



Occupational allergic contact dermatitis due to undeclared benzisothiazolinone in an emulsifying oil

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Running head: contact dermatitis due to benzisothiazolinone

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Isothiazolinones are widely used in cosmetic, household and industrial products for their preservative and biocide properties. The mixture of methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI) in a 3:1 ratio has caused an epidemic allergic contact dermatitis in the 1980s. This led to the use of MI as a stand-alone preservative at increased concentrations, because of its weaker biocidal effect, but sensitization rates have dramatically rises¹. Although the

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use of isothiazolinones in cosmetic formulations has been limited recently, benzisothiazolinone (BIT) and octylisothiazolinone are still used in industrial products².

Case report

A 44-year-old man developed acute eczematous dermatitis on his forearms. He had contact with metals and lubricant fluids during his job as a metal worker. The dermatitis occurred after contact with an emulsifying oil containing BIT at unknown concentration, as reported in the data sheet. Patch tests were performed with the Italian baseline series (F.I.R.M.A. , Florence, Italy) according to SIDAPA, with BIT 0.05% and 0.1% aq., and with the emulsifying oil tested "as is". Patch test chambers (Van der Bend, Brielle, The Netherlands) were applied on the upper part of the back. The readings on day (D) 2, D4 and D7, according to Italian guidelines³, showed positive reactions to MCI/MI 0.02% aq. (+/+/+), to MI 0.2% aq. (+/+/+), to BIT 0.05% (+/+/+), to BIT 0.1% (+/+/+) and to the emulsifying oil (+/+/+).

Thus, the oil was replaced by another product not containing isothiazolinones, according to the data sheet; but the dermatitis worsened. Patch test was performed using the same procedure with the second emulsified oil tested "as is" and was positive (+/+/+).

Chemical analysis was performed using mass spectrometry analytical technique. We compared the second oil with the standard solution of BIT used for the patch tests and in both prepared solutions we detected the same peaks: in negative mode few drops of samples were diluted in acetonitrile/water (60%/40%) solution and a peak at 150 m/z was observed (anion of BIT after proton loss, Online supplemental Fig.1). Subsequently we tested the same solutions by adding sodium ions and we performed a positive mode analysis; we detected a peak concentration at 174 m/z, which corresponds to the molecular sodium adduct (Online supplemental Fig.2). This confirmed the presence of BIT in the second oil as well.

Discussion

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BIT (CAS no. 2634-33-5, molecular weight 151.19 g/mol) is an organic heterobicyclic compound used as a preservative and antimicrobial agent in industrial and consumer products such as cosmetics and paints, at a concentration of not more than 0.1%⁴. Cross-reactivity between isothiazolinones is described in the literature². However, BIT sensitization is also reported to occur independently from other isothiazolinones⁵. The chemical structure of BIT is somewhat dissimilar from the chemical structure of other isothiazolinones, due to its fused 1,2-thiazole and benzene bicyclic ring skeleton⁶; this could explain the low rate of cross-reactivity between BIT and other isothiazolinones.

In our case we can not determine whether the patient was primarily sensitized to BIT, to other isothiazolinones, or if a co-sensitization or cross-reactivity to MCI/MI or MI alone occurred. We emphasize that the second oil should have been isothiazolinone-free, according to the data sheet; only a complex chemical analysis could demonstrate its presence. This case underlines that accuracy and completeness of technical data sheets should be greatly improved to avoid misdiagnosis, especially concerning occupational diseases. We strongly recommend not excluding exposure to proven allergens, even if undeclared in the data sheet, when the clinical history and the stop-restart test are strongly suggestive.

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Figure Legends

Online supplemental Fig.1: Mass spectrometry analytical technique in negative mode used to compare the standard solution of BIT used for the patch tests (a) with the second emulsifying oil (b)

Online supplemental Fig.2: Mass spectrometry analytical technique in positive mode used to compare the standard solution of BIT used for the patch tests (a) with the second emulsifying oil (b)



