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Fragrant and sticky allergens from the pinewood: cohabiting and coreacting

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Conflicts of interest: None to declare.

Running head: Fragrant and sticky allergens from pines
SUMMARY

**Background:** Tree moss (*Pseudevernia furfuracea* (L.) Zopf.), a lichen growing on conifers, is a frequent fragrance sensitizer. Previous studies have shown two subgroups of tree moss-allergic patients: a group sensitized to common allergens of tree and oak moss (*Evernia prunastri*), and another group sensitized to colophonium-derived allergens, which may contaminate tree moss extract.

**Objectives:** To report the results of including tree moss extract in the baseline series and discuss the clinical implications.

**Materials and Methods:** Tree moss extract was included in the baseline series and sensitized patients were assessed for concomitant allergy to colophonium and oak moss, and the relevance of these reactions was analysed.

**Results:** Altogether, 22 of 632 patients (3.5%) had positive reactions to tree moss. Eight patients were sensitized to tree moss only (among fragrance allergens) and 75% had relevant reactions to colophonium. Fourteen patients were sensitized to other fragrance allergens as well and 28.5% had relevant colophonium reactions.

**Conclusions:** The prevalence of positive tree moss reactions is high enough to justify its inclusion in the baseline series. If tree moss is not included, patients with positive colophonium reactions should be informed of possible (false) cross-reactivity to tree moss in order to avoid this labelled fragrance allergen.

**Key words:** allergic contact dermatitis; colophonium; Compositae; fragrance allergy; oak moss; tree moss; lichen; *Pseudevernia furfuracea*
1. INTRODUCTION

Tree moss (*Pseudevernia furfuracea* (L.) Zopf., synonym *Evernia furfuracea* (L.) W. Mann, family Parmeliaceae) is a lichen, consisting of a fungus living symbiotically with a green algae of the genus *Trebouxia*. It typically grows on conifers, especially pine and cedar trees. An extract of tree moss – like that of another lichen, oak moss (*Evernia prunastri* (L.) Ach.) – has been used extensively in the fragrance industry. Both lichens contain atranorin and chloroatranorin, which are degraded to the strong contact allergens atranol and chloroatranol, respectively. Furthermore, when harvesting the tree moss raw material, contamination with the bark and other debris from the host tree will inevitably occur, and this means that the tree moss extract contains colophonium and derived allergens. A German study of 3030 patients, patch tested with oak moss, tree moss, and colophonium, found 2 subgroups of tree moss-sensitive patients: the first comprised patients, who were allergic to common constituents of tree and oak moss, but not colophonium, and the second comprised patients, who were sensitized to colophonium and its constituent (oxidized) resin acids.

As several studies have shown a high prevalence of positive reactions to tree moss, and as there is not consistent cross-reactivity between tree moss and colophonium, or tree moss and oak moss, some authors have suggested that tree moss should be included in the baseline series. We report the results of including tree moss extract in the baseline series and discuss the clinical implications.

2. Methods

Tree moss absolute extract 1% pet. from Chemotechnique Diagnostics (Vellinge, Sweden) was added to the baseline series in January 2018. Other fragrance allergens of the baseline series included fragrance mix I 430µg/cm², *Myroxylon pereirae* (balsam of Peru) 800µg/cm² (TRUE Test Panel 1), fragrance mix I 8% pet., isoeugenol 1% pet., *Evernia prunastri* extract (oak moss absolute) 1% pet., hydroxyisohexyl 3-cyclohexene carboxaldehyde 5% pet., and fragrance mix II 14% pet. from AllergEAZE, SmartPractice, Hillerød, Denmark. Moreover, oxidized linalool 1% and 0.5% pet. as well as oxidized limonene 0.3 and 0.2% pet. from Chemotechnique Diagnostics was included. Colophonium, which may also be considered a marker of fragrance allergy, was also part of the TRUE test Panel 1. The allergens were applied to the back for 2 days, using 8 mm Finn Chambers on Scanpor (SmartPractice), and readings were performed on day (D) 3/4 and D7 according to the latest recommendations.

3. Results

In the first 16 months, 632 patients were patch tested with the tree moss extract. Altogether, 22 patients (3.5%) had positive, 12 had doubtful, and 2 had follicular patch test reactions to the extract.
This places tree moss as number 4 in the ranking of positive reactions to fragrance allergens of the baseline series, only surpassed by hydroperoxides of linalool (1% and 0.3% pet.), fragrance mix I (8% pet. and 430µg/cm²), and fragrance mix II (14% pet.) in our area. The patients with positive reactions comprised 16 females with a mean age of 41 years, and 6 males with a mean age of 66 years. Ten of the 22 positive reactions were considered to be of current or old relevance, based on the patients’ history. More than half of the patients were sensitized to fragrance allergens other than tree moss, and 12 were sensitized to colophonium. The patients could be divided into 2 groups: 8 patients, who were sensitized to tree moss only (group 1), and 14, who were sensitized to other fragrance chemicals (group 2). Tables 1 and 2 show the distribution of reactions to tree moss, colophonium, and oak moss in the 2 groups. In general, the patch test reactions to tree moss were stronger in group 1 (75% ++ or +++ reactions) compared with group 2 (50% ++ or +++ reactions). In group 1, 7 of the 8 patients were sensitized to colophonium, and 6 of these reactions were considered relevant (75%), whereas 5 of the 14 patients in group 2 had colophonium allergy, and 4 were considered relevant (28.5%). Some of the exposures included spruce, tape, wood, band aid, and firewood.

Concerning Compositae sensitization, three of the patients with positive tree moss reactions were sensitized to this plant family as well. In the group with doubtful positive tree moss reactions, two were Compositae-allergic. For comparison, the number of newly diagnosed Compositae-sensitive patients in the study period was 15 (excluding a child who was tested with colophonium, but not tree moss). Thus, 3 of 15 (20%) Compositae-sensitive patients were sensitized to tree moss, and they were also the only Compositae-allergic patients with positive reactions to colophonium. All 3 patients had positive patch test reactions to Compositae mix II 2.5%, whereas only 1 tested positive to the sesquiterpene lactone mix. In the remaining 12 Compositae-sensitive patients, only four were sensitized to other fragrance compounds and only one, with a follicular reaction to tree moss, was sensitized to colophonium.

4. Discussion
The prevalence of positive tree moss patch test reactions of 3.5% is similar to those reported by other Danish studies.6,8 This places tree moss among the 5 fragrance compounds eliciting positive reactions most frequently, and the results support its continued inclusion in the baseline series. Furthermore, the heterogeneity of sensitization to tree moss is confirmed as there were 2 groups of patients with different patterns of sensitization to other fragrance or marker of fragrance compounds. Uter et al in their study of 3030 patients, could not determine the source of primary sensitization, but found it more likely that primary and intense sensitization to colophonium would lead to secondary elicitation by traces of resin acids in tree moss than vice versa.3 The findings in the present study confirm this: most of the colophonium reactions in the 8 patients monosensitized to tree moss were relevant and more often than those of tree moss (Table 1). Colophonium is composed of about 90% resin acids. Oxidized derivatives of abietic acid and dehydroabietic acid are important contact allergens.10 The strength of the reactions to tree moss and colophonium were mostly similar, which suggests more than traces of oxidized resin acids in the tree moss extract – another explanation is intense sensitization as suggested by Uter et al (Table 1).3 Conversely, in patients sensitized to tree moss and other fragrance compounds, the reactions to colophonium were
mostly stronger than those to tree moss, suggesting (false) cross-reactivity to trace amounts of allergens (Table 2).

When tree moss is collected on pine trees in the Massif Central in France, 40-70% of its weight is made up by tree components such as wood, bark, twigs, and needles. The resin acids of colophonium do not only occur in the tree debris, but they also migrate into the lichen. It has been shown that the ratio between 7-oxodehydroabietic acid and dehydroabietic acid is present in a higher concentration in tree moss than in the host tree, suggesting that certain lichen compounds may act as pre-oxidants. Other potential sources of dehydroabietic acid could be the common lichen Xanthoria parietina (common yellow lichen): the resin was detected in X. parietina growing on trees in Israel. Because of high nitrogen dust pollution, X. parietina may also be found on pine trees in the Mediterranean area. In a Canadian study, 3 strains of the fungus honey mushroom, recognized as a species within the Armillaria mellea complex, parasitic on pine and spruce, produced dehydroabietic acid, which occurs widely in higher plants as well as in Cyanobacteria.

Tree moss is a complex natural product, and more than 90 constituents have been detected: in theory, it is possible that patients with positive patch test reactions to tree moss and colophonium are sensitized not only to common oxidized resin acids, but also to other potential allergens of tree moss. The reactions might thus represent both false cross-reactions and cosensitization to unrelated allergens.

According to the manufacturer, the tree moss extract may contain atranol and chloroatranol, and it is obvious from Tables 1 and 2 that patients without colophonium contact sensitization have a fairly high concordance between positive reactions to tree moss and oak moss because of common allergens. Both tree moss and oak moss are among the 26 fragrance allergens that are mandatorily labelled within the EU, and they are thus easily detectable in cosmetic products. Tree moss is not widely used in household products, but may occur in personal care products, men’s products, and fine fragrances for women. If tree moss is not included in the baseline series, it is important to inform patients with relevant colophonium sensitization of the risk of reaction to tree moss and thus inadvertent exposure to common – or coreacting – allergens.

Liverworts of the genus Frullania, such as Frullania tamarisci (L.) Dumort. and Frullania dilatata (L.) Dumort. also grow on trees, notably oaks, and they are a well-known cause of airborne contact dermatitis because of their allergenic sesquiterpene lactones. As they may co-occur with Evernia species, Uter et al also quantified co-reactivity between tree/oak moss and Compositae mix 5%: co-reactivity between oak moss and Compositae mix was almost absent, and that between tree moss and Compositae mix very limited. Even though 20% of the Compositae-allergic patients in the present small study were sensitized to tree moss, they also had relevant positive patch test reactions to colophonium (and positive reactions to Compositae mix). Apart from (false) cross-reactivity between colophonium and tree moss, an association between Compositae sensitization and colophonium are possible explanations. Frullania tamarisci (L.) Dumort. contains, among other compounds, costunolide and (-)-frullanolide, and sensitization to this liverwort may thus elicit positive patch test reactions to the sesquiterpene lactone mix. As the prevalence of sesquiterpene
lactone mix positivity in this study was low, we agree that contamination with, and concomitant allergy to, Frullania seems less likely.

Concomitant contact allergy to lichen and Compositae was reported in 5 of 16 light-sensitive patients, who were patch test positive to various lichens. However, this may reflect cosensitization, as lichens and Compositae plants co-exist in nature and may co-appear in cosmetics. This may be another explanation for the positive and doubtful positive reactions to Compositae among tree moss-sensitive patients in the present study as well.

In conclusion, this study, in accordance with previous reports, confirms that the prevalence of tree moss sensitization is high enough to recommend its inclusion in the baseline series. It also confirms that 2 types of sensitization occur: either concomitant sensitization to tree moss and other fragrance allergens, including oak moss with which it shares some allergens, or concomitant sensitization to colophonium, which may contaminate the tree moss extract and thus cause false cross-reactions. If tree moss is not included in the baseline series, it is recommended to inform patients with colophonium sensitization of this possible source of exposure, especially because tree moss is avoidable being one of the 26 EU-labelled fragrance allergens.
References


3. Uter W, Schmidt E, Lessmann H, Schnuch A. Contact sensitization to tree moss (*Evernia furfuracea* extract, INCI) is heterogeneous. *Contact Dermatitis* 2012; 67: 36-41.


6. Heisterberg M V, Menné T, Johansen J D. Contact allergy to the 26 specific fragrance ingredients to be declared on cosmetic products in accordance with the EU cosmetics directive. *Contact Dermatitis* 2011; 65: 266-275.


<table>
<thead>
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<th>Patient no.</th>
<th>Tree moss a) 1% pet.</th>
<th>Colophonium 1200µg/cm²</th>
<th>Oak moss b) 1%pet.</th>
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<td>++(O)</td>
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Table 1. Distribution of patch test reactions (and relevance) to tree moss, colophonium, and oak moss in 8 patients monosensitized to tree moss (among fragrance chemicals)

C = current; O = old, D = don’t know

a) *Evernia furfuracea* extract (INCI)
b) *Evernia prunastri* extract (INCI)
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<tr>
<th>Patient no.</th>
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<th>Colophonium 1200µg/cm²</th>
<th>Oak moss b) 1% pet.</th>
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Table 2. Distribution of patch test reactions (and relevance) to tree moss, colophonium, and oak moss in 14 patients sensitized to tree moss and other fragrance chemicals

C = current; O = old; D = don’t know
a) *Evernia furfuracea* extract (INCI)
b) *Evernia prunastri* extract (INCI)