

SENSITIZATION CAPACITY OF EPOXY RESIN HARDENERS IN THE GUINEA PIG

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Abstract. Cold-curing resin hardeners were examined regarding their sensitization capacity, by the "guinea pig maximization test". All the aliphatic polyamines caused sensitization. Two of the three cycloaliphatic polyamines sensitized all the animals, while one did not sensitize at all. The aromatic amine sensitized one-fifth of the animals studied. The two polyaminoamides sensitized respectively one-fifth and two-thirds of the animals. Two of the four adducts failed to provoke any reactions. The phenolaccelerated adduct of triethylenetetramine sensitized nearly half of the animals. The adduct of isophorondiamine and epoxy resin sensitized three-fourths of the animals. Judging from the above observations, adducts, when void of aliphatic amines, are probably not potential sensitizers. This may perhaps also be true of the polyaminoamides.

Key words: Guinea pig maximization test; cold-curing hardeners; Aliphatic polyamines; Cycloaliphatic polyamines; Polyaminoamides; Amine adducts

According to clinical experience, epoxy resin hardeners are sensitizers. The polyamines in particular have been reported to cause allergic contact dermatitis (1, 2, 3, 4, 5, 9, 10, 11, 12, 14, 17). Hardeners of the polyaminoamide type have only exceptionally been regarded as sensitizers (10). Lea et al. (7) reported on sensitization in humans provoked by repeated irritancy tests for epoxy resin compounds. Three of 25 humans became sensitized to the hardeners. As far as the present author is aware, only one study has been reported on sensitization in guinea pigs (two animals) with a polyamide hardener. The animals were unresponsive (6).

A search of the literature failed to reveal any attempts to classify the sensitization capacity of various types of epoxy resin hardeners by use of the "guinea pig maximization test". This paper con-

cerns assessment, by means of the GMP test, of the sensitization capacity of common "cold-curing hardeners.

Chemistry

There are two principal classes of epoxy resin hardeners (curing agents), viz. cold-curing and hot-curing. The hot-curing hardeners, which react at high temperature, fall beyond the scope of the present work. The most common cold-curing hardeners, which react at room temperature, are aliphatic and cycloaliphatic polyamines, modified aromatic polyamines, polyaminoamides and amine adducts (Fig. 1).

The main type of reaction between an amine hardener and an epoxy resin generally leads to crosslinkage.

MATERIAL AND METHODS

The methods used were the same as those presented in a previous investigation (15, 16) and were in accordance with the original description of the GMP test (8, 9).

Chemicals. The chemicals used were commercial products and were all supplied by the Swedish Plastics Federation. Their chemical structures are shown in Fig. 1.

Sensitization concentrations. (Table I). Because of their systemic toxicity (13) a weak (0.5% w/v) concentration was used for intradermal and topical sensitization with the polyamines, and a 5% concentration was used for the aromatic amine, polyaminoamides and the adducts, except for one cycloaliphatic diamine and the adduct of phenol-accelerated TETA, when 2% (w/v) concentrations were used for intradermal and topical sensitization.

Induction of sensitization. The animals were sensitized in a two-stage procedure—intradermal injections and topical application.

Table I. Sensitization and challenge to hardeners: 15 animals in each series

Hardener	Vehicle	Sensitization conc. % (w/v) Intradermal and topical	Challenge conc. % (w/v)	Reacting animals % of tested
<i>Aliphatic polyamines</i>				
Ethylenediamine (EDA)	water	0.5	1	60
Diethylene-triamine (DETA)	water	0.5	2	93
Triethylene-tetramine (TETA)	water	0.5	2	80
Dipropylene-triamine (DPTA)	water	0.5	2	55
Tetra-ethylene-pentamine (TEPA)	water	0.5	2	73
Diethylamino-propylamine (DEAPA)	water	0.5	2	80
Trimethylhexamethylene-diamine (TMDA)	water	0.5	2	80
<i>Cycloaliphatic polyamines</i>				
Isophoron-diamine (IDP)	acetone	0.5	2	100
N-aminoethyl-piperazine	water	0.5	2	100
3,3'-Dimethyl-4,4'-diamino-dicyclohexyl-methane	acetone	0.5	2	0
3,3'-Dimethyl-4,4'-diamino-dicyclohexyl-methane	acetone	2.0		
<i>Aromatic amine</i>				
Diaminodiphenyl-methane (DDM)	acetone	5	2	20
<i>Polyaminoamides</i>				
Polyaminoamide based on TEPA	acetone	5	2	67
Polyaminoamide based on TETA	ethanol	5	2	20
<i>Adducts</i>				
Adduct of phenol-accelerated TETA	acetone	2	2	47
Adduct of TETA and propylene oxide	water	5	2	0
Adduct of TETA and propylene oxide, distilled	water	5	2	0
Adduct of isophorondiamine and low MW epoxy resin	acetone	5	2	73
Adduct of DETA and epoxy resin distilled	acetone	5	10	0
non-distilled	acetone	5	10	0

Challenge. Two weeks after the second stage of sensitization, a 24-hour occluded patch test (Al-test, Imeco, Astra Agency) was performed on the flank without chemical depilation. The test concentrations of the hardeners are given in Table I. Animals sensitized with the polyamines DETA, TETA or TEPA were simultaneously patch tested with all these three hardeners. Animals sensitized with the adducts were challenged with the amine from which the adducts are derived.

Reading of challenge reactions. The challenge site was evaluated 24 hours after removal of the patch. Three hours before reading, the test site was shaved with an electric razor. Only obvious redness and swelling was regarded as an allergic response. The reactions were judged by two persons independently.

Controls. The control animals were of the same age and weight as the animals in the experimental groups and were also exposed to CFA and vehicle intradermally. When the sensitized animals in each series were challenged, the control animals were patch tested with the same hardeners in the same concentrations.

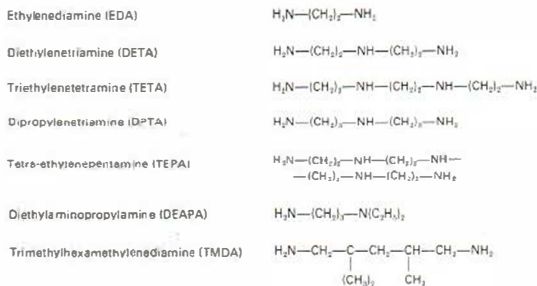
RESULTS

The test results are summarized in Table I.

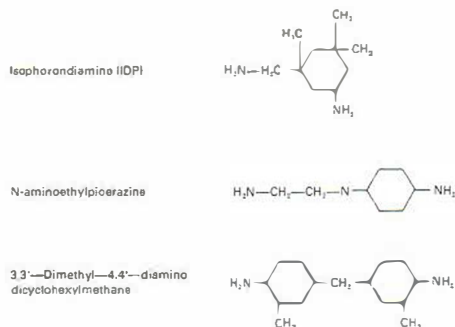
The aliphatic polyamines produced reactions in 55–93% of the animals. Of the reactions to the polyamines the following simultaneous reactions were noted: 67% of the animals sensitized with TETA gave patch test reactions to DETA, 20% of the animals sensitized with DETA gave patch test reactions to TETA, and 40% of the animals sensitized with TEPA gave patch test reactions to DETA and 60% to TETA.

Two of the three cycloaliphatic polyamines produced reactions in all the animals, and seem to be extremely potent sensitizers, while the third, a cycloaliphatic diamine (3,3'-dimethyl-4,4'-diamino-dicyclohexylmethane), elicited no reactions.

Aliphatic polyamines



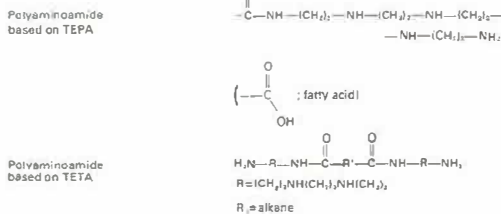
Cycloaliphatic polyamines



Aromatic amine



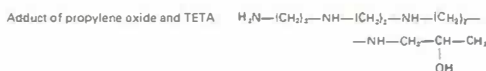
Polyaminoamides



Adducts



Adduct of propylene oxide and TETA



Adduct of isophorondiamine and low MW epoxy resin

Adduct of low MW epoxy resin and DETA

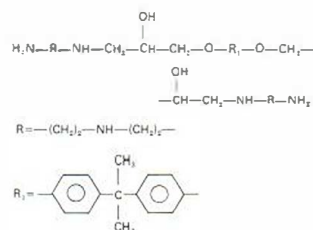


Fig. 1. Hardeners.

The aromatic amine produced reactions in 20% of the animals.

The two polyaminoamides provoked reactions in 67% and 20% respectively. However, 27% of the animals sensitized with the polyaminoamide based on TEPA caused reactions to TEPA and 67% of the animals sensitized with the polyaminoamide based on TETA caused reactions to TETA.

The adduct of phenolaccelerated TETA caused reactions in 47% but none reacted to TETA. The propylene oxide adduct of TETA did not provoke any reactions, while 67% of the animals reacted to TETA. A series with the distilled adduct of propylene oxide and TETA did not evidence reactions and there were no reactions to TETA. The adduct of isophorondiamine and low MW epoxy resin caused reactions in 73% of the animals, while 33% reacted to isophorondiamine but none to epoxy resin (MW 340).

The non-distilled adduct of DETA and epoxy resin provoked no reactions, but 20% reacted to DETA. The distilled adduct of DETA and epoxy resin produced no reactions, but 13% of the animals reacted to DETA.

There were no reactions in the control animals (Table I).

DISCUSSION

All the aliphatic polyamines were found to have a high degree of sensitization. Because of the systemic toxicity of polyamines (13), the concentration used for intradermal and topical sensitization was not more than 0.5% for the polyamines, and 2% for one of the cycloaliphatic polyamines and one of the adducts. However, the sensitization concentration of the two polyaminoamides and three of

the four adducts was as high as 5%, which probably means that the content of free amine was low in these chemicals.

All the aliphatic amines investigated in the present work were commercial products, which means that each might have contained traces of another, varying from batch to batch. It is therefore impossible to decide whether the simultaneous reactions registered were cross reactions or not. Neither pure DETA nor TETA was available.

Two of the cycloaliphatic polyamines proved to be potent sensitizers, while the third seemed to have no sensitizing capacity at all.

The aromatic amine, diaminodiphenylmethane, sensitized one-fifth of the animals.

The two polyaminoamides sensitized two-thirds and one-fifth of the animals, respectively, and sometimes produced reactions to TEPA and TETA, from which each respective polyaminoamide is derived (Fig. 1). Amine-free polyaminoamide was not available for sensitization and it was therefore not possible to assess the sensitization capacity of the polyaminoamide itself.

Two of the four adducts elicited no reactions. Animals induced with the adduct of TETA and propylene oxide, which was distilled and free from TETA, did not react to the adduct or TETA.

Hardeners have usually been found to be responsible for less than 10% of allergic contact eczema cases attributable to epoxy compounds (1, 2, 5, 10, 11). The maximization test illustrates the sensitization capacity of the hardeners.

When there are substantial differences in the hardeners' sensitization capacity in the maximization test, these will probably be reflected in differences in sensitization rate.

However, although the sensitization index is high in the experimental series, this does not necessarily mean that sensitization in industrial work is common. Sensitization depends on a variety of factors, such as concentration, frequency and duration of exposure, as well as presence of irritants.

Because of the high alkalinity of the aliphatic amines, they may disturb the barrier function and also cause irritation. This implies a risk of sensitization to other chemicals, such as epoxy resins.

Hardeners which fail to cause sensitization in the GPM test will probably not cause allergic eczema by industrial exposure to any appreciable extent. It was considered important to define those hardeners which are not sensitizers.

Of the cycloaliphatic polyamines, one proved not to be a sensitizer.

The polyaminoamides are probably not sensitizers. However, this can be decided with certainty only if amine-free polyaminoamide is used for sensitization by the GPM test.

Observations made in the present study illustrate that certain adducts are not sensitizers, provided they do not contain free amine.

The information obtained may be useful in the future choice of hardeners for research and development in the chemical industry. It is therefore considered advisable to investigate other hardeners of cycloaliphatic, polyaminoamide- and adduct-type by means of the GPM test.

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