Contact allergy to Tinosorb® M: recommendations for diagnostic improvement

Anton C. de Groot1, Esther J. van Zuuren2 and Diny Hissink3

1Acdegroot Publishing, Schipslootweg 5, Wapserveen, 8351 HV, The Netherlands, 2Department of Dermatology, Leiden University Medical Centre, Albinusdreef 2, Leiden, 2333 ZA, The Netherlands, and 3The Netherlands Food and Consumer Product Safety Authority, Catharijnesingel 59, Utrecht, 3511 GG, The Netherlands
doi:10.1111/cod.12159

Key words: contact allergy; decyl glucoside; methylene bis-benzotriazolyl tetramethylbutylphenol; sunscreen; Tinosorb® M.

Patients who show a positive patch test reaction to a mixture of chemicals should preferably be further tested with its ingredients, to identify the actual contact allergen(s). Insufficient patient cooperation and a lack of adequate, easily obtainable test materials may frustrate this search, as illustrated by this case of contact allergy to Tinosorb® M.

Case Report

A 56-year-old woman developed an itchy, red and burning eruption on her face and neck 1–2 days after the application of a sunscreen (sun cream SPF 30). Treatment with a corticosteroid cream resulted in rapid improvement. Later, the patient experienced a similar eruption after the use of another sunscreen of a different brand, cream protection SPF 50. The patient was patch tested at the Department of Dermatology, Leiden University Medical Centre, with the European baseline series, and patch and photopatch tested with a photopatch test series [containing a number of ultraviolet (UV) filters] and the two incriminated cosmetic products. At D2 and D3, positive reactions were observed to both sunscreen creams (tested undiluted), with equal strengths (+) on the irradiated and non-irradiated sites. The ingredients were subsequently requested from the manufacturers. After the constituents of one of them had been received (n = 32), the patient was patch tested with these (delivery of the ingredients of the other product was delayed) and retested with the sunscreen cream itself.

Contact allergy to the sunscreen cream was confirmed (D2 +; D3 +), and there was also a positive reaction (D2 +, D3 +) to a mixture of methylene bis-benzotriazolyl tetramethylbutylphenol (nano), decyl glucoside, propylene glycol and xanthan gum 58% in water (test concentration, 14% in water; solid ingredients, 14% of 58% = 8.1%). Xanthan gum was tested separately and gave a negative result. This mixture, which is the UV
filter Tinosorb® M, was also shown to be present in the SPF 50 sunscreen product. The patient was unwilling to be tested further with the ingredients of the second product or other allergens, as she had found another sunscreen not containing Tinosorb M®, which she tolerated well.

**Discussion**

Tinosorb M® is described by its manufacturer (BASF, Ludwigshafen, Germany) as ‘a new technology of UV skin protection. It is the first sun filter using microfine particle technology which acts both as a micropigment and organic UV absorber. Tinosorb M® is a highly efficient sunscreen due to its triple action: UV absorption by a photostable organic molecule, light scattering and light reflection by its microfine structure’. Its applications include ‘skin and sunscreen products’ (http://personal-care.basf.com/ProductDetails?PRD=30482916).

Tinosorb M® is provided as an emulsion that contains the UV filter methylene bis-benzotriazolyl tetramethylbutylphenol (45–55%) (synonym bisoctrizole, CAS no. 103597-45-1). In the EU, its use in cosmetic products has been permitted since 2000, at a maximum concentration of 10%. In a recent opinion of the Scientific Committee on Consumer Safety of the European Commission, it was concluded that the nano form of methylene bis-benzotriazolyl tetramethylbutylphenol (particles of 1–100 nm) can be used safely up to the same maximum concentration (1). Tinosorb M® also contains decyl glucoside (6–10%) (CAS no. 58846-77-8), propylene glycol (0.2–0.6%) (CAS no. 57-55-6), xanthan gum (0.1–0.5%) (CAS no. 11138-66-2), and water (40–42%) (1). These compounds are added to enhance the solubility of the UV filter in cosmetic products; the surfactant decyl glucoside and the emulsifier/surfactant xanthan gum additionally stabilize the emulsion and the UV microparticles in it (1).

Contact allergy to Tinosorb M® was first described by Andersen and Goossens in 2006 (2). Their patient had positive patch test reactions to a sunscreen containing Tinosorb M®, Tinosorb M® 6% in water, decyl glucoside (dilution series 0.5–5% in water and a separate batch of 2% in water), and coco-glucoside 2% in water. It was concluded that the patient suffered from contact allergy to decyl glucoside in Tinosorb M® (2). Later, more cases of contact allergy to Tinosorb M® resulting from its presence in skin care and sunscreen products were reported (3–8). The results of patch tests in these patients are summarized in Table 1.

Two patients were tested with decyl glucoside (no commercial test preparation of which is available), and were both positive. One of them also reacted to coco-glucoside, and the other reacted to cosmetics containing lauryl glucoside, myristyl glucoside, or coco-glucoside. Six patients were tested with lauryl glucoside 3% pet. (Chemotechnique Diagnostics, Vellinge, Sweden), and 5 of them had positive patch test reactions: 1 of these also reacted to shampoos containing glucosides. In a study from the United States, 2 patients with chronic actinic dermatitis reacted to methylene bis-benzotriazolyl tetramethylbutylphenol 10% pet. (probably Tinosorb M®). However, use of this product is not permitted by the Food and Drug Administration, and neither patient could identify previous or current contact with the chemical (9). In not a single case reported have decyl and lauryl glucoside been tested simultaneously. Also, in no single instance was the UV filter methylene bis-benzotriazolyl tetramethylbutylphenol tested as such, as it appears to be unobtainable. The 2 patients of Travassos et al. were considered to be allergic to methylene bis-benzotriazolyl tetramethylbutylphenol (4). Patch test data were not provided. However, we have found that they were tested with Tinosorb M® (Chemotechnique Diagnostics), and were also allergic to decyl glucoside (A. Goossens, pers. comm. 2013). Thus, from these data, it appears likely that at, least in a number of cases, but probably in the (great) majority, decyl glucoside is the actual allergen in Tinosorb M®.

Decyl glucoside (synonym: decyl β-glucopyranoside) is a condensation product of decyl alcohol and glucose. It is an emulsifier, non-ionic surfactant and cleansing agent, and is often used in both rinse-off and leave-on cosmetic products, such as cleansing milks, lotions, and sunscreens, because of the mildness of its effects on the skin (2).

Contact allergy to decyl glucoside in antiseptic gels and cosmetic products, including shampoos, has been reported several times (4, 10–14). Travassos et al. (4) observed 8 cases of cosmetic allergy caused by decyl glucoside between 2000 and 2010; in 5 of these, the cosmetics containing decyl glucoside were ‘sun care’ products. Some of the patients with decyl glucoside allergy described in the literature also reacted to lauryl glucoside and coco-glucoside (10, 14), and one of them was allergic to three sunscreens containing Tinosorb M® (10). The concommitant reactions to decyl glucoside, lauryl glucoside (the condensation product of lauryl alcohol and glucose) and coco-glucoside (the condensation product of coconut alcohol and glucose) may have resulted from cross-reactivity, contamination of one compound with another, or common contaminants of substances used in the production of the glucosides.

---

1 [the INCI name is Methylene Bis-Benzotriazolyl Tetramethylbutylphenol (and) Aqua (and) Decyl glucoside (and) Propylene Glycol (and) Xanthan Gum].
Contact Dermatitis

CONTACT ALLERGY TO TINOSORB® M • DE GROOT ET AL.

Table 1. Test results of published cases of allergic contact dermatitis caused by Tinosorb M® (2–8)

<table>
<thead>
<tr>
<th>Country and year of publication</th>
<th>Patient sex, age</th>
<th>Results of patch tests</th>
<th>Other positive reactions</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Portugal 2009–2012</td>
<td>M, 66</td>
<td>10% pet. ++ 5% pet. ++</td>
<td>NT</td>
<td>(3, 7)</td>
</tr>
<tr>
<td></td>
<td>F, 52</td>
<td>10% pet. +</td>
<td>3% pet. +</td>
<td>Myroxylon pereirae, fragrance mix I, nickel, sunscreens and face cosmetics containing glucosides</td>
</tr>
<tr>
<td></td>
<td>F, 64</td>
<td>10% pet. +</td>
<td>3% pet. +</td>
<td>Sunscreen and shampoos containing glucosides</td>
</tr>
<tr>
<td></td>
<td>M, 64</td>
<td>10% pet. ++</td>
<td>3% pet. +++</td>
<td>Sodium metabisulfite</td>
</tr>
<tr>
<td></td>
<td>F, 39</td>
<td>10% pet. ++</td>
<td>3% pet. +++</td>
<td>–</td>
</tr>
<tr>
<td>United Kingdom 2011</td>
<td>M, 75</td>
<td>10% pet. +</td>
<td>Negative</td>
<td>(5, 6)</td>
</tr>
<tr>
<td></td>
<td>F, 85</td>
<td>10% pet. +</td>
<td>3% pet. +</td>
<td>2-Bromo-2-nitropropane-1,3-diol</td>
</tr>
<tr>
<td>Belgium 2000–2010</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Spain 2007b</td>
<td>F, 54</td>
<td>2% pet. +</td>
<td>NT</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sunscreen containing Tinosorb M®, nickel</td>
<td>(8)</td>
</tr>
<tr>
<td>Denmark 2006</td>
<td>M, 67</td>
<td>6% aqua ++</td>
<td>0.5–5% aqua +</td>
<td>NT</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sunscreen containing Tinosorb M®, methylchloroisothiazolinone/methylisothiazolinone</td>
<td>(2)</td>
</tr>
</tbody>
</table>

F, female; M, male; MCI/MI, methylchloroisothiazolinone/methylisothiazolinone; NT, not tested.

*The 10% pet. preparation is the commercial Chemotechnique Diagnostics test substance, labelled as 10% methylene bis-benzotriazolyl tetramethylbutylphenol.

**In this publication, it is indicated that the patient was tested with methylene bis-benzotriazolyl tetramethylbutylphenol 2% pet.; however, as Tinosorb M® was given as the synonym, and the pure UV filter appears not to be available, it is likely that, in fact, Tinosorb M® with 2% methylene bis-benzotriazolyl tetramethylbutylphenol in pet. was tested.

Although the number of published cases of contact allergy to Tinosorb M® is low (Table 1, our case), it is likely that allergic contact dermatitis caused by this UV filter is not infrequent. Thus, Pereira et al. in Portugal detected 5 cases in a 3-year-period in their clinic in a group of 1033 patients with suspected (photo)contact allergy (3). Also, the members of the European Multicentre Photopatch Test Study performed patch tests and photopatch tests with an extensive series of (photo)contact allergens, including Tinosorb M® (Chemotechnique Diagnostics), in 1031 patients with suspected photoallergic contact dermatitis. There were only 5 cases of photocontact allergy to Tinosorb M®, but 11 cases of contact allergy, the highest number of positive patch test reactions to any allergen tested (15).

Recently, it has been recommended to include ‘methylene bis-benzotriazolyl tetramethylbutylphenol 10% in petrolatum’ to the European photopatch test baseline series (16). This product is available from Chemotechnique, and is indeed labelled as ‘methylene bis-benzotriazolyl tetramethylbutylphenol 10%’, but is actually Tinosorb M®, which also contains decyl glucoside, propylene glycol, and xanthan gum [as already noted by O’Connell et al. (5)]. The concentration of methylene bis-benzotriazolyl tetramethylbutylphenol in the test preparation is 10%, and the concentration of Tinosorb M® in it depends on the concentration of the UV filter in Tinosorb M® (currently, Tinosorb M® 17.5%; information provided by Charlotte Siwmark and Bo Niklasson from Chemotechnique Diagnostics: 26 August 2013). This ‘mislabelling’ has unfortunately led to a great deal of confusion, and may have falsely incriminated the UV absorber methylene bis-benzotriazolyl tetramethylbutylphenol as a contact allergen (4, 6, 8, 9, 15) and possibly as a photocontact allergen (9, 15).

We suggest that contact allergy to Tinosorb M® may not be infrequent. The available data suggest that the allergen in it is decyl glucoside (far) more often than the UV filter methylene bis-benzotriazolyl tetramethylbutylphenol. However, adequate data are lacking, as neither of these chemicals is commercially
available for patch testing. Therefore, we recommend the following:

1. For dermatologists to add the commercial Tinosorb M® product to a series that is routinely tested in patients suspected of having cosmetic allergy or photoallergic contact dermatitis;

2. For dermatologists to add to such a series lauryl glucoside, which will detect a number of cases of contact allergy to decyl glucoside;

3. For commercial parties to describe as accurately as possible the contents of their patch test materials;

4. To avoid confusion, for authors of publications on (contact allergy to) Tinosorb M®/methylene bis-benzotriazolyl tetramethylbutylphenol to describe the materials tested accurately and not use the names as synonyms; and

5. For commercial parties to investigate the possibility of making available patch test materials with decyl glucoside and with the pure methylene bis-benzotriazolyl tetramethylbutylphenol. In response to our suggestions, Chemotechnique has stated that it will be able to provide these separate compounds in the near future (Bo Niklasson, Chemotechnique, information provided 9 September 2013).

References