



Contact allergy to 3-dimethylaminopropylamine in 5140 consecutive Italian patients: A one-year retrospective multicenter SIDAPA study

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3-Dimethylaminopropylamine (DMAPA) (CAS no. 109-55-7) is an aliphatic amine used for the synthesis of betaines often present in the final product as a contaminant;¹ DMAPA is able to induce contact allergy.²⁻⁴ DMAPA may be contained in personal care products and several industrial products such as agricultural chemicals, fabric softeners, water-resistant textile fibers, synthetic dyes and paints, etc. In this study, the prevalence of positive patch test reactions to DMAPA during 2018 in Italian patients was assessed.

METHODS

In 11 patch testing clinics evenly distributed across Italy, 5140 consecutive patients (1615 males, 3525 females; mean age 47.9 years, range 4-93 years) were patch tested for contact dermatitis between January and December 2018 with the SIDAPA (Società Italiana Dermatologia Allergologica, Professionale Ambientale) baseline series (FIRMA Diagent, Florence, Italy).⁵ Patch tests were occluded for 2 days with Haye's Test Chambers (Haye's Service, Alphen aan den Rijn, The Netherlands) on

Soffix tape (Artsana, Grandate, Italy), and readings were performed on day (D)2, D4, and D7.⁵ Patients were asked to return in case of late reactions. Irritant and doubtful reactions were not considered.

RESULTS

Among the 5140 patients tested, 68 (1.3%) (mean age 47.5 years, range 9-81) showed positive reactions to DMAPA, 31 males (1.9%) and 37 females (1.1%). No occupational cases were recorded. Irritant reactions were not registered. Clinical relevance was observed in 55 of 68 DMAPA-positive patients (80.9%): all the cases were related to the repeated daily use of skin cleaners containing betaines. Concomitant sensitization was observed in 44 patients: nickel sulfate in 19 cases (27.9%), methylchloroisothiazolinone/methylisothiazolinone 3:1 in 11 cases (16.2%), and cobalt chloride and methylisothiazolinone in 7 cases (10.3%). Twenty-two (32.3%) of 68 DMAPA-positive patients had a personal history of atopy. The reported duration of the skin lesions ranged from 3 months to 31 years (mean 3.8 years). The body sites most

affected by the skin lesions were the face in 35 cases (51.5%), the trunk in 13 cases (19.1%), the upper limbs in 12 cases (17.6%), the hands in 11 cases (16.2%), and the scalp in 10 cases (14.7%).

DISCUSSION

Our data from 5140 consecutively patch tested patients in Italy during a 1-year period showed a prevalence of 1.3% of contact allergy to DMAPA. This prevalence is lower compared to a previous Italian study,² although still remarkable. In this study, the authors showed 46 positive reactions (3.8%) to cocamidopropylbetaine 1% aq. among 1200 consecutively patch tested patients. Thirty out of the 46 patients were subsequently tested with DMAPA and all were positive, highlighting the sensitizing potential of DMAPA as an impurity of cocamidopropylbetaine.

The sensitizing potential of DMAPA is well known,^{6,7} but there is currently no regulation by the European Union or the United States defining a threshold for this substance in skin care products, nor obligation to report its presence and quantity on packaging labels. The North American Contact Dermatitis Group reported a 1.7% prevalence of positive reactions to DMAPA among 10 877 patients patch tested between 2009 and 2014.³ In 2012, the records of 1092 patch tests performed between 2002 and 2009 were reviewed at the Finnish Institute of Occupational Health reporting a 1.0% prevalence of occupational contact allergy due to DMAPA.⁴ Of note, the authors found irritant reactions to patch tests with cocamidopropyl betaine and its impurities very common, that is, in 39% of the tested patients.

In December 2010, the Cosmetic Ingredient Review Expert Panel reviewed the safety of fatty acid amidopropyl dimethylamines, concluding that they were safe when formulated in nonsensitizing levels, based on quantitative risk assessment,⁸ and considered DMAPA at a concentration of 0.01% in raw cocamidopropyl betaine in finished cosmetic products to not be sensitizing.⁸ In 2019, the Panel advised industry to continue minimizing the concentrations of the sensitizing impurities, highlighting that DMAPA in oleamidopropyl dimethylamine seems to exceed the limit recommended.⁹

Despite this, we found that the majority of the DMAPA-positive patients (39/68; 57.3%), all with clinical relevance, reported the onset of the dermatitis during the last 2 years thus demonstrating that DMAPA is still present at sensitizing concentrations in many products as an impurity. None of our patients reported any recurrence of their dermatitis following strict avoidance of topical products containing betaines.

In conclusion, we believe that legislative interventions on DMAPA to improve consumer safety are advisable. As stated by Burnett et al,⁹ DMAPA should be present in cosmetic products at a concentration lower than 0.01%. We would also stress that DMAPA should be tested in the baseline series.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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