

The importance of propolis in patch testing—a multicentre survey

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Background: Propolis is widely used in 'natural' cosmetics, remedies, and over-the-counter products. The incidence of propolis allergy is increasing, and cross-reaction with fragrance mix I (FMII), colophonium, and *Myroxylon pereirae* can occur.

Objectives: To find out the prevalence and clinical relevance of positive patch tests to propolis and assess cross-reactions with *Myroxylon pereirae*, colophonium, FMI, and beeswax.

Methods: Two thousand eight hundred and twenty-eight subjects in 10 UK centres were patch tested with propolis and beeswax. Generic data were acquired from British Contact Dermatology Society (BCDS) database and further relevant information was requested by survey of participating centres.

Results: The prevalence of propolis allergy was 1.9% (55/2828). Out of these 55 subjects, only 4 (7.2%) were allergic to beeswax, 22 (40%) to *Myroxylon pereirae*, 15 (27.2%) to colophonium, and 6 (10.9%) to FMI. Additional data for 41 propolis allergic subjects were collected by questionnaire. Hands were the most common sites of involvement, and cosmetics were the most common source of contact. Eight out of 12 subjects reported improvement in eczema following avoidance of propolis.

Conclusions: Propolis is an important allergen of increasing frequency and its inclusion in BCDS baseline series is appropriate. Cross-sensitivity to beeswax is rare.

Key words: allergic contact dermatitis; beeswax; patch tests; propolis. © John Wiley & Sons A/S, 2009.

Conflicts of interest: None

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Propolis is composed of beeswax, resin and vegetable balsam, essential and aromatic oils, pollen, and other substances (1). Yellow beeswax is the purified wax obtained from the honeycomb of the bee. White beeswax is derived from yellow beeswax by a bleaching process (2). Propolis has long been known as an occupational contact allergen in beekeepers, musicians, and manufacturers of stringed musical instruments. However, most cases

of propolis allergy are not occupational. Because of its antiseptic, antimycotic, bacteriostatic, astringent, choleric, spasmolytic, antiinflammatory, and anaesthetic properties, this compound is widely used in folk medicine and in the biocosmetic industry. It is found in tablets, powders, lotions, ointments, solutions, creams, toothpaste, chewing gum, etc. (3). More than 250 cases of contact dermatitis have been described in the literature. The increase in

prevalence of contact dermatitis over the last two decades is likely to be due to the use of propolis in pharmaceutical and cosmetic preparations (4). Propolis and *Myroxylon pereirae* share 13 constituents (5) accounting for the cross-sensitization between the two. Cross-sensitization to fragrance mix I (FMI), *Myroxylon pereirae*, and colophonium often occurs because of shared constituents.

Because of its common origin, propolis can be present in beeswax as an impurity. Beeswax is commonly used in cosmetic formulations like lipsticks, ointments and epilating waxes, stiffening agent in ointments and creams, coating in the manufacture of modified-release oral preparations, and occasionally used to adjust the melting point of suppositories (2, 6). Contact sensitization to beeswax appears to be rare, most reported cases being a consequence of contamination with propolis (6). This contamination should be minimized by the high purity requirements of pharmaceutical grade beeswax, which is required for use in pharmaceutical products.

We performed a study to assess the prevalence of propolis allergy in 10 UK centres, to investigate the cross-sensitivity with beeswax, *Myroxylon pereirae*, colophonium, and FMI, and to assess the relevance of propolis allergy.

Materials and Methods

Two thousand eight hundred and twenty-eight subjects undergoing patch testing as part of the investigation for contact dermatitis in UK centres were patch tested with propolis 10% in petrolatum and pharmaceutical grade pure yellow and white beeswax. Propolis was obtained from Chemotechnique (Malmö, Sweden) and beeswax from Fisher Scientific (Loughborough, UK). The patch tests were administered with Finn chambers® or with Chemotechnique IQ chambers® applied on the back with Micropore™ (3M Health Care, Borken, Germany). The patch tests were removed and read at D2 and again at D4, according to the International Contact Dermatitis Research Group recommendations.

Positive reactions were assigned to one of the three relevance categories (current, past, and uncertain), according to the patient's exposure history. The results were entered in the British Contact Dermatology Society (BCDS) database in each centre.

From the BCDS database, information on positive reactions to propolis and cross-sensitivity between propolis and FMI, *Myroxylon pereirae* and colophonium was collected. Further information was gathered for propolis positive subjects about the history of atopy, site and duration of dermatitis, likely sources of allergen exposure, and outcome following allergen avoidance, by a questionnaire survey sent to all participating centres.

Results

Out of 2828 subjects, 1880 (66.4%) were females and 948 (33.6%) were males. Fifty-five subjects (1.94%) had a positive patch test to propolis (40 females and 15 males) and 13 (0.45%) had positive reactions to beeswax [10 to yellow beeswax (4 females and 6 males) and 3 to white beeswax (2 females and 1 male)]. The age range of these subjects was 8–88 years and five subjects were under the age of 15 years. The relevance of positive reactions to propolis, yellow and white beeswax is shown in Table 1. Fifty-one subjects reacted to propolis only, 9 to beeswax only, and 4 subjects reacted to both allergens.

Seventeen of the 55 (30.9%) positive reactions to propolis were considered by the investigators to be due to cross-sensitivity of propolis to other allergens. Figure 1 shows the crude number of propolis allergic subjects with positive reactions to *Myroxylon pereirae*, colophonium, FMI, and beeswax. Four subjects out of 10 with positive reactions to yellow beeswax were allergic to propolis (one was considered to be past relevance, one due to cross-sensitivity, and two were of uncertain relevance).

Additional data for 41 subjects from 7 centres were obtained from the questionnaire survey. This showed the duration of eczema to be from 2 weeks to more than 8 years and 16 of the 41 (39%) subjects had atopic dermatitis. Hands were the most common

Table 1. Relevance of positive reactions to propolis

	Current	Past	Uncertain	Due to cross-sensitivity to other allergens	Total
Propolis	13	4	21	17	55
Yellow beeswax	2	2	5	1	10
White beeswax	0	1	2	0	3

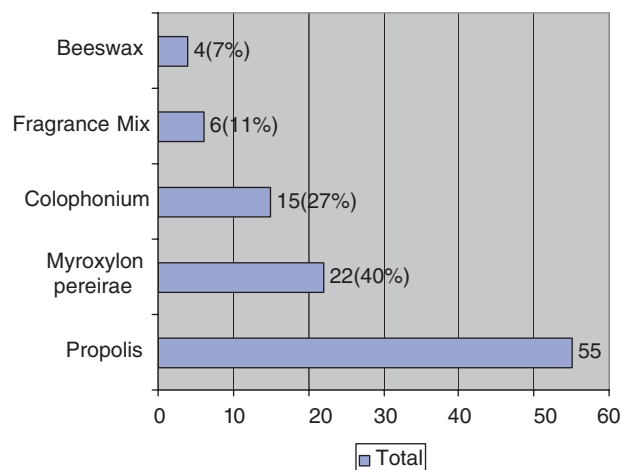


Fig. 1. Bar chart of 55 propolis positive subjects showing positive reactions to *Myroxylon pereirae*, colophonium, fragrance mix I, and beeswax.

sites of involvement in 23 subjects followed by the face in 9. Eczema involved the lower limbs in 7 and was generalized in 5 subjects. Other sites included perineum, genitals, and trunk. Cosmetics were considered the most common source of contact in 21 subjects and the source was not known in 10. Propolis allergy was thought to be occupational in eight and because of self-medication in four subjects. Details about occupation was available in four [one each from manufacturer of metal components (wax moulds), hair dresser, beauty therapist, and oil and gas extraction industry].

Eight out of 12 subjects reported improvement in eczema following avoidance of the substances containing propolis (6 reported marked and 2 reported moderate benefits).

Discussion

The Greek word propolis means ‘defence of the hive’ (*pro*, for or in defence, and *polis*, the city for hive) (7). Propolis is a resinous material collected by bees from the cracks in the barks of the trees and leaf buds. This resin is masticated, salivary enzymes are added, and partially masticated resin is mixed with the beeswax and used in the hive (1). It has a characteristic smell and its colour varies from green, red to dark brown. It is used by bees to seal holes in their honeycombs, smooth out internal walls, and to cover carcasses of dead intruders to prevent their decomposition. The composition of propolis varies depending upon the source plant and local flora and more than 300 constituents have been identified (8, 9).

Propolis is composed of 30% beeswax, 50% resin and vegetable balsam, 10% essential and aromatic oils, 5% pollen, and other substances (1). The following substances have been identified by gas chromatography/mass spectrometry: free aromatic acids (e.g. benzoic, caffeic, cinnamic, coumaric, and ferulic acid), benzyl, methylbutenyl, phenylethyl, cinnalyl, and other esters of these acids, flavonoids, chalcones and dihydrochalcones, terpenoids, sugars, ketones and alcohols (5). The esters of caffeic acid (phenylethyl caffeate and methylbutenyl caffeate) have shown strong sensitizing properties in subjects as well as in guinea-pig experiments. However, other constituents (e.g. isoferulates, flavonoid aglycones, and free aromatic acids) may also play a role in propolis allergy (3).

The prevalence of propolis allergy in our study was 1.9% (55 out of 2828), comparable with that reported (1.2–6.6%) in the past (3). Wohrl et al. (10) identified propolis as an important allergen on its own right [1.3% positive (35 out of 2660)], but its role as a screening tool for fragrance

allergy is limited. In their study, 10 out of 35 propolis allergic subjects (28.5%) did not show concurrent reactions with FMI, *Myroxylon pereirae*, or colophonium. In our study, 19 out of 55 (34.5%) propolis positive subjects did not react to FMI, *Myroxylon pereirae*, or colophonium further confirming its importance as an allergen in its own right. In a multicentre study, the significant increase in propolis sensitivity from 0.5% in 1995–1997 to 1.4% in 2000–2002 (11) was hypothesized to be due to popularity of natural cosmetics containing this substance.

Another study showed significant linear increase in propolis sensitivity from 2% to 13.7% over a period from 1995 to 2002 in 1255 children (3). The European Surveillance System of Contact Allergies reports a propolis sensitivity rate of 3.5% in Austria and Germany and it was suggested that propolis might be an allergen of national or regional importance, or alternatively, it should be considered for inclusion in the baseline series by other departments and regional networks (12). Propolis sensitivity has been reported to be 2.8% in 361 subjects with rosacea patch tested between 1995 and 2002 (13). Propolis is now included in British Contact Dermatitis Society baseline series. Considering higher positive rates in Germany and Austria, it should be included in the European baseline series as well. Giusti et al. (3), in their study of sensitization to propolis in children, found that about 75% of subjects had actual past use of natural products or alternative medicine remedies. In our study, 51.1% (21/41) subjects were identified to have biocosmetics as a source of allergen.

Beeswax is a complex material containing more than 300 constituents. It contains esters of higher fatty acids and alcohols, small quantities of hydrocarbons, acids and other substances, and 50 aroma compounds (14). Granulomatous reaction to surgical bone wax has been reported at the site of application of orbit, foot, and sternum, but contact allergy to beeswax is rare (2) and has been reported with beeswax containing nipple protector and beeswax lip product. In our study, beeswax allergy prevalence was rare [13/2828 (0.45%)] and cross-sensitivity of beeswax to propolis was 4/55 (7%).

Conclusion

Allergy to propolis is important and it is increasing in frequency. Its inclusion in the BCDS baseline series is appropriate. Biocosmetics are the most common cause of reaction and hands seem to be the most commonly affected site. Cross-sensitivity to beeswax is uncommon but should be kept in mind for a subject allergic to propolis.

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