

# No contact allergy to acrylic acid and methacrylic acid in routinely tested dermatitis patients

Magnus Bruze, Martin Mowitz, Erik Zimerson, Ola Bergendorff, Jakob Dahlin, Malin Engfeldt, Marlène Isaksson, Ann Pontén and Cecilia Svedman

Department of Occupational and Environmental Dermatology, Skåne University Hospital, Lund University, 205 02 Malmö, Sweden

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Occupational and non-occupational contact allergy to, and allergic contact dermatitis caused by, acrylates/methacrylates are frequently reported (1–18). However, there is no acrylate/methacrylate test preparation in the European baseline patch test series (19). Therefore, contact allergy to, and allergic contact dermatitis caused by, acrylates/methacrylates may be overlooked when the decision is made on what to patch test with in diagnostic work-up of dermatitis patients (5). There are many sensitizing acrylates/methacrylates to consider regarding whether an acrylate/methacrylate preparation should be included in the European baseline patch test series. Therefore, patch testing with a mix of the acrylates/methacrylates with the highest contact allergy rates when they are routinely tested has been tried, but has been unsuccessful (7). Recently, an Italian article reported contamination with acrylic acid in an electrode gel to be the likely cause of the allergic contact dermatitis (18). The patient reacted positively to a few methacrylates not present in the gel, and these were interpreted as cross-reactions. At least theoretically, acrylic acid and methacrylic acid could be formed by the hydrolysis of acrylates and methacrylates in the skin. Therefore, the acids could be major possible hapten(s) concerning contact allergy to acrylates/methacrylates. To test this hypothesis, in this study the acids were routinely tested in dermatitis patients.

*Correspondence:* Magnus Bruze, Department of Occupational and Environmental Dermatology, Skåne University Hospital, Lund University, Jan Waldenströms gata 16, S-205 02 Malmö, Sweden. Tel: +46 (0)40 331760. E-mail: magnus.bruze@med.lu.se

## Materials and Methods

### Patients

In 2015, 768 dermatitis patients (250 males and 518 females) were patch tested with the Swedish baseline patch test series because of suspected allergic contact dermatitis.

### Patch testing

The Finn Chamber® technique with the chambers (diameter, 8 mm) mounted on Scanpor® tape was used. Chemotechnique Diagnostics (Vellinge, Sweden) provided the Swedish baseline series. Pet. test preparations with acrylic acid and methacrylic acid (both from Acros Organics, Geel, Belgium) were made at our laboratory at 0.1% wt/wt and 2.0% wt/wt, respectively, and temporarily included in the baseline series. The test preparations were stored in a freezer between the patch test occasions, in order to minimize the evaporation of acrylic acid and methacrylic acid from the syringes. Twenty milligrams of the pet. preparations (20) were applied onto the chambers immediately before the application to the back of the patient (21, 22). The patches remained under occlusion on the back for 48 h. Test readings were performed on day (D) 3 or D4 and D7, according to the ICDRG classification used in the ESCD guideline (23, 24).

Among the 768 patients patch tested with the baseline series, 50 patients were additionally tested with series containing acrylates/methacrylates. The concentrations and manufacturers of these test preparations are shown in Table 1.

**Table 1.** Outcome of aimed patch testing with 10 acrylates/methacrylates from Chemotechnique Diagnostics in 7 individuals with at least one positive reaction to acrylates/methacrylates

| Test preparation (% in pet.)                | Patient number |    |     |    |     |    |    |
|---------------------------------------------|----------------|----|-----|----|-----|----|----|
|                                             | 1              | 2  | 3   | 4  | 5   | 6  | 7  |
| 2-Hydroxyethyl methacrylate 2.0%            | ++             | ?+ | +   | –  | ++  | –  | NT |
| Bisphenol A glycerolate dimethacrylate 2.0% | ++             | +  | +   | +  | +   | NT | NT |
| Triethylene glycol diacrylate 0.1%          | –              | ++ | +++ | –  | NT  | NT | NT |
| Hydroxypropyl methacrylate 2.0%             | +              | +  | +   | –  | +++ | ++ | NT |
| 1,4-Butanediol diacrylate 0.1%              | –              | ++ | +++ | –  | ++  | NT | NT |
| Ethylene glycol dimethacrylate 2.0%         | ++             | ?+ | +   | –  | +++ | NT | NT |
| Methyl methacrylate 2.0%                    | –              | –  | NT  | –  | ++  | NT | +  |
| Urethane dimethacrylate 2.0%                | NT             | NT | NT  | NT | +   | NT | NT |
| 1,4-Butanediol dimethacrylate 2.0%          | NT             | NT | NT  | NT | ++  | NT | NT |
| Tetrahydrofurfuryl methacrylate 2.0%        | NT             | NT | NT  | NT | +   | NT | NT |

NT, not tested.

+, ++, +++, positive patch test reaction.

?+, doubtful reaction.

### High-performance liquid chromatography (HPLC)

Samples of the pet. test preparations with acrylic acid and methacrylic acid were investigated by HPLC. The samples were dissolved in heptane (Merck, Darmstadt, Germany). A Luna silica column (Phenomenex, Torrance, CA, USA) constituted the stationary phase, and the elution was isocratic with the mobile phases heptane/ethanol (Kemetyl, Haninge, Sweden) 99:1 vol/vol and heptane/ethanol 95:5 vol/vol for acrylic acid and methacrylic acid, respectively. The injection volume was 20 µl for both acids. The detector was operated in the 190–800-nm range, and the chromatograms recorded at 215 nm were used for quantification of acrylic acid and methacrylic acid. Details of the HPLC instruments and methodology are given elsewhere (22).

### Results

Patch testing with acrylic acid and methacrylic acid did not result in any positive or irritant reactions. Doubtful reactions were seen in 4 patients: 2 with doubtful reactions to acrylic acid, and 2 with reactions to methacrylic acid. One patient reacted to almost all test preparations tested in the baseline series and additional series, including methacrylic acid, so the latter reaction was considered to be a false-positive reaction and therefore disregarded. The additional testing with acrylates/methacrylates

resulted in 26 positive reactions in 7 subjects (Table 1). None of these individuals reacted to acrylic acid and methacrylic acid.

The HPLC analyses of the test preparations at the end of the study period showed that the intended concentrations of 0.1% and 2.0%, respectively, were correct.

### Discussion

To the best of our knowledge, there have been no sensitization studies with acrylic acid and methacrylic acid in animals.

The absence of positive reactions to acrylic acid and methacrylic acid when tested in 768 patients does not necessarily mean that the hypothesis suggesting that these acids are significant sensitizers concerning acrylate/methacrylate contact allergy is wrong. Theoretically, our negative patch test results could be false negatives. One possible reason for a false-negative result could be that there were no or very few contact allergic reactions to acrylates/methacrylates among the 768 tested individuals. However, 26 contact allergic reactions to acrylates/methacrylates were seen in 7 patients without any simultaneous reactions to acrylic acid and/or methacrylic acid (Table 1). Another possible reason for a false-negative result is too low a concentrations of acrylic acid and methacrylic acid in the pet.

preparations, because of factors such as evaporation, polymerization, and degradation. However, chemical analyses of the pet. preparations with HPLC at our laboratory do not support such an interpretation, as the concentrations were the expected ones, that is,

0.1% and 2.0% for acrylic acid and methacrylic acid, respectively.

Thus, it is very likely that acrylic acid and methacrylic acid have a negligible role in contact allergy to acrylates/methacrylates.

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