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Undisclosed presence of methylisothiazolinone in '100% natural' Konjac[®] sponge

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Methylisothiazolinone (MI) (CAS no. 2682-20-4) is causing an epidemic of contact dermatitis throughout Europe and the United States (1, 2). In Europe, MI is permitted in cosmetic leave-on and rinse-off products at a maximum concentration of 100 ppm, and should be labelled (3). We present a case of contact dermatitis caused by undisclosed MI in a Konjac[®] sponge sold in Danish health stores and pharmacies containing ~400 ppm MI.

Case Report

A 38-year-old female agricultural worker, with no history of previous dermatitis, developed vesicular pulpitis of the fingers on both hands with no obvious cause. She also noticed facial dermatitis after using a Konjac[®] sponge bought at the local pharmacy (Bamboo Charcoal; The Konjac Sponge Company, Milton Keynes, UK). She had used the sponge for 3 days, suspected that it caused facial dermatitis, and then stopped using it, after which the facial dermatitis disappeared. Her hand dermatitis improved with topical corticosteroid treatment. She was referred for patch testing. Since being purchased, the moist sponge had been kept in a plastic bag in a closed aqueous environment, and there was no declaration of ingredients. A search of the website of the company did not show any list of ingredients, but it was stated that

the sponge was a '100% natural' product. Patch testing with the European baseline series (TRUE Test[®] panel 1–3; SmartPractice, Hillerød, Denmark) supplemented with the remaining baseline allergens, the Konjac[®] sponge 'as is', dandelion 2.5% pet., *Tanacetum parthenium* 1% pet., Captan 0.5% pet. and Compositae mix II in Finn Chambers[®] on Scanpor[®] tape (SmartPractice, Phoenix, AZ, USA) was performed according to the department's routine procedure, with 2 days of exposure and readings on day (D)3 and D7. Patch tests showed positive reactions to methylchloroisothiazolinone/MI (4 µg/cm²) (+/+), MI 0.2% aq. (++/+), and MI 0.02% aq. (++/+). We suspected MI to be the allergen in the Konjac[®] sponge, and sent it for chemical analysis.

The Konjac[®] sponges were purchased from the local pharmacy (Apoteket Rosengården, Odense, Denmark). MI standard and dichloromethane (DCM; CHROMASOLV HPLC grade) were purchased from Sigma Aldrich (Steinheim, Germany).

Table 1. Concentration of methylisothiazolinone (MI) in Konjac[®] sponges determined by gas chromatography–mass spectrometry

Sponge	Concentration (µg MI/g dried sponge)*
Bamboo charcoal for oily and spot-prone skin	387 ± 3
Rich red clay for dry or mature skin	415 ± 8
For all skin types (white)	320 ± 5
Rich pink clay for tired or devitalized skin	395 ± 6
Green clay for oily and combined skin	441 ± 5

*The concentration of MI is based on three replicates, and is given as the mean ± standard deviation.

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One gram of five different dry Konjac® sponge materials was cut into small pieces. Material from each sponge was extracted with 1 ml of DCM overnight in an 8-ml vial (with occasional shaking). The extraction process was repeated on two other batches of each Konjac® sponge material; hence, three replicates of each sponge were prepared for chemical analysis. The extracts were filtered, and analysed directly by gas chromatography–mass spectrometry (GC-MS). GC-MS data were obtained with a Thermo Fisher Scientific DSQ II Single Quadrupole mass spectrometer (Thermo Fisher Scientific, San Jose, CA, USA) operated at an ionization potential of 70 eV and coupled to a Trace GC Ultra gas chromatograph equipped with a Zebron ZB WAXplus™ column (60.0 m × 0.25 mm, 0.25 µm; Phenomenex, Torrance, CA, USA). The temperature programme was as follows: 80°C for 1 min, and then an increase to 250°C at a rate of 8°C/min with an isothermal step at 250°C for 20 min. The injection volume was 1 µl, with a split ratio of 1:50, and the temperature of the injector and the transfer line was 200°C. Helium was applied as a carrier gas at a flow rate of 1.4 ml/min. The mass spectrometer was operated in scan mode (1 scan/s) over a mass range from 50 to 450 amu.

Compounds suggested by the National Institute of Standards and Technology MS Database (NIST 2008) were verified by comparison of gas chromatography retention times and mass spectra of available authentic reference compounds (MI). The GC-MS analysis resulted in a peak in the total ion chromatogram at retention time 20.98 min, with a molecular ion peak at m/z 115 $[M]^+$ and a fragmentation pattern corresponding to MI. MI in

the Konjac® sponge DCM extracts was quantified from a calibration curve of the MI standard (data not shown). The precision of the GC-MS method used for quantification of MI was determined by three injections of the DCM solution of the Konjac® sponge sample within 1 day (intraday variation) and on two different days (interday variation). The overall intraday and interday variations were <5% for MI.

MI at 387 ± 3 ppm was found in the sponge of the patient causing facial dermatitis. In addition, four other sponges from the same manufacturer were analysed, and similar amounts of MI were found (Table 1).

Discussion

Despite the current epidemic of MI-induced allergic contact dermatitis, authorities in the EU have still not regulated the use of MI in cosmetic consumer products (4, 5). This case of contact dermatitis caused by undisclosed MI in concentrations approximately four times higher than allowed in cosmetics, found in a sponge claiming to be '100% natural and made from pure edible vegetable roots', adds strong support to the request for limitations on the level of MI allowed in consumer products in the EU. Five types of sponge from the company were tested for MI, and it seems reasonable to believe that MI at a concentration of 400 ppm was aimed for in all of the products. Furthermore, this case adds to the number of cases of undisclosed MI in consumer products, and underlines the fact that faulty labelling of consumer products is a significant problem, even in so-called natural/organic products (6–8).

References

- Schwensen J F, Bregnbak D, Johansen J D. Recent trends in epidemiology, sensitization and legal requirements of selected relevant contact allergens. *Expert Rev Clin Immunol* 2015. doi:10.1586/1744666X.2016.1120159. [Epub ahead of print].
- Yu S H, Sood A, Taylor J S. Patch testing for methylisothiazolinone and methylchloroisothiazolinone–methylisothiazolinone contact allergy. *JAMA Dermatol* 2015; 1–6. doi:10.1001/jamadermatol.2015.3606. [Epub ahead of print].
- Council of the European Union. Council Directive 76/768/EEC of 27 July 1976 on the approximation of the laws of the member states relating to cosmetic products. *Journal of the European Union L*. 2008.
- Schwensen J F, White I R, Thyssen J P et al. Failures in risk assessment and risk management for cosmetic preservatives in Europe and the impact on public health. *Contact Dermatitis* 2015; **73**: 133–141.
- Bruze M, Uter W, Gonçalo M et al. Incompetence and failure to regulate methylisothiazolinone. *Contact Dermatitis* 2015; **72**: 353–354.
- Isaksson M, Persson L. 'Mislabelled' make-up remover wet wipes as a cause of severe, recalcitrant facial eczema. *Contact Dermatitis* 2015; **73**: 56–59.
- Schwensen J F, Menné T, Friis U F, Johansen J D. Undisclosed methylisothiazolinone in wet wipes for occupational use causing occupational allergic contact dermatitis in a nurse. *Contact Dermatitis* 2015; **73**: 182–184.
- Vanneste L, Persson L, Zimerson E et al. Allergic contact dermatitis caused by methylisothiazolinone from different sources, including 'mislabelled' household wet wipes. *Contact Dermatitis* 2013; **69**: 311–312.