

- CONTRIBUTIONS TO THIS SECTION MAY NOT UNDERGO PEER REVIEW, BUT WILL BE REVIEWED BY THE EDITOR •

Facial dermatitis caused by undeclared methylisothiazolinone in a gel mask: is the preservation of raw materials in cosmetics a cause of concern?

Stefan Kerre¹ , Tania Naessens², Mart Theunis², Kenn Foubert², An Goossens³  and Olivier Aerts⁴ 

¹Gijmelsesteenweg 14A, 3200 Aarschot, Belgium, ²Natural Products and Food – Research and Analysis (NatuRA), Department of Pharmaceutical Sciences, University of Antwerp (UA), 2610 Antwerp, Belgium, ³Department of Dermatology, University Hospitals KU Leuven, 3000 Leuven, Belgium and ⁴Department of Dermatology, University Hospital Antwerp (UZA) and University of Antwerp (UA), 2650 Antwerp, Belgium

doi:10.1111/cod.12963

Key words: allergic contact dermatitis; CAS no. 2682-20-4; case report; chemical analysis; cosmetics; facial mask; labelling; methylisothiazolinone; raw materials; sodium hyaluronate; spot test.

Certain ingredients added to cosmetic raw materials might theoretically still be present in finished cosmetic products without being labelled. Here, we report a case of facial dermatitis caused by a gel mask containing methylisothiazolinone (MI), which was not mentioned on the packaging. However, its presence could be confirmed and quantified by chemical analysis.

Case Report

An otherwise healthy 56-year-old female patient with rosacea consulted because of acute, itching dermatitis of the face, in terms of erythematous, slightly swollen eyelids, and erythematous papules and infiltrated patches on both cheeks and forehead. The dermatitis had occurred a few days following a facial treatment by a beautician who had applied Bio Balance intensive algoherbal essence gel 'camomille'® (Alpaya Dermaceuticals, Istanbul, Turkey), a 'moisturizing and relaxing natural facial mask'. The product had remained on her face for 15 min before being washed off, and a moisturizing cream was then applied.

The patient was patch tested with our extended Belgian baseline series, a cosmetic series, and her own cosmetics, as well as those applied by the beautician. The culprit facial mask, together with two related facial masks ('rose' and 'lavender') from the same manufacturer, were tested semi-open. Patch tests were performed with IQ Ultra™

chambers (Chemotechnique, Vellinge, Sweden), and read according to ESCD recommendations (1). Readings on day (D) 2 showed reactions to methylchloroisothiazolinone (MCI)/MI 0.02% aq. (+), to MI 0.2% aq. (+), and to all three masks (++) (Fig. 1). On D3, all test reactions had evolved into ++ reactions. No later reactions were reported. The ingredients on the label of the mask did not mention MCI/MI or MI, and both the distributor (Distribicos, Heist-Op-Den-Berg, Belgium) and the manufacturer denied their presence.

A first qualitative chemical analysis of the mask was performed at the department in Antwerp, with an experimental isothiazolinone test kit (Tintometer® Group, Amesbury, UK; <http://www.lovibondwater.com>), originally designed for the detection of isothiazolinones in industrial water systems, which showed the potential presence of isothiazolinones (Fig. 2; File S1). The detailed description of the analytical method of this test is company proprietary information, but, according to the manufacturer, it concerns a colorimetric determination of isothiazoline derivatives based on the formation of a rather non-specific blue colour produced by reducing agents and Folin and Ciocalteu's reagent. Briefly, 5 ml of the gel mask was dissolved in 20 ml of physiological saline, and this aqueous solution was subsequently used for the spot test. Four other cosmetics, that is, three positive controls containing MI, and one negative control free from MI that had been previously investigated by the use of high-performance liquid chromatography with ultraviolet detection (HPLC-UV) (2), were all correctly identified with regard to their MI content by use of this experimental detection method.

Correspondence: Dr Stefan Kerre, Dermatologie aarschot private practise, Gijmelsesteenweg 14A, B-3200 Aarschot, Belgium. Tel: +32 16566141. Email: dermatologieaarschot@gmail.com

Conflicts of interests: None.



Fig. 1. Strong reactions (++) to semi-open tests with three facial masks on day 3.



Fig. 2. Experimental spot test indicating the potential presence of isothiazolinones in the facial gel mask.

Meanwhile, the manufacturer had agreed to provide us with samples of the individual ingredients of the mask (Table 1), which were additionally patch tested at the concentrations present in the finished product. Only the patch test with sodium hyaluronate 0.1% aq. gave clearly positive reactions (++) on D2 and D4) (Fig. 3).

Table 1. Ingredients of the facial gel mask (as provided by the cosmetic manufacturer)

Ingredient (INCI)	%
aq.	70.15
Glycerin	10
Butylene glycol	6
<i>Aloe barbadensis</i> leaf extract	5
<i>Anthemis nobilis</i> flower extract	4
Hydrolysed collagen	2
Carbomer	0.7
Triethanolamine	0.7
Phenoxyethanol	0.5
Panthenol	0.3
Allantoin	0.2
PEG-40 hydrogenated castor oil	0.2
Parfum	0.1
Sodium hyaluronate	0.1
Disodium EDTA	0.05
CI 19140	0.0002



Fig. 3. Strong reaction (++) to a patch test with sodium hyaluronate 0.1% aq. on day 2.

Subsequently, chemical analyses (HPLC-UV) were performed, both of the mask and of the sodium hyaluronate ingredient. These investigations were performed at the Laboratory NatuRA of the University of Antwerp, with a validated method as previously described (2). The presence of MI in the facial mask (147 ppm) and in the sodium hyaluronate solution (326.5 ppm) was thus confirmed. No other isothiazolinone derivatives could be detected.

Discussion and Conclusion

According to the European Cosmetics Regulation, all ingredients should be clearly labelled on the packaging; for some of them, specific concentration limits are in effect (EU directive 1223/2009). Cosmetic products have substantially contributed to the recent epidemic of MI allergy (3), with several of them being mislabelled (2, 4). Other products have been shown to contain MI at concentrations higher than previously permitted (i.e. > 100 ppm) (2, 5).

The preservation of individual cosmetic ingredients with MI has previously been suggested as a possible explanation for the current observation (2), in which a qualitative test detected the presence of isothiazolinones in the mask, and further extensive chemical analyses confirmed the presence of, and enabled quantification of, MI in the mask and in the individual sodium hyaluronate raw material. This case highlights two particularities: (i) a rinse-off cosmetic (i.e. a facial mask) caused severe allergic contact dermatitis attributable to MI that was shown to be present at a concentration of > 100 ppm, although it was

not labelled on the packaging; and (ii) MI was detected at a very high concentration (326.5 ppm) in one of the individual cosmetic raw materials, that is, in the 0.1% sodium hyaluronate solution, which probably explains the presence of the high final concentration of MI (147 ppm) in the finished product.

Hidden exposure to preservatives in cosmetic and non-cosmetic products, in both occupational and non-occupational settings, has been studied before (6–9). Despite recent changes in the EU Cosmetics Regulation, prohibiting MI in leave-on cosmetics and limiting its presence to 15 ppm in rinse-off cosmetics, this case shows that vigilance is still required. Moreover, cosmetic manufacturers should verify the exact nature (including the preservation or other additions) of all raw materials incorporated in their products.

Acknowledgements

We are grateful to the manufacturer, Alpaya Dermaceuticals, Istanbul, Turkey, for their willingness to provide us with the individual ingredients of the gel mask.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

File S1. The working mechanism of the experimental test for isothiazolinone derivatives in industrial water systems (as provided by its manufacturer, Tintometer® Group, Amesbury, UK; <http://www.lovibondwater.com>).

References

- 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.
- Aerts O, Meert H, Goossens A et al. Methylisothiazolinone in selected consumer products in Belgium: adding fuel to the fire? *Contact Dermatitis* 2015; **73**: 142–149.
- Aerts O, Baeck M, Constandt L et al. The dramatic increase in the rate of methylisothiazolinone contact allergy in Belgium: a multicentre study. *Contact Dermatitis* 2014; **71**: 41–48.
- Isaksson M, Persson L. 'Mislabelled' make-up remover wet wipes as a cause of severe, recalcitrant facial eczema. *Contact Dermatitis* 2015; **73**: 56–59.
- Neza E, Centini M. Microbiologically contaminated and over-preserved cosmetic products according rapex 2008–2014. *Cosmetics* 2016; **3**: 1–11.
- Gruvberger B, Bruze M, Tammela M. Preservatives in moisturizers on the Swedish market. *Acta Derm Venereol* 1998; **78**: 52–56.
- Rastogi SC. Analytical control of preservative labelling on skin creams. *Contact Dermatitis* 2000; **43**: 339–343.
- Schwensen JF, Menné T, Friis UF, Johansen JD. Undisclosed methylisothiazolinone in wet wipes for occupational use causing occupational allergic contact dermatitis in a nurse. *Contact Dermatitis* 2015; **73**: 182–184.
- Friis UF, Dahlin J, Bruze M et al. Hidden exposure to formaldehyde in a swab caused allergic contact dermatitis. *Contact Dermatitis* 2014; **70**: 258–260.

Supplemental file: The working mechanism of the experimental test for isothiazolinone derivatives in industrial water systems (as provided by its manufacturer, Tintometer® Group, Amesbury, UK; <http://www.lovibondwater.com>).

The method is a colorimetric determination of isothiazoline (0-7.5 ppm), based on the quantitative blue color formation produced by reducing agents and the Folin and Ciocalteu's reagent.

1. In the first step of the test CDTA is added to remove copper, this has the effect of preventing interference from methylenebisthiocyanate that may be dosed into the water with isothiazolinone.
2. The second step combines two issues – a salt of molybdic acid is added in order to mask the presence of thiocyanate ion that may be present, and pentasodium phosphate is also added to remove hardness.
3. Two set of hydroxide reagents are added in the next two steps, this splits the isothiazolinone ring to form an oxidizable group.
4. Folin and Ciocalteu's reagent is added. This produces a blue color for measurement. Folin and Ciocalteu's measures reducing power.

A calibration is provided either in the form of a comparator disc or color chart.