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Contact sensitization to propolis in the Information Network of Departments of Dermatology (IVDK) 2013-2019 and market survey of propolis commerce in Germany.

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Conflict of interest

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Propolis is a natural product, consists of >100 compounds and shows great compositional variation, depending on its origin.¹ The most common poplar-type propolis is produced by honeybees in China, Europe and North America, and is characterized by several caffeates as major allergens.² The Information Network of Departments of Dermatology (IVDK) and others recently observed increasing rates of propolis sensitization.^{3, 4}

We aimed to identify causes of increasing sensitization to propolis using IVDK and German trade data.

Methods

From 2013 to 2019, 66104 of 79120 consecutive IVDK patients were patch tested with propolis (10% pet) in the baseline series. According to information from Allmiral Hermal and SmartPractice Europe, patch test (PT) preparations contained constantly the same or rather similar poplar-type propolis. Patch tests were performed following German and European guidelines and read on day 3 (day 4 in a few exceptional cases).⁵⁻⁸ Statistical significance on a 5%-level was concluded from non-overlapping 95%-confidence intervals (95%-CI) in corresponding comparisons.

Results

In the study period, 2598 patients (3.9% [95%-CI; 3.8 – 4.1%]) showed positive PT reactions to propolis. Reaction frequencies in female (3.8% [3.6 - 4.0%]) and male (4.2% [3.9 - 4.4%]) patients did not differ significantly. Concerning population characteristics and PT results, table 1 displays differences between 2598 propolis positive patients and 61032 propolis negative patients. Patients with doubtful (n=1883; 2.8%) or irritant reactions (n=591; 0.9%) were excluded from this analysis. Among propolis positive patients, there were significantly more patients aged ≥ 40 years, males, and patients with leg or face dermatitis, whereas occupational and hand dermatitis were diagnosed less often (table 1). As expected, patients sensitized to propolis reacted significantly more often to balsam of Peru (*Myroxylon pereirae*) and colophonium, most probably due to common ingredients, such as (aromatic) resin acids and monoterpenes.¹ In addition, propolis positive patients were significantly more often sensitized to other fragrances, essential oils, and compounds found in topical preparations (table 1).

The upward trend from 3.5% [3.2-3.9%] positive propolis reactions in 2013 to 4.7% [4.2-5.1%] in 2019 (figure 1) was significant (asymptotic Cochran-Armitage trend test; $p < .0001$). If this trend was based on variations in allergen content or concentration in different types of propolis used in consumer products or PT preparations, one would expect that epidemiological (clinical) markers reflect such changes. However, items presented in table 1 showed no substantial variation between the single years of the study period and hence cannot explain this increase (data not shown in detail).

An analysis of propolis import and export in Germany using tridge.com, an internet platform that connects suppliers and buyers⁹, revealed that, from 2016 to 2019, propolis export decreased while its import increased dramatically (figure 1). Imported propolis mainly originated from China (29.9%), Spain (11.2%), the USA (10.9%), Italy (8.1%), and Brazil (6.9%). According to de Groot's classification,¹ poplar-type propolis dominated in Germany every single year. Propolis-import from the USA peaked in 2014 (20.4%) and 2016/2017 (~17%). Propolis from Brazil, which is chemically different from the poplar-type,¹ constantly had a relatively small market share (maximum 16.9% in 2015).

Discussion

Considering patient characteristics, suspected allergen sources and concomitant PT reactions, sensitization to propolis shows an association to skin care and topical medical preparations (table 1). Since 2016, increased import and decreased export of propolis to and from Germany, respectively, probably indicates increased propolis use and exposure, which most likely explains the upward trend of propolis sensitization. Nevertheless, one has to be aware that differences in propolis composition, even between poplar-type propolis species, and heterogeneity of the propolis used in PT preparations as well as in propolis on the (cosmetics) market do exist and affect diagnostic accuracy in patch tested patients, as recently demonstrated in a Swedish study.¹⁰ The compositional (chemical) heterogeneity of commercially available patch test preparations year on year should be studied.

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Figure legend

Figure 1. Propolis in Germany: import of propolis to Germany (black line), export of propolis from Germany (grey line) and propolis sensitization in the IVDK (blue dashed line) between 2013 and 2019.

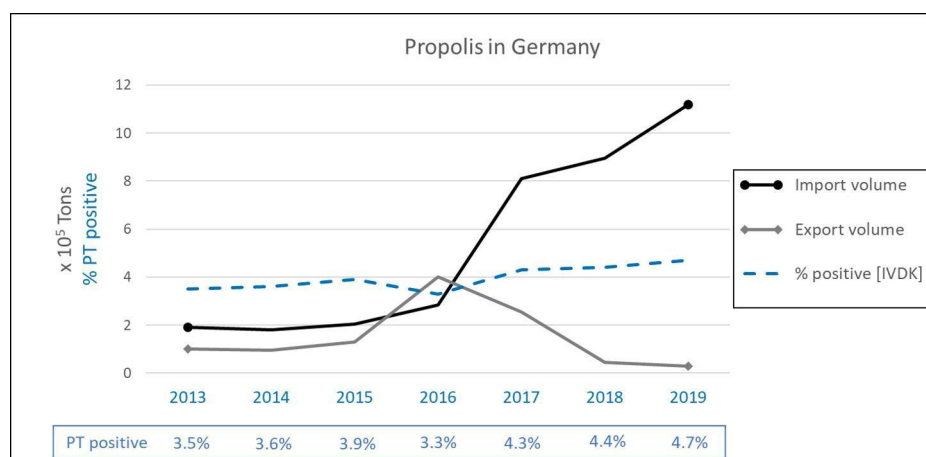


Fig1_300.jpg

Table 1. MOAHLFA-Index, suspected allergen sources and concomitant reactions in propolis positive and negative patients, respectively. Up to three allergen sources could be mentioned by the patients, only items with significant differences are presented. Presentation of concomitant sensitization was limited to the 15 most frequent allergens among propolis positive patients. Vehicle was petrolatum unless aqua (aq) is indicated.

MOAHLFA-Index		Propolis positive patients (n = 2598)		Propolis negative patients (n = 61032)	
		n	% [95%CI]	n	% [95%CI]
Male	M	1002	38.6 [36.7 - 40.5]	21990	36.0 [35.6 - 36.4]
Occupational dermatitis	O	372	14.3 [13.0 - 15.7]	11076	18.1 [17.8 - 18.5]
Atopic dermatitis	A	610	23.5 [21.9 - 25.2]	15170	24.9 [24.5 - 25.2]
Hand dermatitis	H	762	29.3 [27.6 - 31.1]	20168	33.0 [32.7 - 33.4]
Leg dermatitis	L	311	12.0 [10.7 - 13.3]	6063	9.9 [9.7 - 10.2]
Face dermatitis	F	499	19.2 [17.7 - 20.8]	9846	16.1 [15.8 - 16.4]
Age >= 40 years	A	2072	79.8 [78.2 - 81.3]	43403	71.1 [70.8 - 71.5]
Suspected allergen sources					
Cosmetics, creams (leave on products)		1217	46.8 [44.9 - 48.8]	25087	41.1 [40.7 - 41.5]
Drugs, external		398	15.3 [14.0 - 16.8]	8023	13.1 [12.9 - 13.4]
Perfume, deodorant		130	5.0 [4.2 - 5.9]	2156	3.5 [3.4 - 3.7]
Plants (not food)		48	1.8 [1.4 - 2.4]	721	1.2 [1.1 - 1.3]
Concomitant reactions					
Propolis	10%	2598	100.0 [99.9 - 100.0]	0	0.0 [0.0 - 0.0]
Balsam of Peru (Myroxylon pereirae)	25%	923	35.8 [33.9 - 37.7]	3468	5.7 [5.5 - 5.9]
Fragrance mix I	8%	704	27.5 [25.8 - 29.3]	3980	6.6 [6.4 - 6.8]
Gallopheony (Rosin)	20%	479	18.6 [17.1 - 20.2]	1809	3.0 [2.8 - 3.1]
Nickel sulfate	5%	441	17.3 [15.8 - 18.8]	9544	15.9 [15.6 - 16.2]
Fragrance mix II	14%	393	15.3 [13.9 - 16.7]	2427	4.0 [3.8 - 4.2]
Ylang Ylang oil	10%	347	13.4 [12.1 - 14.8]	1054	1.7 [1.6 - 1.8]
Methylidibromo glutaronitrile*	0.2-0.3%	261	10.2 [9.0 - 11.4]	1826	3.0 [2.9 - 3.2]
Potassium dichromate	0.5%	246	9.6 [8.4 - 10.8]	2342	3.9 [3.7 - 4.0]
Cobalt chloride	1%	214	8.3 [7.3 - 9.4]	3263	5.4 [5.2 - 5.6]
Jasmine absolute	5%	211	8.1 [7.1 - 9.3]	607	1.0 [0.9 - 1.1]
Sandalwood oil	10%	197	7.6 [6.6 - 8.7]	515	0.8 [0.8 - 0.9]
Lanolin alcohols	30%	190	7.3 [6.4 - 8.4]	1141	1.9 [1.8 - 2.0]
Compositae Mix II	5%	187	7.4 [6.4 - 8.5]	659	1.1 [1.0 - 1.2]
Methylchloroisothiazolinone / Methylisothiazolinone (MCI/MI)	0.01% aq	183	7.1 [6.1 - 8.1]	2454	4.0 [3.9 - 4.2]

* Patch test concentration changed in 03/2016 from 0.2% pet. to 0.3% pet.