

# 10 years of patch testing with the (meth)acrylate series

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Statistics on 10 years of patch testing with 30 (meth)acrylates were compiled. Altogether 275 patients were patch tested and 48 patients (17.5%) had an allergic reaction to at least 1 (meth)acrylate. The (meth)acrylates most often provoking an allergic patch test reaction were 2-hydroxyethyl acrylate (2-HEA; 12.1%), 2-hydroxypropyl methacrylate (2-HPMA; 12.0%) and 2-hydroxyethyl methacrylate (2-HEMA; 11.4%). No allergic reactions were caused by 2-ethylhexyl acrylate (2-EHA), 2,2-bis[4-(methacryloxy)phenyl]propane (BIS-MA), trimethylolpropane triacrylate (TMPTA), oligotriacrylate 480 (OTA 480), N,N-methylenebisacrylamide (MBAA), or ethyl cyanoacrylate (ECA). The frequency of allergic patch test reactions presented cannot be considered as a "ranking" list of the most sensitizing (meth)acrylate compounds. In order to be able to judge the sensitization capacity of various (meth)acrylate compounds in humans, it would be necessary to have detailed information on the exposure history of the patients studied, including the purity of the (meth)acrylate compounds. Currently, this is not possible because (meth)acrylate-containing products regularly contain undeclared (meth)acrylate compounds.

**Key words:** acrylates; methacrylates; occupational; 2-hydroxyethyl acrylate; 2-hydroxypropyl methacrylate; 2-hydroxyethyl methacrylate; epidemiology; allergic contact dermatitis. © Munksgaard, 1997.

*Accepted for publication 4 August 1997*

Much of the current knowledge of allergy caused by acrylates, methacrylates and epoxy acrylates is based on patch testing with an extensive (meth)acrylate series from Chemotechnique Diagnostics (Malmö, Sweden) comprising about 30 (meth)acrylates. We have earlier reported our 5-year statistics (1), and here further statistical data are given. We have also compared our data to a review by Björkner (2) on the sensitizing capacity of (meth)acrylates based on animal studies. Our patch test results in humans are very different from the anticipated sensitizing capacity of (meth)acrylates based on animal studies.

## Materials and Methods

During 1985-1995, a total of 275 patients with a history of exposure to (meth)acrylates were patch tested with the (meth)acrylate series of Chemotechnique Diagnostics (Malmö, Sweden) (Table 1) containing about 30 (meth)acrylates. Patch testing

and scoring were performed as previously described (3,4) on the back with an occlusion time of 1 day (September 1985-1988) or 2 days (1989-1995). All patients were not uniformly tested to all acrylates (Table 1).

## Results

Altogether 275 patients were patch tested and 48 patients (17.5%) had an allergic reaction to at least 1 (meth)acrylate. The acrylates most often provoking an allergic patch test reaction were 2-hydroxyethyl acrylate (2-HEA; 12.1%), 2-hydroxypropyl methacrylate (2-HPMA; 12.0%) and 2-hydroxyethyl methacrylate (2-HEMA; 11.4%). No allergic reactions were caused by 2-ethylhexyl acrylate (2-EHA), 2,2-bis[4-(methacryloxy)phenyl]propane (BIS-MA), trimethylolpropane triacrylate (TMPTA), oligotriacrylate 480 (OTA 480), N,N-methylenebisacrylamide (MBAA), or ethyl cyanoacrylate (ECA).

Table 1. Allergic (meth)acrylate reactions in (a) 1985–1995, (b) 1985–1990 and (c) 1991–1995; 48 patients showed at least one allergic patch test reaction; the results have been compared to the sensitizing capacity of (meth)acrylates, based on animal studies, according to Björkner (2); Sensitizing capacity: NG, not given; I, weak; II, moderate; III, strong; V, extreme

| (Meth)acrylate series                                          | Abbre-<br>viation | Patch test<br>conc. (%)<br>(w/w) | 1985–1995           |                 |               |                     | 1985–1990       |              |                     |                 | 1991–1995    |                 |              |                         |
|----------------------------------------------------------------|-------------------|----------------------------------|---------------------|-----------------|---------------|---------------------|-----------------|--------------|---------------------|-----------------|--------------|-----------------|--------------|-------------------------|
|                                                                |                   |                                  | allergic/<br>tested | allergic<br>(%) | rank<br>order | allergic/<br>tested | allergic<br>(%) | “top<br>ten” | allergic/<br>tested | allergic<br>(%) | “top<br>ten” | allergic<br>(%) | “top<br>ten” | sensitizing<br>capacity |
| ethyl acrylate                                                 | EA                | 0.1(–0.5)                        | 16/192              | 8.3             | 7             | 9/124               | 7.3             | 8            | 7/68                | 10.3            | 6            | 10.3            | 6            | NG                      |
| butyl acrylate                                                 | BA                | 0.1(–0.5)                        | 12/242              | 5.0             | 12            | 6/124               | 4.8             | 10           | 6/118               | 5.1             |              | 0               |              | NG                      |
| 2-ethylhexyl acrylate                                          | 2-EHA             | 0.1(–0.5)                        | 0/243               | 0               | –             | 0/124               | 0               |              | 0/119               | 0               |              |                 |              | V                       |
| 2-hydroxyethyl acrylate                                        | 2-HEA             | 0.1(–0.5)                        | 16/132              | 12.1            | 1             | 14/124              | 11.3            | 2            | 2/8                 | 25              | 1            | 25              | 1            | NG                      |
| 2-hydroxypropyl acrylate                                       | 2-HPA             | 0.1(–0.5)                        | 14/132              | 10.6            | 4             | 12/124              | 9.7             | 4            | 2/8                 | 25              | 1            | 25              | 1            | NG                      |
| methyl methacrylate                                            | MMA               | 2                                | 20/271              | 7.4             | 8             | 8/124               | 6.5             | 9            | 12/147              | 8.2             | 8            | 12/119          | 10.1         | NG                      |
| ethyl methacrylate                                             | EMA               | 2                                | 18/243              | 7.4             | 8             | 6/124               | 4.8             | 10           | 12/119              | 10.1            | 7            | 12/119          | 10.1         | NG                      |
| n-butyl methacrylate                                           | BMA               | 2                                | 6/243               | 2.5             | 16            | 2/124               | 1.6             |              | 4/119               | 3.4             |              | 4/119           | 3.4          | NG                      |
| 2-hydroxyethyl methacrylate                                    | 2-HEMA            | 2                                | 31/273              | 11.4            | 3             | 13/124              | 10.5            | 3            | 18/149              | 12.1            | 3            | 18/149          | 12.1         | I                       |
| 2-hydroxypropyl methacrylate                                   | 2-HPMA            | 2                                | 29/242              | 12.0            | 2             | 15/124              | 12.1            | 1            | 14/118              | 11.9            | 4            | 14/118          | 11.9         | I                       |
| ethyleneglycol dimethacrylate                                  | EGDMA             | 2                                | 27/272              | 9.9             | 5             | 11/124              | 8.9             | 6            | 16/148              | 10.5            | 5            | 16/148          | 10.5         | I                       |
| triethyleneglycol dimethacrylate                               | TREGDMA           | 2                                | 23/275              | 8.4             | 6             | 11/124              | 8.9             | 6            | 12/151              | 7.9             | 9            | 12/151          | 7.9          | I                       |
| 1,4-butanediol dimethacrylate                                  | BUDMA             | 2                                | 10/274              | 3.6             | 15            | 4/124               | 3.2             |              | 6/150               | 4.0             |              | 6/150           | 4.0          | I                       |
| urethane dimethacrylate                                        | UEDMA             | 2                                | 1/273               | 0.4             | 24            | 0/124               | 0               |              | 1/149               | 0.7             |              | 1/149           | 0.7          | II                      |
| 2,2-bis[4-(2-methacryloxyethoxy)-<br>phenyl]propane            | BIS-EMA           | 1                                | 4/242               | 1.7             | 20            | 2/124               | 1.6             |              | 2/118               | 1.7             |              | 2/118           | 1.7          | IV                      |
| 2,2-bis[4-(methacryloxy)phenyl]propane                         | BIS-MA            | 2                                | 0/241               | 0               | –             | 0/124               | 0               | –            | 0/117               | 0               |              | 0/117           | 0            | V                       |
| 2,2-bis[4-(2-hydroxy-3-methacryloxy-<br>propoxy)phenyl]propane | BIS-GMA           | 2                                | 5/272               | 1.8             | 19            | 4/124               | 3.2             |              | 1/148               | 0.7             |              | 1/148           | 0.7          | I                       |
| 1,4-butanediol diacrylate                                      | BUDA              | 0.1                              | 11/242              | 4.6             | 13            | 6/124               | 4.8             | 10           | 5/118               | 4.2             |              | 5/118           | 4.2          | III-V                   |
| 1,6-hexanediol diacrylate                                      | HDDA              | 0.1                              | 6/274               | 2.2             | 17            | 5/124               | 4.0             |              | 1/150               | 0.7             |              | 1/150           | 0.7          | III-V                   |
| diethyleneglycol diacrylate                                    | DEGDA             | 0.1                              | 13/243              | 5.3             | 11            | 6/124               | 4.8             | 10           | 7/119               | 5.9             | 10           | 7/119           | 5.9          | II                      |
| tripropylene glycol diacrylate                                 | TPGDA             | 0.1                              | 2/243               | 0.8             | 22            | 0/124               | 0               |              | 2/119               | 1.7             |              | 2/119           | 1.7          | IV                      |
| trimethylolpropane triacrylate                                 | TMPTA             | 0.1                              | 0/243               | 0               | –             | 0/124               | 0               |              | 0/119/              | 0               |              | 0/119/          | 0            | IV                      |
| pentaerythritol triacrylate                                    | PETA              | 0.1                              | 3/243               | 1.2             | 21            | 2/124               | 1.6             |              | 1/119               | 0.8             |              | 1/119           | 0.8          | V                       |
| oligo triacrylate 480                                          | OTA 480           | 0.1                              | 0/243               | 0               | –             | 0/124               | 0               |              | 0/119               | 0               |              | 0/119           | 0            | III                     |
| (2,2-bis[4-(2-hydroxy-3-<br>acryloxypropoxy)phenyl]propane     | BIS-GA            | 0.5                              | 5/241               | 2.1             | 18            | 4/124               | 3.2             |              | 1/117               | 0.9             |              | 1/117           | 0.9          | III-V                   |
| urethane diacrylate (aliphatic)                                | al-UDA            | 0.1                              | 2/243               | 0.8             | 22            | 0/124               | 0               |              | 2/119               | 1.7             |              | 2/119           | 1.7          | V                       |
| urethane diacrylate (aromatic)                                 | ar-UDA            | 0.05                             | 2/243               | 0.8             | 22            | 2/124               | 1.6             |              | 0/119               | 0               |              | 0/119           | 0            | II                      |
| triethyleneglycol diacrylate                                   | TREGDA            | 0.1                              | 17/241              | 7.1             | 10            | 12/124              | 9.7             | 4            | 5/117               | 4.2             |              | 5/117           | 4.2          | I                       |
| N,N-methylenebisacrylamide                                     | MBAA              | 1                                | 0/191               | 0               | –             | 0/83                | 0               |              | 0/118               | 0               |              | 0/118           | 0            | NG                      |
| tetrahydrofurfuryl methacrylate                                | THFMA             | 2                                | 7/166               | 4.2             | 14            | 2/16                | 1.6             |              | 5/150               | 3.3             |              | 5/150           | 3.3          | NG                      |
| ethyl cyanoacrylate                                            | ECA               | 2                                | 0/87                | 0               | –             | NT                  | –               |              | 0/87                | 0               |              | 0/87            | 0            |                         |

## Discussion

Most (meth)acrylate-allergic patients react positively to many of the 30–31 (meth)acrylates present in the (meth)acrylate series of Chemotechnique, but it is not clear which of the reactions represent cross-sensitivity and which concomitant sensitization. Koppula et al. (5) proposed that a carboxy ethyl side group would be the common functional group causing cross-reactivity. This residue is also present in, e.g., epoxy diacrylates such as 2,2-bis[4-[2-methacryloxyethoxy]phenyl]propane (BIS-EMA), bis 2,2-bis[4-(methacryloxy)phenyl]propane (BIS-MA) and 2,2-bis[4-(2-hydroxy-3-methacryloxypropoxy)phenyl]propane (BIS-GMA), but these are rather unusual sensitizers (Table 1). In fact, none of our patients had an allergic patch test reaction to BIS-MA. Koppula et al. (5) believe that the carboxy ethyl side group is too hydrophobic and bulky in some (meth)acrylates, and is therefore concealed from the antigen-presenting cells. They listed butyl methacrylate (BMA), BIS-GMA, BIS-EMA, butyl acrylate (BA), butyl diacrylate (BUDA), 1,6-hexanediol diacrylate (HDDA) as belonging to this group. On the other hand, methyl methacrylate (MMA), tetrahydrofurfuryl methacrylate (THFMA), urethane dimethacrylate (UDMA), aliphatic urethane diacrylate (al-UDA) and aromatic urethane diacrylate (ar-UDA) were the acrylates that do not show the functional group and were seldom found to be positive in the Koppula et al. study (5), but, e.g., MMA was often positive in our study. This may be due to concomitant sensitization, or possibly functional groups other than the carboxy ethyl side group are of importance in the cross-reactivity of the (meth)acrylates.

Koppula et al. (5) also concluded that ethyl alpha cyanoacrylate cross-reacts with several other methacrylates, and acrylates such as ethyl acrylate (EA), ethyl methyl acrylate (EMA), 2-hydroxyethyl methacrylate (2-HEMA), ethylene glycol dimethacrylate (EGDMA), diethylene glycol dimethacrylate (DEGDMA) and trimethylolpropane triacrylate (TMPTA). 86 of our patients were patch tested with ethyl cyanoacrylate (ECA, 2% pet, Epikon Oy, Helsinki, Finland) and none reacted to ECA. The patients of Koppula et al. were mainly persons who had been sensitized by nail cosmetics. As EACA, as well as methacrylates and acrylates, are used in nail cosmetics (6,7), it seems plausible to assume that many of the patients of Koppula et al. (5) had *concomitantly* been sensitized to EACA and (meth)acrylates. Our results are in agreement with the opinion expressed by Fisher and Baran (8), i.e., that cyanoacrylates do not cross-react with (meth)acrylates (9). Currently, it is not known whether various types of cyanoacrylates show a

different sensitization pattern, and what is the ideal patch test concentration and vehicle. Furthermore, patients have their own, individualized pattern of cross-reactivity (10), and it cannot be excluded that some individuals may show cross-reactions between cyanoacrylates and (meth)acrylates. Bruze et al. (11) suggested that 10% of ethyl cyanoacrylate in petrolatum (but not in acetone) gave reliable patch test results.

There are great variations in the results obtained in animal sensitization studies as regards the sensitizing capacity of (meth)acrylates (2, 12–14) and, in addition, the correlation between animal studies and clinical experience is not very good (15, 16). Björkner (2) classified, e.g., 2-HEMA, 2-HPMA, EGDMA and TREGDMA as weak sensitizers (Table 1), but these are among the most common sensitizers in our patients (Table 1), as well as in other recent studies (5, 17–19).

It is emphasized that animal tests such as guinea pig maximization tests give information about the sensitization potential, and the extent to which allergens actually cause contact dermatitis is determined by mode of use, etc. Accordingly, the data in Table 1 should be interpreted with caution. In order to be able to judge the sensitization capacity of various (meth)acrylate compounds in humans, it would be necessary to have detailed information about the exposure history of the patients examined and the purity of the (meth)acrylate compounds. Currently, this is not possible because (meth)acrylate-containing products regularly contain undeclared (meth)acrylate compounds (20, 21), and therefore the data in the material safety data sheets and product declarations are not reliable. Accordingly, the allergic patch test reactions in Table 1 cannot be considered as a "ranking" list of the most sensitizing (meth)acrylate compounds.

The (meth)acrylate compounds that provoked many allergic patch test reactions are obviously contact sensitizers in humans, or have a strong tendency to cross-react with sensitizers. Based on a recently proposed classification of contact allergens (22, 23), these (meth)acrylates can be considered *significant human contact allergens*. Because of cross-reactivity, sensitized persons will often have allergic reactions also to many other (meth)acrylate compounds. (Meth)acrylate compounds, including cyanoacrylates (5, 8, 9, 11, 24), that did not provoke any allergic patch test reactions in our patient material may also be significant human contact allergens (5).

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