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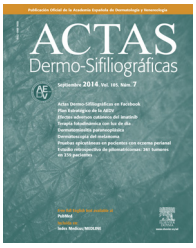

NOVELTIES IN DERMATOLOGY

Update on Allergic Contact Dermatitis Due to Methylchloroisothiazolinone/Methylisothiazolinone and Methylisothiazolinone☆

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Abstract The combination of methylchloroisothiazolinone (MCI) and methylisothiazolinone (MI) is widely used as a preservative in cosmetics, household, and industrial products. Furthermore, MI at a concentration of 100 ppm has been permitted in cosmetic products since 2005. Recently, a considerable increase in cases of contact dermatitis to both MCI and MI have been noted, and this warrants closer monitoring by relevant authorities and, probably, stricter legislation. In fact, MI at a test concentration of 2000 ppm was recently included in the European baseline patch test series. The clinical manifestations of allergy to MCI/MI and MI are highly variable and diagnosis is often missed. In the standard patch test series of the Spanish Contact Dermatitis and Skin Allergy Research Group (GEIDAC), MCI/MI is tested at 100 ppm, but at this concentration, up to 50% of cases might go undetected. Furthermore, our data indicate that MCI/MI at 200 ppm would make it possible to diagnose more cases of contact allergy to MI. To improve the diagnosis of contact allergy to MCI/MI and MI, we believe that the test concentration of MCI/MI should be increased to 200 ppm in the GEIDAC standard series and that MI should be added in the GEIDAC standard series.

PALABRAS CLAVE
Dermatitis de contacto;
Conservantes;
Cosméticos;
Metilcloroisotiazolinona;
Metilisotiazolinona

Actualización En La Dermatitis De Contacto Alérgica Por Metilcloroisotiazolinonametilisotiazolinona Y Metilisotiazolinona

Resumen La combinación de metilcloroisotiazolinona (MCI) con metilisotiazolinona (MI) es ampliamente empleada como conservante tanto en productos de higiene y domésticos como industriales. Desde 2005 está permitido el uso de MI a 100 ppm en cosméticos. En los últimos años se está detectando un aumento considerable de los casos de dermatitis de contacto a los 2 conservantes, por lo que es necesaria una monitorización estrecha por parte de las

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autoridades y probablemente unas medidas legislativas más estrictas. De hecho, MI a 2000 ppm se ha incluido recientemente en la batería estándar Europea. La forma de presentación clínica es muy variable, y en ocasiones es difícil sospechar una alergia a MCI/MI y MI. MCI/MI se testa en la batería estándar del GEIDAC a 100 ppm, pero con esta concentración se podría estar dejando de diagnosticar hasta la mitad de los casos. Además, según nuestros datos MCI/MI a 200 ppm permite diagnosticar más casos con alergia a MI. Para llegar a un buen diagnóstico consideramos que se debería aumentar la concentración del parche de MCI/MI a 200 ppm e incluir MI en la batería estándar del GEIDAC.

Introduction

The combination of methylchloroisothiazolinone (MCI) and methylisothiazolinone (MI), which is more commonly known as Kathon CG, has been and continues to be widely used as a preservative in cosmetic, household, and industrial products. After formaldehyde releasers, MCI/MI is the second most common cause of contact allergy to preservatives in Europe.[1] During the 1980s, a large number of patients were reported to be allergic to MCI/MI. Since it was originally thought that the allergenicity of the combination lay in MCI, use of MI alone was authorized at high concentrations in cosmetic products in 2005. The first cases of MI-induced allergic contact dermatitis soon began to emerge.[2] We are currently witnessing a considerable increase in the number of patients who are allergic to MCI/MI and MI,[3] and some authors have warned of a possible epidemic.[3,4] MI was named allergen of the year in 2013 by the American Contact Dermatitis Society and included in the European standard series.[5] Moreover, it is very likely that a considerable number of cases of allergy to MCI/MI or MI go undetected with the concentration of MCI/MI used in the patches of the European and Spanish standard series.[6,7]

The primary objective of this article is to provide an update on allergic contact dermatitis caused by MCI/MI and MI. We review the main sources of exposure and current legislation on the use of these allergens in both domestic and industrial products. We also provide available clinical and epidemiological data on allergy to MCI/MI and present our approach to diagnosis and treatment.

Molecular Structure and Sensitization Studies

5-Chloro-2 methyl-4-isothiazolinone/2-methyl-3,4-isothiazolinone (MCI/MI) and 2-methyl-3,4-isothiazolinone (MI) are members of the isothiazolinone group. Isothiazolinones are heterocyclic organic components used as biocides owing to their marked antibacterial and antifungal activity within a wide range of pH values. MCI/MI is used as a preservative at a ratio of 3:1. MI is less potent than MCI/MI and, as such, must be used at higher concentrations in order to be sufficiently biocidal. The only difference in the molecular structure of these substances is the presence of a chloride in MCI that leads to a different type of interaction with the allergenic proteins. The resulting formation of a very electrophilic and, therefore, very reactive intermediate, makes MCI more allergenic.[8] (Fig. 1) The results of studies in animals and healthy volunteers show that MCI is 30 times more potent than the nonhalogenated form MI and that MI was a mild-to-moderate sensitizer with no ability to induce respiratory sensitization. In a further 2 studies in which concentrations of MI of 100-600 ppm were analyzed, healthy volunteers could only be sensitized at concentrations of 600 ppm or higher.[9] In the murine local lymph node test, MI was classified erroneously by some authors as a moderate sensitizer. It was subsequently shown that the results pointed to MI as a strong sensitizer.[10] Scientific committees and evaluators from the United States of America and the European Union concluded that MI at 100 ppm was safe for use in cosmetic products. However, despite the so-called safe concentrations of MI, postmarketing studies revealed cases of allergy to this preservative in cosmetic products.[1,2,9,11] Finally, the relatively high incidence detected in studies on patients with eczema performed in skin allergy units highlights the marked allergenicity of these substances.[12,13]

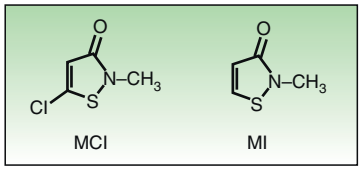

Figure 1 Molecular structure of MCI and MI. MCI indicates methylchloroisothiazolinone; MI, methylisothiazolinone.

Sources

MCI/MI and MI are widely used in consumer and in industrial products.

Consumer Products

The preservatives are found in cosmetics and personal hygiene products (rinse-off and leave-on) such as soaps, gels, shampoos, leave-on products for scalp care, sunscreens, deodorants, moisturizing creams, intimate wipes, baby wipes, and makeup remover wipes (Fig. 2). They are also present in cleaning products such as washing up liquid, detergents, stain removers, window cleaning solution, grease remover, and air fresheners.