

Contact allergy to beeswax and propolis among patients with cheilitis or facial dermatitis

Gunnar S. A. Nyman^{1,2}  | Mimmi Tang^{1,2} | Annika Inerot^{1,2} | Amra Osmanovic^{1,2} | Per Malmberg³ | Lina Hagvall^{1,2} 

¹Department of Dermatology and Venereology, Region Västra Götaland, Sahlgrenska University Hospital, Gothenburg, Sweden

²Department of Dermatology and Venereology, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

³Department of Chemistry and Chemical Engineering, Centre for Imaging Mass Spectrometry, Chalmers University of Technology, Gothenburg, Sweden

Correspondence

Mr Gunnar S. A. Nyman, Department of Dermatology and Venereology, Institute of Clinical Sciences, Sahlgrenska Academy University of Gothenburg SE-413 45 Gothenburg, Sweden.
Email: nyman@cutis.nu

Abstract

Background: Beeswax, both white and yellow, has many uses, such as in lip balm. This material can cause contact allergy, although not many cases have been described.

Methods: Ninety-five patients with contact cheilitis, facial eczema or a suspicion of contact allergy to beeswax were patch tested with yellow and white beeswax and with propolis, in addition to the Swedish baseline series. Patients who reacted positively to beeswax were additionally tested with caffeic acid, and two derivatives thereof that are believed to be important haptens in propolis.

Results: Seventeen patients had positive reactions to beeswax. Fourteen of these patients had been tested with both yellow and white beeswax. Among those 14, eight had positive reactions to both types of wax, five only to yellow wax, and one only to white wax. Of the 10 wax-positive patients tested with caffeic acid derivatives, three reacted positively. Fourteen beeswax-positive patients also had positive reactions to propolis.

Conclusion: Patch testing cheilitis patients is important, as contact allergy is common. Our suggestion is to patch test, apart from the baseline series and the patient's own products, also with beeswax and propolis. Many beeswax-allergic cheilitis patients would not have been diagnosed with a relevant contact allergy if only the Swedish baseline series had been used.

KEYWORDS

beeswax, caffeic acid, cera alba, cera flava, cheilitis, contact allergy, propolis, RRID: SCR_001905

1 | INTRODUCTION

Beeswax is produced by the wax glands of honeybees (*Apis mellifera*). The main raw materials for wax formation are the honey sugars fructose, glucose, and sucrose.¹ Beeswax is naturally yellow in colour (cera flava), but becomes white when purified or bleached.^{1,2} Beeswax can cause contact allergy, and some cases of contact cheilitis, as well as cosmetic and occupational contact dermatitis, caused by beeswax have been described.³⁻⁹ It is not known whether there is any difference in allergenicity between white and yellow beeswax. Moreover,

the relationship between beeswax and propolis from the perspective of allergenicity is not known, although many cases of reactions to beeswax appear to be attributable to contamination with propolis.^{5,7}

Propolis or bee glue is another commonly used bee-related product, manufactured by bees from plant material mixed with beeswax.¹⁰ Propolis is often an impurity in beeswax.^{1,11} The main haptens in propolis are believed to be caffeic acid and its derivatives.¹² Beeswax and propolis are different products, although they are sometimes referred to as the same substance.¹³ As natural products, beeswax and propolis are not exactly chemically defined, but they may share

some components, as propolis contains beeswax, and beeswax can be contaminated with botanical material from propolis.^{1,10}

Eczema on the lips (cheilitis) is relatively common,¹⁴ and can be caused by contact allergy.^{13,15–17} There are some case reports of cheilitis caused by beeswax, propolis, and honey.^{4,7,9,15,18} Beeswax is a component in many lip balms and lipsticks, and is thus of interest for further investigation.⁴ Contact allergy to beeswax has not been very well investigated.

The main aim of this study was to investigate the frequency of contact allergy to beeswax and propolis among patients with suspected contact-allergic cheilitis, eczema around the lips, or suspicion of contact allergy to products containing beeswax. We also sought to investigate possible differences regarding contact allergy to yellow and white beeswax by examining the haptens present in the waxes. Furthermore, we were interested in the relationship between contact allergy to beeswax and to propolis, fragrance markers and plant substances in the Swedish baseline series. Finally, we wished to study whether certain previously identified haptens in propolis, namely caffeic acid and its esters, were significant haptens among patients reacting positively to beeswax.

2 | PATIENTS AND METHODS

2.1 | Chemicals

Yellow beeswax (*cera flava*) was obtained from Apoteket (Stockholm, Sweden), and white beeswax (*cera alba*) was obtained from ACO Hud Nordic (Upplands Väsby, Sweden). Caffeic acid ($\geq 98.0\%$), caffeic acid 1,1-dimethylallyl ester ($>98.0\%$), and caffeic acid phenethyl ester ($\geq 97\%$) (Figure 1) were all obtained from Sigma-Aldrich Sweden (Stockholm, Sweden).

The purity levels of caffeic acid, caffeic acid 1,1-dimethylallyl ester and caffeic acid phenethyl ester were determined by the use of nuclear magnetic resonance (NMR). ¹H-NMR spectra were acquired with CDCl₃ as the solvent on a JEOL (Tokyo, Japan) Eclipse⁺ 400-MHz spectrometer. No impurities could be detected.

2.2 | Analysis of beeswax

The surface hapten content of samples of yellow and white beeswax was examined with time-of-flight secondary ion mass spectrometry (ToF-SIMS). A ToF-SIMS 5 instrument (IONTOF, Münster, Germany) equipped with a liquid metal primary ion source was used to record ToF-SIMS spectra of negative ions with a mass resolution of $m/\Delta m = 8000$ full width at half maximum at m/z 500. The software SURFACE LAB (version 6.3; IONTOF) was used to analyse all ToF-SIMS data. Signals for [C][−], [CH][−], [C₂][−], [C₃][−] and [C₁₆H₃₁O₂][−] were used for calibration. In total, four samples of each type were analysed.

2.3 | Patch test materials

Patch testing was performed with yellow and white beeswax, both “as is,” and with propolis 10% pet., in addition to the Swedish baseline

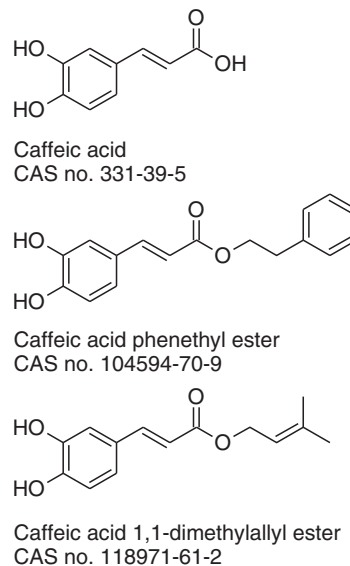


FIGURE 1 Chemical structures of caffeic acid and derivatives used in patch testing

series. The propolis patch test preparation and the Swedish baseline series were obtained from Chemotechnique Diagnostics (Vellinge, Sweden). The baseline series and the propolis patch test preparations were used within a period of 12 months, during which time they were stored in a refrigerator. The white beeswax patch test preparation was acquired at the time of its introduction in 2013. Patch testing was performed with caffeic acid 5.0%, 0.5%, 0.05%, 0.005% and 0.0005% pet., and with caffeic acid phenethyl ester and caffeic acid 1,1-dimethylallyl ester, both 1.0%, 0.1%, 0.01%, 0.001% and 0.0001% pet. Maximum test concentrations were chosen according to earlier studies by Hausen and Wollenweber.¹⁹ Patch test preparations of caffeic acid, caffeic acid phenethyl ester and caffeic acid 1,1-dimethylallyl ester were prepared in house, stored at -20°C until use, and used within 6 weeks after preparation.

2.4 | Patients and patch testing

In this retrospective study, the cohort consisted of 95 patients, comprising 83 females and 12 males. The mean age was 45.3 years (range, 18–83 years; median, 44 years). Inclusion criteria were a suspicion of contact allergic cheilitis ($N = 55$), eczema around the lips or on the face ($N = 32$), or a suspicion of contact allergy to products containing beeswax ($N = 8$). An age of <18 years was an exclusion criterion. Patch testing was performed at the Department of Occupational and Environmental Dermatology, Sahlgrenska University Hospital, Gothenburg, and the Dermatology Private Practice, Telegrafan, Borås, from August 2009 until October 2016. A history of atopic eczema was recorded in 41 of 80 patients (51%). For 15 patients, there was no information on atopy.

Consecutive dermatitis patients who were patch tested with the Swedish baseline series at the Dermatology Department at Sahlgrenska University Hospital during the study period were used as a control

TABLE 1 Positive reactions to yellow or white beeswax and propolis in the group of 95 patients with contact cheilitis, facial dermatitis, or suspicion of beeswax allergy

	No. tested	No. positive	Percentage positive	CI
Cera flava or cera alba	95	17	18	11-28
Cera flava	95	16	17	10-27
Cera alba	49	9	18	9-24
Propolis	84	16	19	11-30

Abbreviations: CI, confidence interval.

group. The control group was used to compare frequencies of positive reactions to plant and fragrance haptens. Twenty control patients were patch tested, and had negative results with yellow beeswax.¹⁵

Patients with positive patch test reactions to beeswax were contacted for further testing with caffeic acid and the two esters. Ten of 17 accepted further testing. Patch test preparations of ~20 mg were applied in small Finn Chambers (diameter, 8 mm; inner area of 0.5 cm²; Epitest, Tuusula, Finland) on Scanpor tape (Norgesplaster, Vennesla, Norway) to each patient's back, left occluded for 2 days, and then removed by the patient. The amounts used for patch testing were 75 mg for yellow beeswax and 79 mg for white beeswax. Readings were performed on day (D) 3-D4 and D7, and positive reactions were graded by a dermatologist following the standard procedure recommended by the European Society of Contact Dermatitis.²⁰

Clinical relevance was assessed by checking products used with regard to beeswax. If patients regularly used products declared to contain beeswax at the same location as the dermatitis, the patch test reaction to beeswax was considered to be clinically relevant. Clinical relevance was rated as current, previous, or unknown. The study was approved by the local ethics committee.

2.5 | Statistics

All data were analysed with R version 3.0.3 (R Foundation for Statistical Computing, Vienna, Austria; RRID:SCR_001905). Fisher's exact test was used to compare the frequencies of positive reactions between the patient cohort and the control group. All tests were two-sided, and $P < 0.05$ was defined as statistically significant. Confidence intervals of frequencies of contact allergy were calculated with the Mid-P exact test and OPENEPI (<http://openepi.com>).

3 | RESULTS

3.1 | Patch testing

In the cohort, 17 of the 95 patients (18%) showed positive reactions to yellow or white beeswax (Table 1). Patch test reactions to propolis were seen in 19% of the patients. One doubtful reaction was seen to cera flava, one to cera alba, and one to propolis. In the beeswax-positive patients, 16 of 17 positive reactions were rated as being currently clinically relevant. The main product used was a brand of Swedish lip balm and emollient declared to contain beeswax. Nine of 17 patients with positive reactions had used this type of product. Seven of the patients also had reactions to their own products "as is." A history of atopic eczema was recorded in 11 of the 17 beeswax-positive patients (65%) (Table 2). Concomitant positive reactions to propolis were found in 14 of the 17 patients who reacted positively to beeswax, and 14 of the 16 patients who reacted positively to propolis also reacted positively to beeswax.

Concomitant reactions to plant substances and fragrances in the baseline series, that is, sesquiterpene lactone mix, colophonium, lichen acid mix, *Myroxylon pereirae* resin (MPR), and fragrance mix I (FM I), in the group of patients are shown in Table 3. Significantly more

TABLE 2 Concomitant reactions to plant substances and fragrance markers of the baseline series among patients with positive reactions to beeswax, and the clinical relevance regarding beeswax

	Participant																
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Sex	F	F	F	F	F	M	F	F	F	F	M	M	F	F	M	F	F
Age (y)	59	22	31	29	18	36	31	50	67	41	80	60	51	42	37	31	21
Atopic dermatitis	+	+	+	+	+	–	+	+	–	+	–	–	–	+	–	+	+
Cera alba	+	NT	NT	–	+	–	NT	+	–	++	+	++	–	++	+++	–	+
Cera flava	+	++	+	+	+	+	+	++	+	++	+++	–	+	++	+++	+	+
Propolis	+	–	++	+	+	+	++	++	–	++	+++	–	++	++	+++	++	+++
MPR	++	–	++	–	+	–	–	+	–	–	+	++	+	++	–	–	++
FM I	++	–	–	–	+	–	–	+	–	–	–	++	–	+	–	–	++
Colophonium	++	–	–	–	+	–	+	++	–	–	–	–	–	–	–	–	++
SLM	–	–	–	–	–	–	–	–	+	–	–	–	–	–	–	–	–
Lichen acid mix	+	–	–	–	–	–	–	–	–	–	–	–	–	+	–	–	–
Relevance regarding beeswax	C	C	C	C	C	C	C	C	C	C	C	C	C	U	C	C	C

Abbreviations: C, current clinical relevance; F, female; FM I, fragrance mix I; M, male; MPR, *Myroxylon pereirae* resin; NT, not tested; SLM, sesquiterpene lactone mix; U, unclear clinical relevance.

TABLE 3 Reactions to plant substances and fragrance markers in the patients with contact cheilitis or facial dermatitis (N = 93) as compared with unselected test patients in Gothenburg 2009 to 2014 (N = 2497)

	No. tested	Percentage positive	CI	Unselected test population (%)	CI	P-value
Colophonium	9	10	5-18	2.2	1.68-2.85	0.004
SLM	1	1	0-5	0.8	0.50-1.22	NS
MPR	14	15	9-25	4.5	3.71-5.38	0.0002
FM I	12	13	7-22	7.1	6.10-8.19	0.021
FM II	1	1	0-5	2.4	1.85-3.07	NS
Lichen acid mix	1	1	0-5	0.7	0.41-1.07	NS
One or more of the above	10	11	5-19	10.9	9.65-12.2	NS

Abbreviations: CI, confidence interval; FM I, fragrance mix I; FM II; fragrance mix II; MPR, *Myroxylon pereirae* resin; NS, not significant; SLM, sesquiterpene lactone mix.

concomitant reactions to colophonium, MPR and FM I were found than in our general test population. Colophonium, MPR and FM I were also more commonly positive in the beeswax-positive group than in the general test population, although statistical analysis was not possible, owing to low numbers (Table 4).

Ten beeswax-positive patients were tested with caffeic acid and two ester derivatives, previously identified as haptens in propolis (Figure 1).¹² Among these patients, three reacted to caffeic acid phenethyl ester and/or caffeic acid 1,1-dimethylallyl ester. None had a positive test reaction to caffeic acid (Table 5).

3.2 | Chemical analysis

Mass spectrometry analysis of the surface of the yellow and white beeswax showed an abundance of lipids and other fatty acid-related species (Supporting Information Figure S1). The waxes differed clearly in caffeic acid $[C_9H_7O_4]^-$, caffeic acid phenethyl ester $[C_{17}H_{15}O_4]^-$ and caffeic acid 1,1-dimethylallyl ester $[C_{14}H_{15}O_4]^-$ contents

(Figure 2). The contents of all three substances were higher in yellow beeswax than in white beeswax.

4 | DISCUSSION

There are not many articles in the literature describing contact allergy to beeswax. Apart from some case reports,^{2-5,7} only one systematic survey on a general test population in the United Kingdom has been published; that study found that 0.45% of patients were beeswax-positive.¹¹ Contact allergy to beeswax seems to be rather uncommon relative to the extent of beeswax usage.

Although 20% to 30% beeswax in pet. or oil has been tested before, beeswax is tested "as is" in most studies,^{2-5,11} and this latter approach is what we have chosen. To our knowledge, this study is the first to systematically investigate the frequency of beeswax contact allergy among patients with cheilitis, facial eczema, or anamnestic suspicion of contact allergy to beeswax. We found a high proportion of positive reactions, almost all of which were clinically relevant. If similar results are obtained in further studies, this will imply that beeswax or relevant haptens therein should be included when patch testing is performed in these types of patient.

In its natural form, beeswax is yellow, being contaminated with material from pollen and propolis.¹ The wax can be whitened by purifying or bleaching it.^{1,21} Thus, it is difficult to determine the exact chemical difference between yellow and white beeswax. It is unknown whether contact allergy to beeswax is caused mainly by a hapten within beeswax, or by impurities in the product. We have not found many studies comparing contact allergy between white and yellow beeswax.¹¹ Contact sensitization to beeswax has been proposed to be mainly attributable to contamination with propolis.⁴ One argument for this possibility is that many patients with positive patch test reactions to yellow beeswax show concomitant reactions to propolis,^{5,7} but some also react to white beeswax, and a few have negative patch test results with propolis, which could indicate that some substance in beeswax itself can be sensitizing.^{4,11}

To our knowledge, there have been no systematic studies on the frequency of contact allergy to propolis in Sweden. The frequency in

TABLE 4 Concomitant reactions to plant substances and fragrance markers of the baseline series among patients with positive patch test reactions to beeswax (N = 17) as compared with unselected test patients in Gothenburg 2009 to 2014 (N = 2497)

	Beeswax-positive patients (n)	Beeswax-positive patients (%)	CI	Unselected test population (%)	CI
Colophonium	5	29	11-65	2.2	1.68-2.85
SLM	1	6	3-29	0.8	0.50-1.22
MPR	9	53	26-97	4.5	3.71-5.38
FM I	5	29	11-65	7.1	6.10-8.19
Lichen acid mix	1	6	3-29	0.7	0.41-1.07
One or more of the above	5	29	11-65	10.9	9.65-12.2

Abbreviations: CI, confidence interval; FM I, fragrance mix I; MPR, *Myroxylon pereirae* resin; SLM, sesquiterpene lactone mix.

TABLE 5 Results of complementary patch testing with caffeic acid and its esters among beeswax-positive patients (N = 10)

	Patient number									
	1	4	5	6	8	9	10	11	15	16
Sex	F	F	F	M	F	F	F	M	M	F
Age (y)	65	34	24	40	52	67	42	81	41	32
Year tested	2015	2014	2015	2015	2015	2015	2015	2015	2016	2016
White beeswax	+	—	+	—	+	—	++	+	+++	—
Yellow beeswax	+	+	+	+	++	+	++	+++	+++	++
Propolis 10% pet.	+	+	+	+	++	—	++	+++	+++	++
Caffeic acid 5% pet.	—	—	—	—	—	—	—	—	—	—
Caffeic acid 0.5% pet.	—	—	—	—	—	—	—	—	—	—
Caffeic acid 0.05% pet.	—	—	—	—	—	—	—	—	—	—
Caffeic acid 0.005% pet.	—	—	—	—	—	—	—	—	—	—
Caffeic acid 0.0005% pet.	—	—	—	—	—	—	—	—	—	—
Caffeic acid phenethyl ester 1% pet.	—	—	—	—	—	—	—	+++	?+	++
Caffeic acid phenethyl ester 0.1% pet.	—	—	—	—	—	—	—	+++	—	++
Caffeic acid phenethyl ester 0.01% pet.	—	—	—	—	—	—	—	++	—	+
Caffeic acid phenethyl ester 0.001% pet.	—	—	—	—	—	—	—	++	—	—
Caffeic acid phenethyl ester 0.0001% pet.	—	—	—	—	—	—	—	+	—	—
Caffeic acid 1,1-dimethylallyl ester 1% pet.	—	—	—	—	—	—	—	+++	+	++
Caffeic acid 1,1-dimethylallyl ester 0.1% pet.	—	—	—	—	—	—	—	+++	—	++
Caffeic acid 1,1-dimethylallyl ester 0.01% pet.	—	—	—	—	—	—	—	+++	—	—
Caffeic acid 1,1-dimethylallyl ester 0.001% pet.	—	—	—	—	—	—	—	++	—	—
Caffeic acid 1,1-dimethylallyl ester 0.0001% pet.	—	—	—	—	—	—	—	+	—	—

Abbreviations: F, female; M, male; pet., petrolatum.

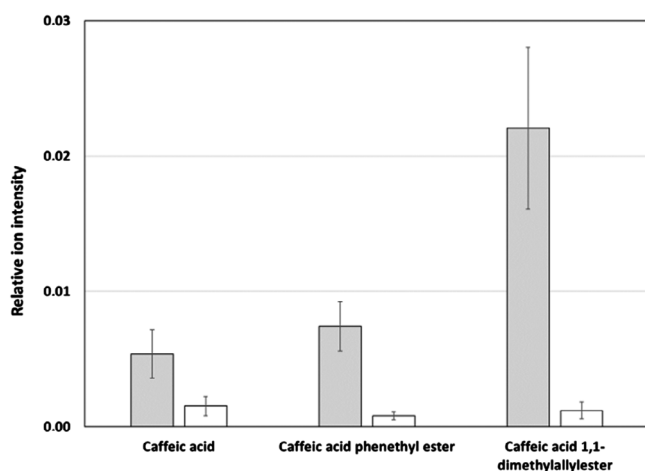


FIGURE 2 Relative surface contents of caffeic acid and esters in yellow beeswax (grey) and white beeswax (white) as analysed with secondary ion mass spectrometry. The waxes differed significantly ($P < 0.05$) in caffeic acid [$C_9H_7O_4$][−], caffeic acid phenethyl ester [$C_{17}H_{15}O_4$][−] and caffeic acid 1,1-dimethylallyl ester [$C_{14}H_{15}O_4$][−] contents. Error bars are 95% confidence intervals (n = 4)

this study is rather high, probably because we used a selected patient cohort. In the literature, reported frequencies of contact allergy to propolis are lower, but these frequencies were determined in

unselected patient cohorts.^{11,22} Concomitant patch test reactions between propolis, plant substances and fragrance markers are well known.^{11,23,24} To a large extent, this overlap is considered to result from shared constituents between propolis and MPR.¹¹ An additional cause, however, might be simultaneous exposure and sensitization. Concomitant reactions between beeswax and propolis, plant substances and fragrance markers are not well known, and it is not understood whether these reactions are attributable to remains of propolis in beeswax, shared constituents, or sensitization to several of the constituents at different times. In this study, there was a high frequency of contact allergy to beeswax in patients with cheilitis, facial eczema, and suspicion of contact allergy to beeswax. This finding has not been reported previously.

Caffeic acid and its esters have been suspected to be important allergens in propolis, as both caffeic acid phenethyl ester and caffeic acid 1,1-dimethylallyl ester were strong sensitizers in guinea-pig experiments and were present in propolis.¹⁹ All of our three patients with positive test reactions to caffeates also had strong reactions to propolis, which might suggest that those reactions could actually be attributable to the patients' concomitant contact allergy to propolis (Table 5). Here, we also show that there is a clear difference between yellow and white beeswax with regard to the contents of caffeic acid phenethyl ester and caffeic acid 1,1-dimethylallyl ester, whereby

yellow beeswax shows significantly higher levels. This is the first study to use imaging mass spectrometry as an analytical tool for natural products with complex matrices. One advantage of imaging mass spectrometry is that any material can be analysed without a complicated work-up, during which important analytes are at risk of being lost or chemically modified. Furthermore, compounds in tissue and cells can be imaged without the use of target-specific markers such as antibodies or probes. Imaging mass spectrometry is thus a promising tool for the identification of haptens in materials with complex compositions.

Clinically, beeswax was not shown to contain caffeic acid esters as important haptens, as propolis does, but caution is necessary when conclusions are drawn, owing to the low number of study subjects. The difference between the levels of those esters in yellow and white beeswax might point to the importance of those haptens in beeswax. If they do have importance, it is probably as prohaptens or prehaptens, via catechols activated to quinones, as esters and catechols are not normally chemically strong sensitizers. The difference could also be attributable to the presence of propolis in yellow beeswax.

Relevant positive patch test reactions have been found in 6% to 84% of patients with eczematous cheilitis.^{14,16,25–27} Causative allergens include fragrances, MPR, colophonium, antioxidants such as propyl gallate, octyl gallate, and dodecyl gallate, and propolis and several of the patient's own products.^{26–28} In the studies of contact allergic cheilitis, patch testing with beeswax has rarely been performed.^{4,9,15} The results of the present study, however, indicate that it might be important to patch test with beeswax in patients with cheilitis and facial dermatitis. The culprit allergen in beeswax remains to be identified, as does the relationship between beeswax and propolis regarding important allergens. Possible chemical differences between the two and their relevance to contact allergy need to be further investigated.

5 | CONCLUSION

Contact allergy to beeswax and propolis seems to be common among patients with cheilitis, eczema around the lips, or adverse reactions to products containing beeswax. Caffeic acid and its esters appear not to be the main haptens causing contact allergy to beeswax. The causative haptens in beeswax remain to be identified, and the relationship between contact allergy to propolis and contact allergy to beeswax remains to be characterized. As contact allergy is common among patients with eczematous cheilitis, patch testing is important.^{14,28,29} Our suggestion for identifying the culprit is to patch test not only with the baseline series and patient's own products, but also with beeswax and propolis.

ACKNOWLEDGEMENTS

We would like to thank Martin Gillstedt for help with statistical analysis and Britt-Marie Ehn for help with patch testing and study logistics.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to report.

ORCID

Gunnar S. A. Nyman  <https://orcid.org/0000-0002-3627-5124>

Lina Hagvall  <https://orcid.org/0000-0002-9141-9215>

REFERENCES

1. Bogdanov S. Beeswax: quality issues today. *Bee World*. 2004;85:46–50.
2. Rothenborg HW. Occupational dermatitis in beekeeper due to poplar resins in beeswax. *Arch Dermatol*. 1967;95:381–384.
3. Camarasa G. Occupational dermatitis from beeswax. *Contact Dermatitis*. 1975;1:124–124.
4. Lucente P, Cavalli M, Vezzani C, Orlandi C, Vincenzi C. Contact cheilitis due to beeswax. *Contact Dermatitis*. 1996;35:258–258.
5. García M, Pozo MD, Díaz J, Muñoz D, Fernández De Corrés L. Allergic contact dermatitis from a beeswax nipple-protective. *Contact Dermatitis*. 1995;33:440–441.
6. Schwartz L, Peck SM. The irritants in adhesive plaster. *Public Health Rep*. 1935;50:811–819.
7. Junghans V, Geier J, Fuchs T. Allergy to propolis caused by beeswax-containing ointment. *Am J Contact Dermat*. 2002;13:87.
8. Kohl L, Blondeel A, Song M. Allergic contact dermatitis from cosmetics. *Dermatology*. 2002;204:334–337.
9. Schena D, Fantuzzi F, Girolomoni G. Contact allergy in chronic eczematous lip dermatitis. *Eur J Dermatol*. 2008;18:688–692.
10. de Groot AC. Propolis: a review of properties, applications, chemical composition, contact allergy, and other adverse effects. *Dermatitis*. 2013;24:263–282.
11. Rajpara S, Wilkinson MS, King CM, et al. The importance of propolis in patch testing—a multicentre survey. *Contact Dermatitis*. 2009;61:287–290.
12. Hausen BM, Evers P, Stüwe HT, König WA, Wollenweber E. Propolis allergy (IV) studies with further sensitizers from propolis and constituents common to propolis, poplar buds and balsam of Peru. *Contact Dermatitis*. 1992;26:34–44.
13. Cuell A, Thompson DA. Too bee or not to bee? A case of contact cheilitis to beegle and lip balm allergens. *Br J Dermatol*. 2016;175:184.
14. Lim SW, Goh CL. Epidemiology of eczematous cheilitis at a tertiary dermatological referral centre in Singapore. *Contact Dermatitis*. 2000;43:322–326.
15. Nyman G, Hagvall L. A case of allergic contact cheilitis caused by propolis and honey. *Contact Dermatitis*. 2016;74:186–187.
16. Lim JTE, Ng SK, Goh CL. Contact cheilitis in Singapore. *Contact Dermatitis*. 1992;27:263–264.
17. Francalanci S, Sertoli A, Giorgini S, Pigatto P, Santucci B, Valsecchi R. Multicentre study of allergic contact cheilitis from toothpastes. *Contact Dermatitis*. 2000;43:216–222.
18. Jacob SE, Chimento S, Castaneda-Tardan MP. Allergic contact dermatitis to propolis and carnauba wax from lip balm and chewable vitamins in a child. *Contact Dermatitis*. 2008;58:242–243.
19. Hausen BM, Wollenweber E. Propolis allergy. (III). Sensitization studies with minor constituents. *Contact Dermatitis*. 1988;19:296–303.
20. Johansen JD, Aalto-Korte K, Agner T, et al. European Society of Contact Dermatitis guideline for diagnostic patch testing—recommendations on best practice. *Contact Dermatitis*. 2015;73:195–221.

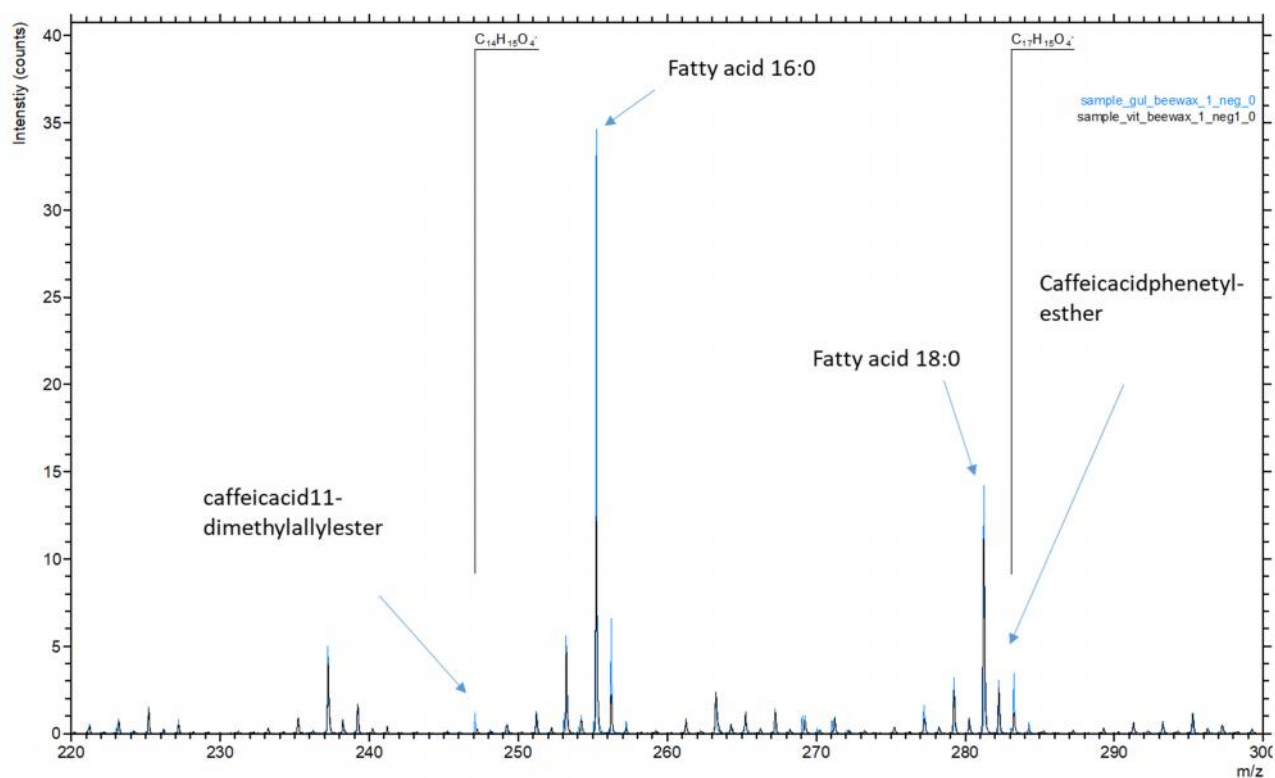
21. Bonnekoh B, Merk HF. Airborne allergic contact dermatitis from benzoyl peroxide as a bleaching agent of candle wax. *Contact Dermatitis*. 1991;24:367-368.
22. Uter W, Spiewak R, Cooper SM, et al. Contact allergy to ingredients of topical medications: results of the European Surveillance System on Contact Allergies (ESSCA), 2009–2012. *Pharmacoepidemiol Drug Saf*. 2016;25:1305-1312.
23. Shi Y, Nedorost S, Scheman L, Scheman A. Propolis, colophony, and fragrance cross-reactivity and allergic contact dermatitis. *Dermatitis*. 2016;27:123-126.
24. Petersen HO. Hypersensitivity to propolis. *Contact Dermatitis*. 1977;3:278-278.
25. Kanthraj GR, Sheno SD, Srinivas CR. Patch testing in contact cheilitis. *Contact Dermatitis*. 1999;40:285-285.
26. Zoli V, Silvani S, Vincenzi C, Tosti A. Allergic contact cheilitis. *Contact Dermatitis*. 2006;54:296-297.
27. O'Gorman SM, Torgerson RR. Contact allergy in cheilitis. *Int J Dermatol*. 2016;55:e386-e391.
28. Strauss RM, Orton DI. Allergic contact cheilitis in the United Kingdom: a retrospective study. *Am J Contact Dermat*. 2003;14:75-77.
29. Zug KA, Kornik R, Belsito DV, et al. Patch-testing North American lip dermatitis patients: data from the North American Contact Dermatitis Group, 2001 to 2004. *Dermatitis*. 2008;19:202-208.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Nyman GSA, Tang M, Inerot A, Osmancevic A, Malmberg P, Hagvall L. Contact allergy to beeswax and propolis among patients with cheilitis or facial dermatitis. *Contact Dermatitis*. 2019;81:110–116. <https://doi.org/10.1111/cod.13306>

Supplementary Figure 1



Comparison of negative ion mass spectra from the surface of yellow beeswax (blue line) and white beeswax (black line). The spectra show differences in c16:0 fatty acids, c18:0 fatty acids, caffeic acid phenethyl ester [C₁₇H₁₅O₄]⁻ and caffeic acid 1,1- dimethylallyl ester [C₁₄H₁₅O₄]⁻ content. The mass range from *m/z* 220 to *m/z* 300 is shown.