

Compositae-Associated Allergic Contact Dermatitis from Bisabolol

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Background: Compositae-related chemicals cause allergic contact dermatitis (ACD) in children with atopic dermatitis (AD). Moisturizers can be an overlooked exposure source.

Objective: To evaluate ACD in children with recalcitrant AD and a reported history of intolerance to Aquaphor Healing Ointment (AHO) moisturizer.

Methods: We retrospectively reviewed charts of children patch-tested to the ingredients of AHO moisturizer who had a history of intolerance, as well as of additional patch-tested patients with exposure to bisabolol in their personal hygiene products and without a history of product intolerance.

Results: Seven patients, six of whom had AD, had been referred to our clinic with a history of intolerance to the moisturizer. They were patch-tested with their moisturizer and the components provided by Beiersdorf. Of these, four had positive reactions to their AHO moisturizer and to bisabolol, a Compositae derivative.

Conclusion: Bisabolol, a sesquiterpene alcohol, should be considered a potential cause of ACD in children with AD and a history of moisturizer intolerance.

BISABOLOL, a monocyclic sesquiterpene alcohol (Fig 1), is one of the primary active ingredients in *Matricaria chamomilla* (German chamomile), a member of the Compositae (Asteraceae) family. Because of bisabolol's purported antiinflammatory, antibacterial, and skin-soothing properties, this extract is used in numerous products, especially "natural" ones targeted at children with sensitive skin.¹ It may be an overlooked cause of Compositae-associated allergic contact dermatitis (ACD). Sesquiterpene alcohol is structurally similar to sesquiterpene lactone (SQL) (Fig 2), one of the most important allergens in the Compositae family, so there may be the potential for cross-reactivity between the substances.

In early 2009, after evaluating three patients with reported pruritus, stinging, and worsening of their dermatitis when using Aquaphor Healing Ointment (AHO) (Beiersdorf AG, Hamburg, Germany), we acquired the AHO ingredient panel from the manufacturer. Unfortunately, these patients were not available to undergo confirmatory testing with the individual components of AHO. However, because two of the original three

patients had patch-tested positively to their AHO and all three had positive patch-test reactions to Compositae and SQL, the ingredient bisabolol was considered a potential culprit.² At that time, there were two reports in the European literature confirming bisabolol as an allergen.^{3,4}

We here report patch-test evaluation results for seven children with a history of intolerance (namely, pruritus and "stinging") to their AHO moisturizer who were tested with the product ingredient panel.

Materials and Methods

We reviewed our charts for pediatric and adolescent patients who had been referred to our tertiary care contact dermatitis center, had a self-reported history of "intolerance" to their AHO moisturizer, and had been tested with the individual product ingredients. Subsequent patients with a history of intolerance to AHO moisturizer who were referred to our center were offered testing with the panel of the individual moisturizer ingredients as well (Table 1).

Seven patients were found to have met the above criteria upon chart review; none of these patients had been using another moisturizer at the time of "intolerance." Six patients had been tested with the Rady Children's Hospital standard chemicals (allergEAZE, SmartPractice, Calgary, Alberta, Canada) whereas one patient was tested with the Thin-Layer Rapid Use Epicutaneous (T.R.U.E.) Test panels 1.1, 2.1, and 3 (Allerderm, Phoenix, AZ) in addition to

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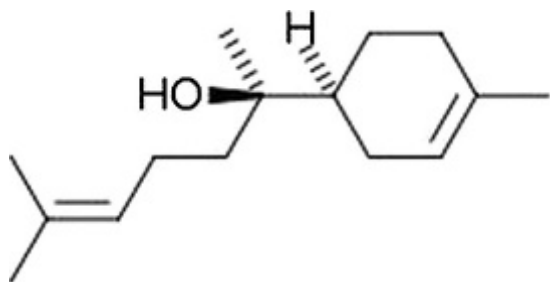


Figure 1. Structure of bisabolol.

selected chemicals from the Rady standard panel that were thought to be potentially relevant (eg, *Compositae* mix 6% in petrolatum and SQL mix 0.1% in petrolatum). Chemicals were applied to allergEAZE patch-test chambers (SmartPractice); patches had been applied for 48 hours and then read at 48 hours as well as between 72 and 96 hours after application.

The patients tested in 2008 (patients 1–3) were tested with the AHO panel with a bisabolol concentration of 0.5% and 1% in petrolatum as there were no references in the literature to concentrations in children. In 2009, we began testing with bisabolol at concentrations of 1% and 5% in petrolatum, the same concentrations that have been used for testing adults in Europe. In 2009, bisabolol 5% in petrolatum (pet) was added to the Rady standard panel and was used only if the patient had frequently used a product containing bisabolol as an ingredient. An additional 16 patients (12 with a diagnosis of atopic dermatitis) who had a history of prior exposure to bisabolol in their personal care products and who did not specifically report an intolerance to the product were also tested at our center.

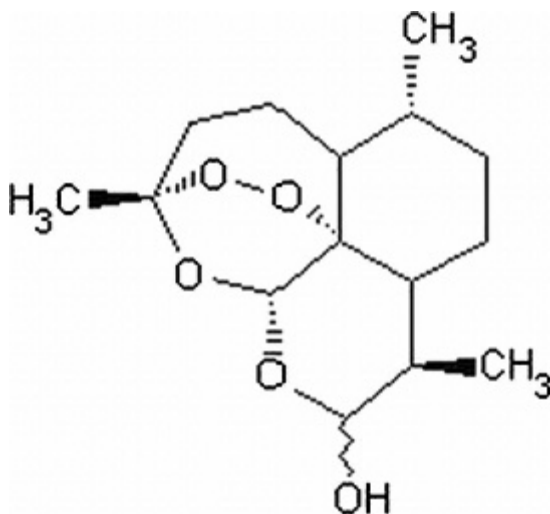


Figure 2. Structure of sesquiterpene lactone.

Table 1. Current Aquaphor Healing Ointment Substituent Panel*

Lanolin 30% pet
Ceresin wax 30% pet
Panthenol 5% pet
Glycerin 10% aqueous
Undiluted mineral oil
Bisabolol 5% pet
White petrolatum

pet = in petrolatum.

*Chemicals supplied by Beiersdorf AG, Hamburg, Germany.

Results

Of the 7 patients with self-reported intolerance to AHO who were tested with the manufacturer's supplied ingredient panel for AHO, 4 had positive patch-test reactions at 72 hours to their own AHO moisturizer in addition to bisabolol and to SQL or *Compositae* or both. The results are presented in Table 2; notably, there were no appreciable reactions at 48 hours.

Furthermore, 5 of the 7 patients had negative reactions to both the allergEAZE lanolin and the Beiersdorf lanolin; however, two patients (patients 1 and 2) did have false-negative reactions to the "standardized" commercially available lanolins but reacted positively to the Beiersdorf lanolin. Of clinical relevance, the 4 patients with confirmed allergy to bisabolol improved with avoidance of their moisturizer and *Compositae*-related chemicals (SQL and bisabolol). Notably, the additional 16 patients who were also tested with bisabolol all had negative test results.

Discussion

Compositae has been documented as a cause of ACD in adults; in the recent past, it has also been linked to ACD in children.^{5,6} Of interest, a study by Belloni Fortina and colleagues reported a statistically significant difference in the prevalence of positive patch-test reactions to *Compositae* mix in children with atopic dermatitis (AD) when compared to those without AD.⁵ Likewise, in the cases we reviewed, 6 of the 7 patients with self-reported moisturizer intolerance who were tested with the AHO ingredient panel also had the diagnosis of AD; 4 of these 6 patients had positive patch-test reactions to their own AHO and bisabolol. We considered these reactions to be true positive reactions and clinically relevant because significant improvement was noted when AHO and *Compositae*-related chemicals (SQL and bisabolol) were avoided. Furthermore, the 16 additional patients (12 with AD) with reported exposure and "intolerance" to AHO all

Table 2. Summary of Patients

<i>Patient</i>	<i>Age (yr)</i>	<i>Gender</i>	<i>Clinical Presentation</i>	<i>Prior Reaction to AHO Use</i>	<i>Relevant Patch-Test Results</i>
1	3	F	Severe generalized recalcitrant AD	Positive	(++) AHO (ME) Bisabolol 0.5% (+) Bisabolol 1% (+) Compositae mix (+) SQL mix (-) Lanolin (T.R.U.E. Test*) (+) Lanolin (Beiersdorf) (+) Panthenol
2	14	F	Worsening AD with eyelid and perioral involvement	Possible	(-) AHO (-) Bisabolol 0.5% and 1% (++) Lanolin (Beiersdorf) (-) Lanolin (allergEAZE [†])
3	13	F	Dermatitis on shins and feet	Possible	(-) Reactions to AHO and all components: (-) Bisabolol 0.5% and 1% (-) Lanolin (Beiersdorf and allergEAZE [†])
4	12	M	Recalcitrant AD with eyelid involvement	Positive	(+) AHO (ME) Bisabolol 1% (+) Bisabolol 5% (+) Compositae mix (-) SQL mix (-) Lanolin (Beiersdorf and allergEAZE [†])
5	7	M	Recalcitrant AD with marked perioral and periorbital component	Possible	(+) AHO (-) Bisabolol 1% (+) Bisabolol 5% (+) Compositae mix (-) SQL mix (-) Lanolin (Beiersdorf and allergEAZE [†])
6	5	F	Recalcitrant AD	Possible	(-) AHO (-) Bisabolol 1% and 5% (-) Compositae mix (-) SQL mix (-) Lanolin (Beiersdorf and AllergEAZE [†])
7	5	M	AD and ACD from nickel, with ID reaction and poor response to allergen avoidance	Possible	(+) AHO (+) Bisabolol 1% (+) Bisabolol 5% (+) Compositae mix (+) SQL mix (-) Lanolin (Beiersdorf and allergEAZE [†])

ACD = allergic contact dermatitis; AD = atopic dermatitis; AHO = Aquaphor Healing Ointment (Beiersdorf AG, Hamburg, Germany); F = female; ID = idiopathic reaction; M = male; ME = macular erythema; SQL = sesquiterpene lactone; T.R.U.E. = Thin-Layer Rapid Use Epicutaneous.

*Allerderm, Phoenix, AZ.

[†]SmartPractice Canada, Calgary, Alberta, Canada.

tested negatively, and no reactions to bisabolol were noted before 72 hours, suggesting that bisabolol 5% pet is not a low-grade irritant. That said, we recognize that further testing is necessary to investigate the pharmacokinetics of bisabolol as well as the irritancy threshold potential.

On a final note, ACD from lanolin (wool wax) alcohol, specifically in association with AHO, has been reported.⁷ It is also important to recognize that there is the potential for false-negative reactions when moisturizers with lanolin as a substituent are evaluated (even when lanolin is the culprit) because of naturally occurring variations in the composition of lipids.⁸ Provocative use testing with the patient's moisturizer in addition to testing with standardized lanolin 30% pet, Amerchol L-101 50% pet, and the moisturizer manufacturer's lanolin may be necessary to rule out lanolin causation of ACD.

Many current products on the market (such as moisturizers, lotions, ointments, cleansers, sunscreens, antiperspirants, and cosmetics) that are made to soothe the skin contain Compositae-associated allergens and bisabolol in particular. Our results suggest that the consideration of ACD from moisturizer ingredients in patients with AD recalcitrant to standard treatments is warranted.

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