceae	2		
				<i>Rumex</i>	1		

Table 1 (continued)

Region	Average pollen concentrations		Allergenic pollen		Sensitization		Ref.
	pollen/m ³ air/year	comments	Ref.	most frequent types	%	prevalence, %	
Portimão	30,989	Data from 2003 to 2006 obtained during the spring	35	<i>Olea europaea</i> Poaceae <i>Quercus</i> sp. Urticaceae	40.8 15.2 14.4 10 ¹	35 - - 55 ¹	- - - -
				<i>Plantago</i> sp. Chenopodiaceae- Amaranthaceae	9.9 4.8 3.0		
Islands							
Azores	7,043	Data from 2006 to 2009	42	<i>Urtica membranacea</i> Poaceae Cupressaceae Pinaceae <i>Parietaria/Urtica</i>	27.4 13.0 11.0 9.9 9.2	42 - - - -	- - - -
Madeira	1,635	Data from 2003 to 2008, obtained from Funchal station	27	Urticaceae	20.6	27	
	3,894	Data from 2006 to 2009	42	Poaceae Cupressaceae Pinaceae Myrtaceae <i>Platanus</i> Chenopodiaceae- Amaranthaceae	16.2 13.6 9.0 5.9 2.6 1.3	Grasses (17.2%; n = 116) Pellitory/ <i>Parietaria</i> (7.5%; n = 116) Plane/ <i>Platanus</i> (5.2%; n = 116) Pine/ <i>Pinus</i> (2.6%; n = 116) Timothy grass/ <i>Phleum</i> (1.7%; n = 116) Goosefoot/ <i>Chenopodium</i> (1.7%; n = 116)	Allergic respiratory disease (50% female; average age = 13.0±8.6 years; 4–44 years old)
Portugal							
				Grasses (34.4%) Olive/ <i>Olea</i> (21.3%) Pellitory/ <i>Parietaria</i> (17.5%) Mugwort/ <i>Artemisia</i> (16.3%) Ragweed/ <i>Ambrosia</i> (12.4%) Hazel/ <i>Corylus</i> (7.4%) Plane/ <i>Platanus</i> (7.0%) Alder/ <i>Alnus</i> (6.8%) Birch/ <i>Betula</i> (6.8%) Cypress/ <i>Cupressus</i> (5.1%)		-	15

The allergic pathologies, gender, and average age of the patients are also shown. Pairing of data and reference is indicated with superscript letters.

Table 2. Average fungal spore indices in the Portuguese regions, relative distribution of the most frequent allergenic fungi and sensitization rates

Region	Average spore concentration		Ref.	Allergenic fungi		Sensitization		Ref.		
	spores/m ³ air/year	spores/m ³ air/day		comments	most frequent	%	Ref.		prevalence, %	allergic pathologies manifested by the sensitized population
North										
Porto	-	402.7	Data from January 1 to December 31, 2003	74	<i>Cladosporium</i> <i>Ganoderma</i> Aspergillaceae <i>Ustilago</i> <i>Coprinus</i> <i>Alternaria</i> <i>Botrytis</i> <i>Cladosporium</i>	74.5 11.7 2.9 2.5 1.4 1.3 1.3	74	-	-	
	2-2,198 2-2,299	403 412	Data from January 2003 to December 2004	81	<i>Cladosporium cladosporioides</i> <i>Ganoderma</i>	71 59.5 30 14 81 3.4 80 6 68 1.1 80 1 81 5.6 80 3 81 1.2 80 1.2 80 1.0 80 0.9 80	81 80 68 81 80 80 68 80 80 80 80			
	-	531	Data from 2005 to 2007	80	<i>Alternaria</i>					
	300	-	Data from January to December of 2005	68	<i>Agaricus</i> Aspergillaceae <i>Agroclype</i> Smuts Rusts <i>Aspergillus/Penicillium</i>					
Center										
Coimbra	323	-	Data from January to December 2005	68	<i>Cladosporium cladosporioides</i> <i>Alternaria</i>	33 7	68	Aspergillus fumigatus (46%; n = 340) Cladosporium herbarum (38%; n = 340) Aspergillus niger (36%; n = 340) Alternaria tenuis (34%; n = 340) Penicillium roqueforti (32%; n = 340) Fusarium moniliforme (31%; n = 340) Curvularia spicifera (29%; n = 340) Candida albicans (28%; n = 340) Rhizopus nigricans (26%; n = 340) Alternaria (8.9%; n = 275) ^a	18-75 years old ^a Asthma, rhinitis, chronic sinusitis, conjunctivitis, mycosis, nasal polyposis (20-60 years old; average age = 37 years) ^b	9 ^a 88 ^b
Cova da Beira (Castelo Branco)	-	-	-	-	-	-	-	Fungi (23.5%; n = 686) ^c Fungi (11.2%; n = 1,096) ^d Fungi (8.4%; n = 835) ^e	Rhinitis and nonallergic rhinitis, some patients revealed asthma, sinusitis, pharyngitis, urticaria and drug allergy (≥18 years old) ^c 41% female; average age = 30.5 years ^d 58.3% female; average age = 26.4±16.9 years ^e	57 ^c 49 ^d 89 ^e
Lisbon	-	1.803	Data from January to December 2013	116	<i>Cladosporium cladosporioides</i> <i>Cladosporium herbarum</i> <i>Alternaria</i>	54 4 1	116	-	-	-
	312	-	Data from January to December 2005	68	-	-	68	-	-	-

Table 2 (continued)

Region	Average spore concentration		Allergenic fungi		Sensitization		Ref.
	spores/m ³ air/year	spores/m ³ air/day	spores/m ³ comments	Ref.	most frequent	%	Ref.
South							
Évora	463	-	Data from January to December 2005	68	<i>Cladosporium herbarum</i>	40	68
Beja	-	500–2,000	Data from April 2012 to July 2014	117	<i>Alternaria</i>	3	-
Portimão	470	-	Data from January to December 2005	68	<i>Cladosporium herbarum</i> <i>Alternaria</i>	51 3	68
Islands							
Azores	-	-	-	-	-	-	-
Madeira	2,931	-	Aerobiology of anamorphic fungal spores from 2003 to 2008	70	<i>Cladosporium</i> <i>Alternaria</i> <i>Fusarium</i> <i>Torula</i> <i>Botrytis</i>	78 5.4 4.7 3.9 1.9	70
Portugal							
					<i>Cladosporium herbarum</i> <i>Cladosporium cladosporioides</i> Ascosporos <i>Coprinus</i> <i>Agaricus</i> <i>Alternaria</i> <i>Leptosphaeria</i> <i>Arthrinium</i> Uredosporos <i>Botrytis</i>	50.8 11.2 5.9 5.2 4.0 3.3 2.7 2.2 2.1 2.0	68
					<i>Cladosporium</i> (10.3%) <i>Alternaria</i> (8.5%) <i>Aspergillus</i> (6.9%)	-	15

The allergic pathologies, gender, and average age of the patients are also shown. Pairing of data and reference is indicated with superscript letters.

1,096) in a population of Cova da Beira (Castelo Branco), as determined by Loureiro et al. [49]. In Évora, the sensitization prevalence to Oleaceae pollen type reached 39.2% ($n = 27$) [50]. The sensitization to *Olea* pollen allergens is frequently associated with other atopic sensitizations, such as allergy to grasses (discussed further). In fact, it is often difficult to know whether sensitization to grasses prevails or whether it is olive that prevails. Moreover, polysensitization to olive pollen in association with other allergens is more frequent than monosensitization [47].

With respect to the Oleaceae family, 4 allergens were identified and characterized in Portuguese olive cultivars, namely Ole e 1, Ole e 2, Ole e 5, and Ole e 9, with Ole e 1 being predominant. The reactivity of pollen extracts containing these allergens against sera from patients sensitized to *Olea europaea* pollen was verified by Morales et al. [51] and Ribeiro et al. [52]. Olive pollinosis is clinically characterized by oculorhinitis and/or bronchial asthma, with a higher prevalence of rhinoconjunctival symptomatology [53]. A particular aspect of olive allergy is that in subjects with sensitization to the allergens of this pollen the clinical symptoms are frequently not limited to the pollination season (May–June) but are present all year round [22].

Sensitization to Other Pollen Aeroallergens

Maple (*Acer negundo*) and Willow (*Salix babylonica*)

Ribeiro et al. [54] identified a probable sensitization to pollen of *Acer negundo* and *Salix babylonica* in the Porto region, noting a positive correlation between pollen concentrations and hospital admissions due to asthma and dyspnea. Both pollen types prevailed from January to April in Porto city at high to moderate allergic risk levels. Taking into account the increasing occurrence of these trees capable of producing large amounts of pollen mostly released at the beginning of the pollen season [54], the population's exposure risk to these aeroallergens can greatly increase in the Porto region.

Grasses (Pollinating Mostly in Spring and Early Summer)

Nettle (Urtica)

The pollen of the Urticaceae family is significantly represented in the pollen spectrum of the Portuguese districts. The main pollination period of *Urtica* is between May and June in the northern regions of Portugal, and between the end of January and May in the southern regions [55]. *Urtica* pollen type was also observed in winter in the southern-central regions of the country [34, 42], as

well as in Ponta Delgada. The highest levels of *Urtica* pollen were observed in Porto, Coimbra and Lisbon, and the lowest in the Algarve region [55].

Grasses (Poaceae Family)

Poaceae pollen occurs throughout the country. Poaceae make the second most abundant pollen type in Porto, to be found mainly between April and August [56]. In the atmosphere of Beja, the Poaceae pollen type is the most prevalent, especially between May and June [36]. In Funchal (Madeira), the prevalence of the Poaceae pollen type (16.02%) is preceded by Urticaceae (20.64%) [27].

In northern, central and eastern Europe, the main grass flowering period usually starts at the beginning of May and ends in July. In the Mediterranean area, grass pollination occurs about 2–3 weeks earlier at sea level than in mountainous regions [28].

Sensitization Rates to Grasses

Grass pollen is the most important cause of pollinosis throughout Europe and also in the Mediterranean area [22]. Loureiro et al. [49] determined the prevalence of sensitization to grasses in a sensitized allergic population in the Cova da Beira region (Castelo Branco) to be 44.9% ($n = 1,096$). In the population with rhinitis referred to the Hospital da Cova da Beira between 2003 to 2007, the sensitization to grasses reached 64.7% ($n = 686$) [57]. A previous survey in Cova da Beira over a 5-year period (1995–2000) involving patients with positive STPs ($n = 1,096$) revealed a sensitization rate to grasses of 51.3% [58].

In a study performed by Chambel et al. [48] on a population of patients from the Immunoallergology Unit of Dona Estefânia Hospital – Hospital Center of Lisbon Central, high sensitizations rates were found to grass pollen allergens (97%; $n = 34$). The reactivity against Par j 2 allergen in particular and also to Phl p 1, Phl p 4, Phl p 5, and Cyn d 1 was observed in more than 50% of the patients studied. In the Porto region, the antigenic and allergenic profiles from 8 common grass species were investigated using immunochemical techniques. In almost all pollen extracts, the IgE binding proteins of 12–13 kDa were detected and considered to be the potential causal agent of the allergic respiratory diseases in atopic patients [56].

In turn, Diamantino et al. [59] performed a retrospective study of the clinical files of children in the pediatric age at the Hospital of Espírito Santo Évora between January 2002 and June 2005. The study included children with an age under 8 years with pollen sensitization. All children were sensitized to grass pollen, 38% ($n = 32$) of them

were monosensitized. The frequency order of grass pollen sensitization was orchard grass/*Dactylis* (94%), barley/*Hordeum* (75%), timothy grass/*Phleum* (72%), meadow grass/*Poa* (69%), oat/*Avena* (66%), meadow fescue/*Festuca* (63%), wheat/*Triticum* (59%), rye/*Secale* (53%), perennial rye grass/*Lolium* (50%), and maize/*Zea* (31%) [59].

In Madeira, the grass sensitization prevalence in the population was approximately 17.2% ($n = 116$), followed by timothy grass (*Phleum pratense*) with 1.7% ($n = 116$) [60]. Despite the very long Poaceae pollen season in Madeira Island, the pollen risk from grasses lasts only a few days per year, presenting a nil to low allergenic risk during most of the time [61].

Weeds (Pollinating Mostly in Spring and Early Summer)

Pellitory (*Parietaria*)

The *Parietaria* pollen type occurs throughout the country, prevailing in spring and summer especially in the northern-central regions and in the islands [27, 34, 42, 43]. The country-wide data show that *Parietaria* pollen is detected until mid-August to mid-September in Porto city, and from the end of July to early September in Coimbra. In Lisbon *Parietaria* pollinates from December to February, while this occurs in Évora and Portimão (Algarve) cities between November and December [55].

Parietaria is the main allergenic genus of the Urticaceae family which comprises 2 common allergenic species: *P. officinalis* and *P. judaica*. *P. judaica* grows in coastal Mediterranean areas, and this allergenic plant, which is responsible for many cases of severe pollinosis, has 2 very long flowering periods: its pollen first appears in early spring and persists into the summer months [22]. Overall, the long persistence in the atmosphere of the *Parietaria* pollen type in the Mediterranean area is responsible for a multiseasonal symptomatology [53].

Sensitization Rates to *Pellitory* (*Parietaria*)

According to Sousa et al. [62], this pollen type appears to be an important source of weed sensitization in the Porto region. In a population of 415 patients with pollen allergy previously evaluated by SPTs, 34.2% showed specific IgE levels to *Parietaria* sp. pollen extracts. Among these, 84.5% were only positive to *P. judaica*, 8.5% to *P. officinalis*, and 7.0% to both pollen types. The immunoreactivity of *P. judaica* pollen extracts was also tested against 21 sensitized patient sera revealing the presence

of 2 protein bands around 12 kDa and 2 possible glycoprotein bands of around 22 and 18 kDa [62].

The prevalence of sensitization to *P. judaica* was determined by Loureiro et al. [49] in a sensitized allergic population in the Cova da Beira region (Castelo Branco) to be 23.4% ($n = 1,096$). Moreira [63] also performed a study in the same region, reporting sensitization rates to *P. judaica* of 41.2% ($n = 17$) in elderly subjects, whereas young adults were mostly sensitized to other aeroallergens such as those from grass pollens (70.8%; $n = 24$). In Coimbra, the sensitization to *Parietaria* pollen was lower compared to the previous Portuguese regions, reaching a value of 9.6% ($n = 275$) [9].

English Plantain (*Plantago*)

The pollen of *Plantago* usually arises in mid-April in Porto city and can be detected in the atmosphere until the end of summer [26]. According to the Portuguese Aerobiology Network (<http://www.rpaerobiologia.com/>) [37], this pollen type is frequent in Portugal almost all year round. The highest counts of *Plantago* pollen were recorded in spring, mainly in April and May, and from early November onwards, pollen counts decline until February.

Sensitization Rates to English Plantain (*Plantago*)

In a study by Miranda et al. [64] in northern regions of Portugal there was a higher sensitization prevalence of *Plantago lanceolata* allergens in Trás-os-Montes and Alto Douro compared to Porto regions (littoral and inland). In those regions 35% of patients ($n = 472$) had only sensitization to *Plantago lanceolata*. In turn, Sánchez Mesa et al. [50] determined the sensitization prevalence rate to *Plantago* allergens at 21.42% ($n = 27$) in Évora city.

Sorrel (*Rumex*)

Rumex pollen is mainly found in spring in Porto, Évora and Beja regions [26, 34, 36, 42] and in Ponta Delgada during the summer season.

Species of *Rumex*, *Plantago*, and Poaceae are more abundant in Atlantic and continental areas with an extensive area of grasslands and pastures [29]. *Rumex* is an annual plant that presents an irregular pollen production pattern. In general, *Plantago* and *Rumex* and some Poaceae species adjusted their flowering onset date to the availability of soil water resources. If rainfall prevails in the winter and early spring months, it favors *Plantago* and *Rumex* pollen production. In contrast, rain events during the pollination process negatively affect the pollen release [65]. No information was found regarding the sensitization rates to *Rumex* pollen in the country.

Weeds (Beginning Pollination in Spring and Extending throughout the Summer and Early Autumn)

Sunflower Family (*Asteraceae*) and Goosefoot (*Chenopodiaceae-Amaranthaceae*)

In spring *Asteraceae* and *Chenopodiaceae* pollen was found in the Évora region [34, 42]. During the summer *Chenopodiaceae* pollen was detected in the Beja region [36] and in Ponta Delgada. In addition, *Chenopodiaceae* are present in Porto atmosphere until autumn [26].

Mugwort (*Artemisia*) is an important allergenic taxon in the *Asteraceae* family. It is present in both urban and suburban areas and in the Mediterranean area, flowering from September to the end of October [47]. Both *Artemisia* and *Amaranthaceae* pollen types are representative of the Mediterranean area, especially in the southeast. Some species are adapted to low water availability, and for that reason they are most abundant in semiarid climates of the southeastern Iberian Peninsula [29].

Many members of the *Amaranthaceae* family have been involved in inducing allergic diseases [66], and the clinical incidence of chenopod pollinosis has increased mainly in desert areas and arid environments [67]. No information was found regarding the sensitization rates to *Chenopodiaceae-Amaranthaceae* pollen. Nonetheless, a sensitization value of 9.6% ($n = 275$) to *Artemisia* pollen was determined in a population of atopic adults in Coimbra [9].

Fungi

Alternaria

Alternaria prevails in spring in Funchal (Madeira) and in summer and autumn in Porto city [68–70]. Across the Portuguese regions *Alternaria* spore levels varied between 7% in Coimbra and 3% in Évora and Portimão (Algarve) [68]. The *Alternaria* genus is considered an important pathogen in plants, and their allergens are among the most important causes of respiratory allergic diseases in Europe. *Alternaria* spore production tends to increase as temperatures reach optimal growing conditions in the 2 seasonal growing periods in the Mediterranean climate, spring and autumn [71]. The seasonal occurrence of *Alternaria* in the atmosphere of Portugal is in agreement with similar variations that have been reported from other regions [72, 73].

Aspergillus/Penicillium

These fungal spores are prevalent during the summer and early autumn (July and October) in Porto and show

lower levels during the winter season (January–February) [74]. For this city, Aira et al. [69] reported the prevalence of *Aspergillus/Penicillium* during the autumn. Both genus comprise xerophilic species able to survive in very dry environments. Their conidia are particularly resistant to lack of water and drought [75], features that explain the seasonal dynamics of these fungal spores in the atmosphere. Thus, the concentration of *Aspergillus* spores tends to increase during the summer and autumn season [76, 77]. Ebner et al. [77] reported increased concentrations for *Penicillium* in the spring and autumn. The exposure to *Aspergillus* and *Penicillium* sp. is associated with adverse health effects for humans and animals. The symptomatology often involved various bronchopulmonary diseases such as bronchopulmonary aspergillosis, aspergilloma, alveolitis, etc. [78, 79].

Cladosporium

Cladosporium represents the most frequent fungal spore type in the atmosphere throughout the country [68, 70, 80]. In general, the southern regions (including Lisbon) show higher concentrations of fungal spores in the air than those of Porto and Coimbra. The spores' average weekly concentration determined on the mainland varied between 200 and 400 spores/m³ in Coimbra and between 200 and 1,800 spores/m³ in Lisbon [68]. In Porto and Coimbra the most prevalent species is *Cladosporium cladosporioides* (30 and 33%, respectively), while in Lisbon, Évora, and Portimão (Algarve) the most abundant fungus is *Cladosporium herbarum* (47, 40, and 51%, respectively) [68].

Other Fungal Genera

Agaricus and *Agrocybe* spores are often found in the Porto atmosphere. *Epicoccum* and *Ganoderma* spores were observed throughout the year, and *Corynespora*, *Didymella*, *Drechslera*, *Fusarium*, *Pleospora*, *Rhizopus*, *Torula*, and *Ustilago* showed sporadic occurrence in Porto, in low concentrations [81]. In Funchal (Madeira) atmosphere fungal spores peaks are observed in the spring (April–June) and autumn (September–November). The lowest spore levels were observed between December and February [81]. During spring fungal spores other than *Alternaria* and *Cladosporium*, such as *Botrytis*, *Drechslera*, and *Torula*, prevail in Funchal, while *Epicoccum*, *Fusarium*, and *Nigrospora* spores attain maximum concentrations in autumn [70]. Other allergenic genera were detected in Funchal, although in concentrations below 1% of the total: *Epicoccum* (all year), *Curvularia* (predominates in August and November), *Spegazzinia* (predomi-

nates from April to August), and *Polythrincium* (predominates in spring and autumn) [70, 82].

Overall, anamorphic fungi (previously imperfect fungi) represent the major component of the airborne fungal spores in Portugal, with *Cladosporium* spores featuring prominently. Spores of fungal taxa occur in the air throughout nearly the whole year. The highest fungal spore concentration and diversity were detected during late spring-early summer and autumn seasons, similarly to the works of Halwagy [83] and Jothish and Nayar [84]. In other European cities, peak concentrations are reached during summer and are characterized by the prevalence of *Cladosporium* and *Alternaria* from April to September-October [85–87].

Sensitization Rates to Fungi

There are 3 Portuguese regions with sensitization levels described so far: Coimbra, Cova da Beira, and Madeira.

A study by Santos et al. [88] at the Immunoallergology Service of Coimbra University Hospitals, between January 2001 and December 2005, showed that the fungal species most frequently involved in patients' sensitizations were *Aspergillus fumigatus* (46%; $n = 340$), *Cladosporium herbarum* (38%; $n = 340$), *Aspergillus niger* (36%; $n = 340$), and *Alternaria tenuis* (34%; $n = 340$). In turn, Newson et al. [9] reported a prevalence sensitization rate to *Alternaria* of 8.9% ($n = 275$) in the Coimbra region. In addition, Santos et al. [88] found Alt a 1 (possible major allergen) in *Alternaria alternata* extract and minority molecular allergens, namely, Asp f 9, Asp f 2, Can CYP, Cla h 6, and Pen ch 13 in the remaining extracts. Loureiro et al. [89] determined the prevalence of sensitization to fungal spores in the allergic population of Cova da Beira to be 8.4% ($n = 835$). Similar values were also reported in other national studies [9, 90]. In the study by Lourenço et al. [57], the sensitization prevalence to fungal spores in the population of Cova da Beira equaled 23.5% ($n = 686$). The sensitization prevalence to fungal spores in a population in Madeira island ($n = 116$) was determined by Cardoso [60] as follows, in descending order: *Alternaria alternata* (14.7%), *Aspergillus* (10.3%), *Cladosporium* (6%), and *Penicillium notatum* (1%).

The most prevalent fungal spores detected in the atmosphere of Portugal are considered common aeroallergens in the literature. Adverse health effects associated with fungal exposure are widely documented, although diverse. The incidence of mold allergy is estimated at 6–24% in the general population, up to 44% among atopics, and 80% among asthmatic patients [91]. The occurrence of common aeroallergens such as *Alternaria* and

Cladosporium can induce allergenic symptoms including rhinitis, alveolitis [92] and asthma [79]. The less well-studied Ascomycetes and Basidiomycetes aeroallergens also occurred in the atmosphere of Portugal. Both fungal classes possess allergenic species with harmful potential among subjects with respiratory allergies [93, 94]. Basidiomycetes produce large quantities of spores that are dispersed by the wind over long distances. Some species can release great amounts of spores in a day [94], many of which are important aeroallergens associated with allergic symptoms [91].

House Dust Mites, Cockroaches, Cat and Dog Epithelium

The main mite species present in the Portuguese houses were determined by Todo-Bom et al. [95]. The most prevalent species was *Dermatophagoides pteronyssinus*, followed by *D. farinae* and *Lepidoglyphus destructor*. *D. farinae* was prevalent in the Lisbon region, *L. destructor* in Portalegre, *Glyciphagus domesticus* and *Euroglyphus maynei* in Évora. In the south, the most prevalent mite was *D. pteronyssinus* followed by *L. destructor*. This last species in particular was also common in samples collected in Coimbra and Leiria cities [95] (Fig. 2). A high prevalence of mite fauna in all regions of the country was confirmed later on in the presentation of the Acarologic Map of Portugal by Chieira et al. [96, 97]. *D. pteronyssinus* showed an average frequency of 88.7%, and *L. destructor* corresponded to the second most frequent mite species in the Portuguese houses with 43.8%. *Blomia tropicalis* revealed one of the lowest occurrence frequencies across mainland Portugal (average frequency of 3.1%) but expressive rates in the Azores (77.5%) and Madeira (51.8%). *B. tropicalis* has been described as the most important and ubiquitous mite species in tropical and subtropical regions of the world whose clinical importance has also been increasingly recognized over the years [98].

In a study conducted at nurseries and kindergartens in Porto and Lisbon cities between March 2011 and February 2012, the most frequent allergen was Der p 1. Der p 1 was quantified in 69% of the samples, while Der f 1 allergen was detected in 10% of samples. It was also found that concentrations of mites obtained in spring were higher than in winter [99]. In addition, predominance of Der f 1 allergen during the spring was observed in Porto city while in a survey performed by Plácido et al. [100], the indoor levels of Der f 1 were always less than 1 µg/g dust in 11% of samples. Overall, both surveys reported Der 1 and Der 2

Table 3. Relative rates of sensitization to house dust mites, cockroaches and animal epithelia in Portugal

Region	Aeroallergen	Frequencies	Allergic pathologies manifested by the sensitized population	Ref.
North				
Vila Real	Mites	73% (<i>n</i> = 365)	Atopic children, with asthma, rhinitis, and/or eczema (39.2% female; average age = 7.7 years)	118
	<i>D. pteronyssinus</i>	50.4% (<i>n</i> = 365)		
	<i>D. farinae</i>	49.9% (<i>n</i> = 365)		
	<i>L. destructor</i>	35.3% (<i>n</i> = 365)		
Porto	<i>D. pteronyssinus</i>	62.8% (<i>n</i> = 196)	Rhinitis, rhinoconjunctivitis, and/or asthma or cutaneous symptoms (urticaria/angiodema and/or eczema) (61.2% female; average age = 30.8 years) ^a	119 ^a
	<i>D. farinae</i>	54.6% (<i>n</i> = 196)		
	<i>L. destructor</i>	50.5% (<i>n</i> = 196)		
	<i>Blatta orientalis</i>	96.2% (<i>n</i> = 27) ^a	Atopic patients with respiratory allergy (30 with asthma) (79.4% female; 6–54 years old) ^b	108 ^b
		21–65% (<i>n</i> = 34) ^b		
	<i>Blatella germanica</i>	18–36% (<i>n</i> = 34) ^b	Atopic population sensitized to indoor allergens (average age = 29±12 years) ^c	101 ^c
		3.7% (<i>n</i> = 27) ^a		
	Cat	28.1% (<i>n</i> = 196)		
	Dog	96.2% (<i>n</i> = 27)		
		11.7% (<i>n</i> = 196)		
Center				
Coimbra	Mites	88% (<i>n</i> = 450)	65.1% female; average age = 46 years ^d	9 ^d
	<i>D. pteronyssinus</i>	26.9% (<i>n</i> = 275) ^d	Allergic respiratory disease (asthma and/or rhinitis) (10–68 years old) ^e	102 ^e
	<i>D. farinae</i>	21.7% (<i>n</i> = 275) ^d		
	<i>Blatella germanica</i>	32.4% (<i>n</i> = 450)		
	Cat	44% (<i>n</i> = 450)		
Cova da Beira (Castelo Branco)	<i>D. pteronyssinus</i>	47.1% (<i>n</i> = 17) ^f	Patients observed for suspected allergic symptoms ^f 41% female; average age = 30.5 years ^g	63 ^f
		32.5% (<i>n</i> = 1,096)		49 ^g
	<i>D. farinae</i>	41.2% (<i>n</i> = 17) ^f		
		29.1% (<i>n</i> = 1,096)		
	Cat	16.1% (<i>n</i> = 1,096)		
	Dog	10.4% (<i>n</i> = 1,096)		
Covilhã (Castelo Branco)	Mites	61.4% (<i>n</i> = 686)	Rhinitis and nonallergic rhinitis, some patients revealed asthma, sinusitis, pharyngitis, urticaria, and drug allergy (≥18 years old)	57
	Cat	32.7% (<i>n</i> = 686)		
	Dog	29.4% (<i>n</i> = 686)		
Lisbon	Mites	94.3% (<i>n</i> = 409) ^h	Patients with pollinosis and positive skin tests for 1 or more pollen allergens (61.4% female; average age = 33.2±12.9 years) ^h	120 ^h
	<i>D. pteronyssinus</i>	77% (<i>n</i> = 40) ⁱ		
		52% (<i>n</i> = 640)		
		44% (<i>n</i> = 126) ^j	Rhinitis (53% female; 18–65 years old; average age = 34±11 years) ⁱ	122 ⁱ
	<i>D. farinae</i>	48% (<i>n</i> = 640)		
		44% (<i>n</i> = 126) ^j	Complaints of respiratory allergy and/or allergic conjunctivitis, with a predominance of patients having asthma and rhinitis or rhinoconjunctivitis and some complaints of urticaria (62% female; 9–68 years old; average age = 32 years) ^j	121 ^j
	<i>Euroglyphus</i>	31% (<i>n</i> = 640)		
	<i>Lepidoglyphus</i>	28% (<i>n</i> = 640)		
	<i>Tyriphagus</i>	23% (<i>n</i> = 640)		
	Cat	43% (<i>n</i> = 40) ⁱ	48.5% female; average age = 17.1 years ^l	103 ^l
		19.4% (<i>n</i> = 167) ^l		
	Dog	43% (<i>n</i> = 409) ^h		
		43% (<i>n</i> = 40) ⁱ		
		18.4% (<i>n</i> = 167) ^l		123
South				
Évora	Mites	22% (<i>n</i> = 32)	Allergic rhinitis; conjunctivitis; asthma and rhinitis (≤8 years old; average age = 5.3±1.44 years)	59
Islands				
Azores	<i>D. pteronyssinus</i>	95.1% (<i>n</i> = 103)	Allergic respiratory disease (95.1% of the patients had complaints of rhinitis, 68.9% of conjunctivitis, 49.5% of asthma, and 50.5% of cutaneous allergies) (46.6% female; 4–47 years old)	19
	<i>Blomia tropicalis</i>	77.1% (<i>n</i> = 103)		
	<i>Lepidoglyphus destructor</i>	77.1% (<i>n</i> = 103)		
	<i>D. farinae</i>	58.3% (<i>n</i> = 103)		

Table 3 (continued)

Region	Aeroallergen	Frequencies	Allergic pathologies manifested by the sensitized population	Ref.
Madeira	<i>D. pteronyssinus</i>	65.5% (<i>n</i> = 116)	Allergic respiratory disease (50% female; 4–44 years old; average age = 13.0±8.6 years)	60
	<i>D. farinae</i>	60.3% (<i>n</i> = 116)		
	<i>Blomia tropicalis</i>	48.3% (<i>n</i> = 116)		
	<i>Lepidoglyphus</i>	32.8% (<i>n</i> = 116)		
	<i>Acaro siri</i>	31% (<i>n</i> = 116)		
	<i>Glyciphagus</i>	22.4% (<i>n</i> = 116)		
Portugal	Mites	26% (<i>n</i> = 48) ^m	Population of patients presenting with suspected allergic disease (median age = 33 years) ⁿ	104 ^m
	<i>D. pteronyssinus</i>	68.8%		
	<i>D. farinae</i>	68.0%		
	<i>Blatella</i>	33.4%		15 ⁿ
	Animal epithelium	13% (<i>n</i> = 48) ^m		
	Cat	25.4%		
	Dog	20.7%		

Pairing of data and reference is indicated with superscript letters.

allergen concentrations greater than the threshold sensitization value of 2 µg/g of dust, a fact that increases the risk of developing sensitization to house dust mites.

With regard to allergens of cockroaches, *Blatella germanica*, *Periplana americana*, and *Blatta orientalis* have been recognized as an important cause of allergic disease. Notwithstanding their clinical relevance, few Portuguese surveys analyzed those specific aeroallergens [101, 102].

In the Lisbon region, Marinho et al. [103] studied a population of 167 patients from the Immunoallergy Out-patient Clinic of Dona Estefânia Hospital concerning exposure to pets and the occurrence of clinical manifestations. 67.1% of patients aged less than 16 years and 80.8% in total had a regular contact with pets, 62.2% in the house and 37.8% at school/work or at a friend's house. The contact with a dog was the more prevalent one, corresponding to 80% of the cases with regular contact; 46% of patients were exposed to cats, and 37% had a regular contact with other animals.

Sensitization Rates to Mites, Cockroaches, and Animal Epithelium

According to Araújo et al. [104], mite aeroallergens are the most prevalent allergens nationwide. Moreover, the sensitization to mite aeroallergens is also the most frequent (26%; *n* = 48), followed by the animal epithelium sensitization prevalence rate of 13% (*n* = 24). Table 3 summarizes the sensitization rates to mites, cockroaches, and animal epithelium in the country determined by different research groups.

D. pteronyssinus is a house dust mite particularly frequent in Europe, Asia, and the American continent. Due to its allergenic potency and ubiquitous distribution, its allergens are widely used in the diagnosis and treatment of allergic diseases. The Portuguese population is potentially exposed to a wide number of other mite species, namely *L. destructor*, *D. farinae*, *G. domesticus* and *E. maynei*. Such storage mites and house dust mites have been reported in other regions of the world with milder climates. Their allergenic potential has been determined, reaching high sensitization rates in the atopic population [105, 106].

The prevalence of sensitization to common aeroallergens including mite allergens was determined in 2 European multicenter studies including Portugal. Burbach et al. [15] reported sensitization rates to *D. pteronyssinus* and *D. farinae* of 68.8 and 68%, respectively, to all countries. In turn, the sensitization to *D. pteronyssinus* and *D. farinae* was investigated in the Coimbra area where the sensitization rates reached 26.9% (*n* = 275) and 21.7% (*n* = 275), respectively [9].

In Madeira Island, *D. pteronyssinus*, *D. farinae*, and *B. tropicalis* aeroallergens were responsible for the highest sensitization rates reaching 65.5, 60.3, and 48.3% in the population, respectively [60]. These data are in agreement with those obtained in other similar studies in patients sensitized to mites [15, 107]. Cuesta et al. [101, 108] assessed the prevalence of cockroach sensitization in a population of Porto city (Table 3). A higher risk of cockroach sensitization was observed among the atopic popu-

lation sensitized to other indoor allergens such as house dust mites, danders, and fungi. Almost all patients (88.6%, $n = 155$) had had or had contact with pets (dog, 83.1%; cat, 51.4%). 61.7% of patients were atopic, 19.4% sensitized to cat and 18.4% to dog danders.

Pathologies Manifested in the Sensitized Population

The patients subjected to SPTs for pollen and fungus allergens, diagnosed with some type of respiratory allergic disease, reported mostly asthma, rhinitis and nonallergic rhinitis symptoms (Tables 1, 2). Symptoms of urticaria, angioedema, sinusitis, and conjunctivitis were also described among the sensitized patients. For the patients sensitized to house dust mites, cockroaches and animal epithelia (Table 3), these main morbidities were reported as well as cutaneous symptoms like eczema.

Correlation between Aeroallergen Exposure and Sensitization Rates

Pollen

A statistically significant correlation between the annual average pollen concentrations and the sensitization prevalence was detected (Spearman correlation coefficient = 0.819, $p < 0.000$, $n = 18$). The role of pollen on the pathogenesis of allergic diseases is well established. Rhinitis, asthma, and conjunctivitis are the typical clinical scenarios of pollen allergy and often occur in the same patient simultaneously during the pollen season [109]. In fact, these ailments were frequently experienced by the various sensitized population age groups by the different research groups across the country (Table 1). In general, asthma and allergic rhinitis are more common in young people, yet their prevalence in the elderly is increasing [110]. Asthma is a chronic inflammatory disease of the airways characterized by recurrent episodes of wheezing, chest tightness, and breathlessness [111]. In turn, allergic rhinitis is a disorder of the upper airways resulting from IgE-mediated inflammation of the nose upon contact of the nasal mucosa with allergens. This disease, also called allergic rhinosinusitis, since histopathological changes also affect the paranasal sinuses, typically presents sneezing, nasal pruritus, and obstruction. It is often associated with allergic conjunctivitis [110].

Fungi

With regard to the variable annual average spore concentrations and the sensitization prevalence, there was no significant statistical correlation (correlation coefficient =

-0.632 ; $p = 0.368$; $n = 4$). Despite the lack of association between fungal spore exposure and the sensitization levels observed in the studies reviewed, the sensitized population revealed symptoms of asthma, rhinitis and other respiratory disease symptoms. Further, a prevalence of *Cladosporium* fungal spores was observed in the atmosphere of Portugal, and a frequent occurrence of *Alternaria* spores across the country. *Cladosporium* spore exposure has been associated with asthma exacerbations or worsened symptoms in sensitized individuals. In turn, a number of authors have noted that *Alternaria* and *Cladosporium* can induce allergenic symptoms [92] and asthma [79, 91].

In general, it has been more difficult to demonstrate a causal relationship between airborne fungus exposure and symptoms than for pollens. This difficulty is due to the significant number of fungal species, many of which are reported to cause hypersensitivity reactions and the lack of strict seasonal patterns of exposure [112].

Mites, Cockroaches, and Animal Epithelium

The symptoms experienced by the population sensitized to the above-mentioned aeroallergens were mainly rhinitis, asthma, and conjunctivitis (Table 3). The house dust mites in particular have been described to induce specific IgE. Most of the investigation has focused on *D. pteronyssinus* with regard to major allergens, epitopes, and thresholds for sensitization and asthma development. Other mites such as the storage mite *L. destructor* and *B. tropicalis* have been implicated in allergic rhinitis episodes in the geographic areas where they are endemic [112].

Cockroaches' allergens have also been reported to cause asthma and allergic rhinitis [112], with the German cockroach (*B. germanica*) and the American cockroach (*P. americana*) being the most common species to cause allergies [113]. Several studies have shown the significance of their allergens in the induction and exacerbation of the respiratory allergic diseases [9].

Lastly, epithelia of cats and dogs have been reported to induce IgE antibodies and to trigger allergic rhinitis symptoms [112]. The small allergenic particles of cats and dogs can scatter easily in the air and adhere to clothing for further dispersal. It has been shown that even in pet-free homes and public places a pet owner's clothing represents an important source of allergen dispersal in those places [5].

Conclusions

In this work the data for the most important aeroallergens in Portugal were compiled and presented in a simplified manner by season of the year. It is assumed that the patients' molecular profile is related to the specific allergen type, to which they were previously exposed. As such, the sensitization levels reported in distinct surveys are generally correlated with the aeroallergen levels. Based on published data, the correlation between pollen exposure and sensitization rates was demonstrated, which is not the case for the fungi probably due to low sampling numbers [114–117].

It was shown that the critical periods of exposure to pollen aeroallergens are between spring and early autumn, when the sensitized population is exposed to a more different pollen quantity and variety.

The pollen spectrum in the Portuguese territory can be considered as having Mediterranean characteristics, revealing some taxa with allergenic importance such as Cupressaceae, *Olea*, Poaceae, *Quercus*, and Urticaceae. As in Europe, the main pollination period of various types of allergenic pollen in Portugal covers about half of the year, from spring to autumn. In addition, there is a low winter season (from December to the end of March), marked by the presence of the pollens of trees such as Cupressaceae and Betulaceae. Considering the aerobiological data, other pollen allergens like *Casuarina*, *Corylus*, and *Rumex* should be included in the allergen panel for SPTs. It is important to emphasize that the information compiled and illustrated in this review is limited to studies conducted in Portugal. As such, it is deemed essential to access the information provided by the Portuguese Aerobiology Network in order to follow the temporal and spatial variations of allergenic pollen in the atmosphere of the country. This network provides information in the form of alerts and forecasts, representing a useful tool in the diagnosis, prevention and a better approach of allergic respiratory disease.

In the case of fungi, several fungal genera occur throughout the year, revealing well-defined seasonal patterns throughout Portugal. The highest fungal spore concentration and diversity were detected during late spring-early summer and autumn seasons. Anamorphic fungi (previously imperfect fungi) represent the major component of the airborne fungal spores in Portugal, with *Cladosporium* being the most prevalent fungal spore type.

With regard to mites, *D. pteronyssinus* and *D. farinae* corresponded to the most prevalent species in the country, followed by *L. destructor*, a storage mite. Beyond these

mites, *B. tropicalis*, a species common for subtropical regions, was also detected in the Azores and Madeira islands.

The sensitization prevalence levels to common aeroallergens in several Portuguese regions remain unknown, in particular with regard to some interior northern and southern districts of mainland Portugal and to the Azores.

Finally, the present review revealed a high number of surveys carried out in Portugal on aeroallergen identification and several studies devoted to allergic sensitization in the atopic population.

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Statement of Ethics

This article does not contain any studies with human or animal subjects performed by the author.

Disclosure Statement

The author declares no conflict of interest.

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Supplementary Material. Trees, Weeds and Grasses – General definitions and plant species with allergenic importance

Trees

Trees are defined as a woody perennial plants which minimum height can range between 3-6 m, with a main stem or several stems, and more or less defined crown [124]. Some definitions also mention a particular height or stem diameter as distinctive criteria between trees and shrubs.

In general, tree pollen allergies are mainly elicited by allergenic trees belonging to the orders Fagales, Lamiales, Proteales, and Pinales [125]. Within the order Fagales the members of the Betulaceae (i.e., alder/*Alnus*, birch/*Betula*, hornbeam/*Carpinus*, hazel/*Corylus*, and hop hornbeam/*Ostrya*) and the Fagaceae (i.e., beech/*Fagus*, chestnut/*Castanea* and oak/*Quercus*) are most frequently implicated in allergies. Within the order Lamiales, only the Oleaceae family contains allergenic wind-pollinated tree species, which are European ash (*Fraxinus excelsior*), common privet (*Ligustrum vulgare*), olive (*Olea europea*), and lilac (*Syringa vulgaris*). In the Proteales order, allergenic species are exclusively found within the Platanaceae family. Plane trees (*Platanus*) are important sources of airborne allergens and comprise two allergenic trees, i.e., the London plane tree (*Platanus acerifolia*) and the oriental plane (*Platanus orientalis*). Lastly, within the Pinales the following genus of Cupressaceae family contains clinically relevant allergens (*Chamecyparis*, *Cryptomeria*, *Cupressus*, *Hesperocyparis*, and *Juniperus*) (www.allergen.org) [126].

Grasses (Poaceae family)

Grasses are ubiquitous plants in most parts of the world and they are one of the most important airborne allergen sources worldwide. The grass family (Poaceae) comprises 9,000 species occurring in almost habitats, being cultivated for food (e.g. cereal, corn, rice, sugar cane), animal forage, among other uses [127-128]. Grass pollen is a major outdoor cause of hay fever, being also responsible for triggering allergic asthma [129]. The clinically most relevant source of pollen allergens is found within the Poaceae family [109]. Among this, the Pooideae subfamily is prevalent in temperate climates and the most abundant allergenic species within the Pooideae are Timothy grass (*Phleum pratense*) [130], Perennial ryegrass (*Lolium perenne*), Orchard grass (*Dactylis glomerata*), common wild oat (*Avena fatua*), slender wild oat (*Avena barbata*) [109, 131-132] and smooth meadow grass (*Poa pratensis*). The Panicoideae subfamily also comprises important sources of pollen allergens such as Bahia (*Paspalum notatum*), mostly in subtropical regions [133]. Depending on climate and geography, grass pollens represent the most important contributors of airborne allergens during spring and summer [128].

Weeds

The term describes plants outside the order of trees or grasses and does not specify any botanical family. Important allergenic weeds belong to the plant families Asteraceae, Amaranthaceae, Urticaceae, Euphorbiaceae, and Plantaginaceae [134]. The Asteraceae family includes ragweed (*Ambrosia*), mugwort (*Artemisia*), sunflower (*Helianthus*), and feverfew (*Parthenium*). The Amaranthaceae plant family comprises two important allergenic weeds, i.e., goosefoot (*Chenopodium album*) and Russian thistle (*Salsola kali*) [134]. *S. kali* can be found extensively worldwide, being responsible for multiple sensitizations. Is one of the species of the Amaranthaceae family best characterized from an allergenic point of view [135]. The Urticaceae family contains the allergenic weed pellitory (*Parietaria*), which is commonly found in the countryside and urban areas, growing on walls and soils with high nitrogen content. The Euphorbiaceae family contains other important sources of sensitizing allergens, such as latex from the *Hevea brasiliensis* tree, seeds of castor bean (*Ricinus communis*) and the pollen of annual mercury (*Mercurialis annua*). The *Plantago* genus of the Plantaginaceae family, grows on moist meadows and roadsides, invades lawns, and spreads steadily, flowering from May to October. English plantain or ribwort pollen is an important cause of pollinosis in the temperate regions of North America, Australia, and Europe [134].

Suppl. Table 1. Most important allergenic plants at the Portuguese territory. The family/genus names are shown above each photograph (Photos: Irene Camacho and Roberto Camacho; Photos of *Castanea*, Fagaceae and all grasses except *Avena* and *Lolium* were obtained from Flora-On: Flora de Portugal Interactiva. (2014). Sociedade Portuguesa de Botânica. www.flora-on.pt, consulted in November 21st of 2016.

TREES	<i>Casuarina</i>	<i>Corylus</i>	<i>Castanea</i>	Cupressaceae	Fagaceae			
								
	<i>Olea</i>	<i>Palmae</i>	Pinaceae	<i>Platanus</i>	<i>Salix</i>			
								
WEEDS	Asteraceae	Cheno-Amaranthaceae	<i>Rumex</i>	<i>Plantago</i>	<i>Parietaria</i>			
								
GRASSES	<i>Avena</i>	<i>Dactylis</i>		<i>Fetua</i>	<i>Holcus</i>	<i>Lolium</i>	<i>Phleum</i>	<i>Poa</i>
								

Supplementary Material. Vegetation landscape and bioclimatic characteristics at the Portuguese territory

Vegetation landscape

Portugal is located in the western part of the Iberian Peninsula, bordered by the North Atlantic Ocean and Spain. The country also comprises the Archipelagos of Azores and Madeira. The Azores is sits 1,100 km west of Lisbon, and Madeira sits north of the Canary Islands.

About one-third of the Portugal mainland is covered by forest and woodland, and another third has agricultural areas. In the northern half of the country prevails the maritime pine (*Pinus pinaster*). Along the western half of Portugal and interior parts of central and southern regions the Blue gum (*Eucalyptus globulus*) plantations are abundant, and in the southern half of Portugal prevails evergreen oak woodlands. The main forest land cover type in south-western of Portugal is composed by Cork oak woodlands (*Quercus suber*) whereas holm oak (*Quercus rotundifolia*) prevails in the southeast [136-138].

Over one-quarter of the country is covered by scrubland, mostly in the northern third and southeastern regions, being dominated by the genus *Cytisus* (Fabaceae) and *Cistus* (Cistaceae), often occurring together in sedimentary sands and sandstones. In the limestone areas normally composed by heather scrub, the garrigue-like scrubland (*Quercus coccifera*) predominate [136].

Agricultural areas are present throughout the entire country, mostly in the coastal plains of central Portugal along the main river valleys, as well as in the southeastern parts of the country.

In northern and central Portugal, the agricultural landscape is composed by small parcels of diverse crops, vineyards, and olive groves while in the southeastern is more extensive and homogeneous, dominated by dryland farming of cereal crops [136].

In **Azores**, much of the islands of the archipelago are covered by dense evergreen forest. The land has been used for agriculture and settlement but the native vegetation still persists in several isolated areas, dominated by Azores heather (*Erica azorica*), Azorean picconia (*Picconia azorica*), Cape myrtle (*Myrsine africana*), common heather (*Calluna vulgaris*), faya tree (*Myrica faia*), whortleberry (*Vaccinium cylindraceum*) and *Sphagnum* spp. Plantations of the exotic conifer *Cryptomeria japonica* are quite common. Much of the forest is covered by juniper (*Juniperus brevifolia*), *Ilex perado* spp. *Azorica*, and other species such tree heather (*Erica azorica*) and laurel (*Laurus azorica*) [139].

In regards to **Madeira**, about two-thirds of the island is a natural park, possessing the largest continuous and best preserved area of humid laurel forest. The laurel forest is covered by the most common trees belonging to the Lauraceae family, like the Canary Laurel (*Apollonias barbuja*), Laurel (*Laurus novocanariensis*), fetid Laurel (*Ocotea foetens*) and Madeira mahogany (*Persea indica*) [140]. In the urban areas thrives exotic plants from around the world. The most common trees in Funchal city (the capital) are *Agathis robusta*, *Casuarina equisetifolia*, *Jacaranda mimosifolia*, *Spathodea campanulata*, *Tipuana tipu*, besides several other species from families like Arecaceae, Cupressaceae and Cyatheaceae. In the urban landscape there are many patches of land used for agricultural purposes, mostly cultivated with *Musa acuminata*, *Vitis vinifera* and with horticultural production. Uncultivated land presents a variety of weeds and grasses, dominated by *Arundo donax*, *Dactylis* spp. and *Parietaria* spp. The exotic forest is dominated from the genera *Acacia*, *Eucalyptus* and *Pinus* [140-141].

The **climate** in the Portuguese territory varies considerably due to its location, and for that reason there is a strong contrast between coastal (western) and mainland (eastern) areas [142]. The climate is warm temperate, mostly Mediterranean, characterized by hot, dry summers and cool, wet winters [136]. Mainland Portugal includes both temperate and Mediterranean territories [142]. The north western half of Portugal, which includes the cities of Porto and Coimbra, reveals Meso-temperate and Meso-Mediterranean thermoclimates. The district of Castelo Branco (eastern centre) and the city of Évora, located in Alentejo in the south eastern region of Portugal, also exhibits Meso-Mediterranean features. In contrast, the central and south eastern part of Portugal, which includes Lisbon, Beja and Algarve, shows a Thermo-Mediterranean thermoclimate. The climate in Azores is Mediterranean pluvisesonal oceanic / Temperate hyper-oceanic sub-Mediterranean, and Temperate / Hyper-oceanic-sub-Mediterranean in Madeira [142-143].



Suppl. Fig. 1. Map of Portugal (the scale is relative to the mainland territory).

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