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SENSITIZATION CAPACITY OF ACRYLATED PREPOLYMERS IN ULTRAVIOLET CURING INKS TESTED IN THE GUINEA PIG

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Abstract. One commonly used prepolymer in ultraviolet (UV) curing inks is epoxy acrylate. Of 6 men with dermatitis contracted from UV-curing inks, 2 had positive patch test reaction to epoxy acrylate. None reacted to the chemically related bisphenol A dimethacrylate. The sensitization capacity of epoxy acrylate and bisphenol A dimethacrylate performed with the "Guinea pig maximization test" (GPM) shows epoxy acrylate to be an extreme sensitizer and bisphenol A dimethacrylate a moderate sensitizer. Cross-reaction between the two substances occurs. The epoxy resin oligomer MW 340 present in the epoxy acrylate also sensitized some animals.

Key words: Acrylic acid; Acrylated prepolymer; Bisphenol A dimethacrylate; Cross-reaction; Epoxy acrylate; Epoxy resin; Methylmethacrylate; Sensitization capacity; Ultraviolet curing ink

The introduction of the ultraviolet (UV) curing inks in printing plants seems to have many advantages compared with conventional printing technology, such as reduction in energy consumption as well as elimination of air pollution (15). During the last year, however, reports have been published concerning skin problems experienced by those men working with or manufacturing UV-curing inks or varnishes (2, 4, 5, 12, 13, 14, 16).

UV-curing inks contain three basic components: a reactive base prepolymer, a photo-initiator (usually a benzophenone), and a multifunctional acrylic monomer used as a "diluent" with "cross-linking" properties.

The prepolymers are synthetic resins with terminal acrylate groups. The most common are acrylated polyesters, acrylated polyethers, acrylated urethanes and acrylated epoxy resins. In many formulations the base prepolymer portion of the inks constitutes as much as 80%.

In a previous investigation 6 men with dermatitis contracted from UV-curing inks, 2 had a positive patch test reaction to the prepolymer used (2). According to the manufacturer this prepolymer was a diacrylate ester of bisphenol A epoxy resin (Fig. 1).

Some of the same features that give epoxy resins their superior performance in thermal systems are not always found with acrylated epoxy resins. They have too high a viscosity and impart excessive hardness to the coating. Other types of acrylated prepolymers have therefore been developed. One of these, a difunctional unsaturated methacrylic monomer based on bisphenol A (called bisphenol A dimethacrylate) is said to have such good properties that it can replace epoxy acrylates not only in UV-curing inks, but also in conventional epoxy resins (Fig. 1). Bisphenol A dimethacrylate is also believed by the manufacturer to be less irritating and allergenic and thus meets the requirements of safer handling and application.

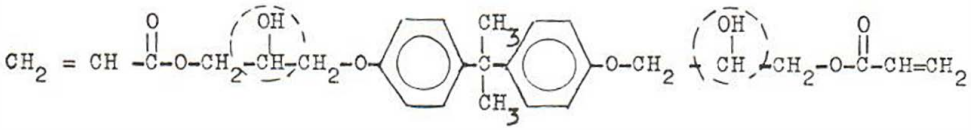
The purpose of this study was to assess with the "Guinea pig maximization test" (9, 10) the sensitizing capacity of epoxy acrylate and bisphenol A dimethacrylate and to investigate if any cross-reaction between these two chemically related prepolymers occurs and to confirm the clinical test results.

MATERIAL AND METHODS

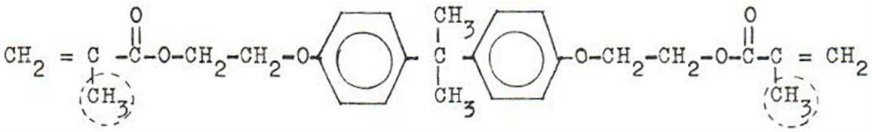
The induction and challenge were in accordance with the original description of the GPM test (7, 9, 10). A booster dose was also given intradermally with the sensitizing chemicals 48 hours after the challenge application.

Animals. Albino female guinea pigs, weighing 300–400 g, were used.

Chemicals. The acrylates used for sensitization and challenge were epoxy acrylate and bisphenol A dimethacrylate (Fig. 1). Challenge was also performed with epoxy resin of bisphenol A type (epoxy oligomer MW 340), bisphenol A, acrylic acid and methylmethacrylate (MMA). Thin-layer chromatography (6) revealed the presence of epoxy resin oligomer MW 340 in the epoxy acrylate but not in the bisphenol A dimethacrylate.



Acrylated epoxy resin



Methacrylic monomer based on bisphenol A

Fig. 1. Diacrylate ester of bisphenol A epoxy resin (epoxy acrylate) and methacrylic monomer based on bisphenol A (bisphenol A dimethacrylate).

Topical irritancy. The topical irritancy of the chemicals was studied by a 24-hour closed patch test in 6 animals not used in the test. A challenge patch test concentration was used which did not give any reaction.

Sensitization concentrations. Preliminary investigations were performed in 6 animals to establish the optimal sensitization concentration of the test substances for intradermal and topical induction without causing systemic toxicity.

The final concentrations chosen for intradermal induction with epoxy acrylate were 5% in liquid paraffin and with bisphenol A dimethacrylate 10% in liquid paraffin. For topical induction, both acrylates were used in 100%.

Challenge. All animals were tested with epoxy acrylate in a concentration of 10% in acetone and with bisphenol A dimethacrylate in a concentration of 25% in acetone. Only evident redness and/or swelling was regarded as an allergic response. The reactions were evaluated blind and an assistant chose the cages of the animals at random.

Cross-testing. In order to maintain the allergenic potential, those animals sensitized to epoxy acrylate received, 48 hours after challenge application, a booster dose with 0.1 ml of epoxy acrylate in a concentration of 5% in liquid paraffin intradermally in the shoulder region (11). The control animals got the same amount of the vehicle alone and in the same way as the experimental group. One week later the animals were rechallenged with 10% epoxy acrylate, 1% epoxy oligomer MW 340, 1% bisphenol A, 0.5% acrylic acid and 1% methylmethacrylate, all in acetone.

The other group which was sensitized to bisphenol A dimethacrylate also got a booster dose intradermally above the shoulder region 48 hours after challenge application but with 0.1 ml of bisphenol A dimethacrylate 10% in liquid paraffin. In the same way, the control group received 0.1 ml of the vehicle alone. One week later the animals were rechallenged with 25% bisphenol A dimethacrylate, 1% epoxy oligomer MW 340, 1% bisphenol A, 0.5% acrylic acid and 1% methylmethacrylate, all in acetone.

Controls. At the same time as the animals in the experimental groups were sensitized, the control animals in each series were also exposed intradermally to Freund's complete adjuvant (CFA) and vehicle. When the sensitized animals in each series were challenged, control animals were also patch tested with the same chemicals and in the same concentrations.

Table I. *Challenge reactions in 20 animals sensitized to epoxy acrylate*

Challenge concentrations in acetone

Animals	Epoxy acrylate 10%	Bisphenol A dimethacrylate 25%
Number	18	9
Per cent	90	45
Controls	0	0

Table III. *Challenge reactions in 20 animals sensitized to bisphenol A dimethacrylate*

Challenge concentrations in acetone

Animals	Bisphenol A dimethacrylate 25%	Epoxy acrylate 10%
Number	8	14
Per cent	40	70
Controls	0	0

Table II. *Cross reactions in 20 animals sensitized to epoxy acrylate after a booster dose*
Challenge concentrations in acetone

Animals	Epoxy acrylate 10%	Epoxy MW 340 1%	Bis-phenol A 1%	Acrylic acid 0.5%	Methyl-methacrylate 1%
Number	20	5	1	1	0
Per cent	100	25	5	5	0
Controls	0	0	0	0	0

RESULTS

Induction with epoxy acrylate. The test results are summarized in Table I. Eighteen (90%) of 20 animals exposed to epoxy acrylate became sensitized. Nine animals (45%) also reacted to bisphenol A dimethacrylate. None of the control animals reacted.

The rechallenge of the animals one week after a booster dose with epoxy acrylate shows that 100% of the 20 animals were sensitized. Five (25%) of the animals reacted to epoxy oligomer MW 340, one to the bisphenol A, one to acrylic acid, but none to methylmethacrylate (Table II).

None of the control animals reacted to any of the compounds.

Induction with bisphenol A dimethacrylate. The test results are summarized in Table III. Eight (40%) of 20 animals exposed to bisphenol A dimethacrylate became sensitized. Fourteen animals (70%) also reacted to epoxy acrylate. None of the control animals tested simultaneously reacted.

After a booster dose with bisphenol A dimethacrylate, the rechallenge one week later showed that 9 (45%) of 20 animals were sensitized. Six of the 20 (30%) reacted positively to epoxy oligomer MW 340, 2 to acrylic acid but none to bisphenol A and methylmethacrylate. One of the 6 animals positive to epoxy oligomer 340 had a negative test reaction to bisphenol A dimethacrylate. None of the control animals reacted to any of the compounds (Table IV).

DISCUSSION

Ninety per cent of the guinea pigs were sensitized to epoxy acrylate which can be classified as an extreme sensitizer (10). Forty-five per cent of the animals reacted positively when tested with bisphenol A dimethacrylate, suggesting a certain cross-reaction between epoxy acrylate and bisphenol A dimethacrylate. This is not in agreement with the previous clinical findings in which 2 of 6 men with dermatitis from UV-curing inks reacted to epoxy acrylate but none cross-reacted to bisphenol A dimethacrylate (2). However, this material is small. After a booster dose with epoxy acrylate and rechallenge, all animals became sensitized, a further indication of the strong sensitizing capacity.

Forty per cent of the guinea pigs were sensitized to bisphenol A dimethacrylate which can be classified as a moderate sensitizer (10), 70% of the animals also reacted to epoxy acrylate. It is surprising that the secondary allergen elicited reaction in more animals than did the primary allergen.

The only difference in molecule structure between epoxy acrylate and bisphenol A dimethacrylate is two hydroxyl- and methyl groups (Fig. 1). Epoxy acrylate is an extremely potent sensitizer compared with the moderate sensitizer bisphenol A

Table IV. *Cross reactions in 20 animals sensitized to bisphenol A dimethacrylate after a booster dose*
Challenge concentrations in acetone

Animals	Bisphenol A dimethacrylate 25%	Epoxy MW 340 1%	Bis-phenol A 1%	Acrylic acid 0.5%	Methyl-methacrylate 1%
Number	9	6	0	2	0
Per cent	45	30	0	10	0
Controls	0	0	0	0	0

dimethacrylate. Methacrylates are less potent sensitizers than corresponding acrylates (1).

Of the 20 animals sensitized to bisphenol A dimethacrylate, 6 also reacted to epoxy oligomer MW 340. TLC showed no presence of epoxy oligomer MW 340 (12). The reaction cannot be explained at present but requires further investigations.

One of the animals sensitized to bisphenol A methacrylate also reacted to bisphenol A and acrylic acid, which could be due to a hyperreactivity in this animal. It seems rather difficult to sensitize guinea pigs to acrylic acid (8).

Information from the manufacturer about tests made according to Draize for skin irritation (3) show that "the primary irritation index" for epoxy acrylate is less than 0.5 and non-irritant, and for bisphenol A dimethacrylate 1.7, which means slightly irritant. Compared with the sensitization class for these acrylates, it shows the discrepancy between skin irritation and the sensitizing capacity and it is important to inform manufacturers and workers about the difference between these two methods and between allergenic and irritant effects on the skin.

The epoxy acrylate molecule is formed by letting the epoxy oligomer react with acrylic acid, to impart acrylic-type terminal unsaturation to the prepolymer. It seems probable that the whole molecule of epoxy acrylate acts as an allergen and not the terminal acrylic groups, as they did not react to acrylic acid.

Of the animals sensitized to epoxy acrylate, 25% reacted positively to epoxy oligomer MW 340. TLC showed presence of free epoxy resin in the epoxy acrylate. The patients were not sensitized to epoxy resin. The guinea pig maximization test shows, however, that there is a potential risk of sensitization with the epoxy resin contaminant when working with epoxy acrylates in UV-curing inks.

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