

Occupational allergic contact dermatitis from 2,3-epoxypropyl trimethyl ammonium chloride (EPTMAC) and Kathon® LX in a starch modification factory

TUULA ESTLANDER, RIITTA JOLANKI AND LASSE KANERVA
Finnish Institute of Occupational Health, Helsinki, Finland

2,3-epoxypropyl trimethyl ammonium chloride (EPTMAC) is used in the production of cationic starch (CS) for the paper industry. It has been shown to be a sensitizer in guinea pigs, but cases of human sensitization are few. 4 workers were previously sensitized to the substance in a Finnish plant. This report describes 3 process men from another plant examined because of recurring dermatitis. 18 workers were involved in production, and had free access to all work sites. 3 process men, whose work involved drying the CS, had dermatitis, although they had only occasional contact with the cationizing chemical. 2 were already verified to be allergic to EPTMAC and had had variable dermatitis for 8–12 years. One had had dermatitis on his face for 1 year. Patch testing with a dilution series (1%, 0.5%, 0.2%, 0.1% pet.) confirmed their allergy to the cationizing chemical containing EPTMAC, but tests with CS were negative. In addition, 2 had contact allergy to Cl+ Me-isothiazolinone from contact with Kathon® LX used as a slimicide in the process. In long-standing (years) recurrent dermatitis, re-examination of patients with verified exposure history and skin tests is necessary. In line with our previous study, sampling the process materials, maintenance work and contamination of work sites and gloves caused sensitization. The results also confirm that EPTMAC is a strong human contact sensitizer. 0.2%–0.5% pure EPTMAC in pet. seems to be the optimal patch test concentration.

Key words: glycidyl trimethyl ammonium chloride; oxiranemethanaminium; N,N,N-trimethyl chloride (CAS 3033-77-0); quaternary ammonium compound; cationic starch; paper industry; slimicide; Kathon® LX; methylchloroisothiazolinone (CAS 26172-55-4); methylisothiazolinone (CAS 2682-20-4); allergic contact dermatitis; occupational. © Munksgaard, 1997.

Accepted for publication 21 December 1996

Modified cationic starch (CS) is added to paper to increase its strength both in pulp and sizing. In Finland, CS is manufactured in automatic modification processes using starch from potatoes, barley or wheat (1–3) (Fig. 1). 2,3-epoxypropyl trimethyl ammonium chloride (EPTMAC) (Fig. 2) (CAS 3033-77-0; glycidyl trimethyl ammonium chloride; oxiranemethanaminium, N,N,N-trimethyl chloride) is used as a cationizing chemical in the process as a water-based commercial product. Additional substances in the cationizing process include e.g.,

bases, acids, antimicrobials and antifoaming agents.

EPTMAC is a sensitizer in guinea pigs (4), but cases of human sensitization are very few (1–3). 4 workers, 3 process men and a laboratory technician, were previously sensitized to the chemical during the production of the CS in one Finnish plant (1–3). This report includes 3 process men

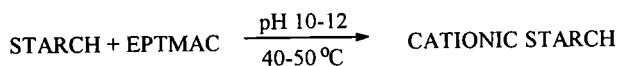


Fig. 1. Modification of starch.

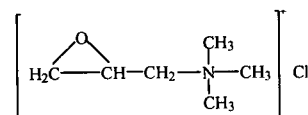


Fig. 2. Structure of 2,3-epoxypropyl trimethyl ammonium chloride (EPTMAC).

from another plant examined at the Finnish Institute of Occupational Health (FIOH) because of recurring dermatitis.

Patients and Methods

Patch tests

Patch tests were done on the backs of patients, using the Finn Chamber[®] method with 2-day application time, and read as previously described (3, 5). They included a modified European standard series (Chemotechnique Diagnostics AB, Sweden), containing the active ingredients of Kathon[®] CG, i.e., methylchloroisothiazolinone (CAS 26172-55-4) and methylisothiazolinone (CAS 2682-20-4), Cl+ Me-isothiazolinone at 200 ppm in aqua (aq.) and other relevant series such as a modified epoxy series (Chemotechnique) supplemented by 3 epoxy acrylates, bisphenol A, epichlorohydrin, 8 non-bisphenol A epoxy compounds, 2 reactive diluents and 5 amine hardeners (6, 7), a series of antimicrobials, and in 1 case (patient no. 2), a modified series of plastics and glues (Chemotechnique).

Other test substances included copper sulphate 2% aq., oleamidopropyl dimethylamine 0.1% aq., cocodiethanolamide 0.5% petrolatum (pet.), cocamidopropylbetaine 1% aq., 3-dimethylaminopropylamine 1% pet. and 9 chemicals or materials from the workplace.

The cationizing chemical (containing 65–75% EPTMAC in water according to the material safety data sheet) was tested as a dilution series (Table 2). PVC and nitrile rubber glove materials were tested in a chamber with a drop of water, and acetone and 4–5 samples of CS were tested as such.

Prick and other tests to detect type I sensitization

Prick tests were done with a series of common environmental allergens (Allergologisk Laboratorium A/S, Denmark) and with 4 natural rubber latex allergens. 2 of the latex test substances were prepared as described by Turjanmaa (8). In the case of patient no. 2, total IgE and birch pollen specific IgE-antibodies were also determined.

Patients

18 workers were involved in the production of CS. 3 process men who worked in the department where CS was dried to powder form developed dermatitis after 3–7 years in the job. Details of these patients are given in Table 1. 2 of them (patient nos. 1, 2) were already verified to be allergic to EPTMAC chemical and had had variable dermatitis for 12 and 8 years on their hands and at other sites, including the face and legs. Patient no.

2 was atopic and had had atopic dermatitis of short duration. Patient no. 3 had had occasional dermatitis on his face for 1 year. He had used protective gloves made of nitrile rubber or PVC only occasionally. Patient nos. 1 and 2 had used the gloves daily. Every worker wore any gloves available at each work site. The workers' main task (90% of each shift) was to follow the automatic drying process, to take samples of the CS, to take such samples to the laboratory, and also to take care of maintenance, when required, in other parts of the factory.

Results

Patch test results are given in Table 2. Tests with EPTMAC cationizing chemical 1% pet. and a dilution series of the compound elicited allergic reactions in all 3 patients. Patient no. 3 reacted ++ to EPTMAC 0.2% pet. and + even to 0.1% pet., whereas the other 2 had weaker ?+ or + reactions to these concentrations. Tests with CS and the epoxy series were negative in all patients.

Tests with other series and substances were also negative except with the standard series. Patient nos. 1 and 2 had ++ reactions to Cl+ Me-isothia-

Table 1. Analysis of 3 process men with dermatitis in a starch modification factory

Patient no.	1	2	3
age (years)	48	30	32
work with drying of cationic starch in 3-shifts	yes	yes	yes
duration of occupation before dermatitis (years)	3	3	7
duration of dermatitis before diagnosis (years)	12	8	1
site of dermatitis	hands, legs	face, hands arms, legs, feet	face
use of PVC or nitrile rubber gloves	2h daily	1.5 h daily	occasional
previous dermatitis	no	yes	no
atopy own/family	no/yes	yes/yes	no/no
no. of patch test sessions/year	2/1986, 1996	3/1994, 1996 (2×)	1/1996

Table 2. Patch test results of 3 process men with dermatitis in a starch modification factory

Patient no.	1	2	3
Cationizing chemical containing 65–75% EPTMAC in water			
1% pet.	+++	++	++
0.5% pet.	+++	++	++
0.2% pet.	+	?+	++
0.1% pet.	?+	?+	+
0.05% pet.	–	–	–
standard series			
Cl+me-isothiazolinone			
0.02% aq.	++	++	–
epoxy series	–	–	–
other series	–	–	–
11 own materials ^a	–	^b	–

^a Kathon LX was not tested

^b PVC glove in a drop of water and acetone ++, retesting negative.

zolinone from contact with Kathon® LX used to preserve CS as a water solution. Patient no. 2 also had a ++ reaction to the PVC glove material, but retesting with the material, 10 control tests as well as tests with the glove ingredients, were all negative. Irritation or even glove contamination during patch tests could have caused the reaction.

Prick tests were negative in all except patient no. 2, who was atopic and positive to birch pollen. Correspondingly, birch pollen specific IgE was slightly elevated, 0.7 kU/l, as well as the total IgE, 150 kU/l.

Discussion

EPTMAC is a low-molecular-weight (MW 152) quaternary ammonium compound containing an epoxide group in its molecule (Fig. 1). In addition to the manufacture of CS, it also has many new applications, e.g., in the production of cellulosic textile fibres to improve their dyeing properties, as well as in the production of hair dye and skin care formulations, dispersing and emulsifying agents, fabric softeners, surfactants and adsorbents for removal of dyes from wastewater (9–13).

In the manufacture of cationic starch, EPTMAC is chemically reactive only during the 1st cationizing phase of the process, when it reacts with starch in an alkaline milieu (Figure 1). Its reactivity is lost when the epoxide rings are prised opened and the chemical is fixed in the starch molecule during the last phase of the process (2). Patch testing with a dilution series (Table 2) and 25 negative controls (20 previously made with 0.2% pet (2) and 5 freshly made with 0.5% pet.) confirmed sensitization of all 3 process men to EPTMAC cationizing chemical.

The cationizing chemical is a Finnish product prepared from epichlorohydrin, trimethylamine and water, which can also contain, according to the material safety data sheet, in addition to EPTMAC and water, 2,3-dihydroxypropyl trimethyl ammonium chloride (CAS 34004-36-9) 0.5–3%, 3-chlor-2-hydroxypropyl trimethyl ammonium chloride (CAS 3327-22-8) 2–7% and epichlorohydrin less than 10 ppm, but not trimethylamine (2). Our previous experience (2) and the dilution series positive down to 0.1% pet. indicate that EPTMAC itself was the probable sensitizer in the cationizing chemical, although sensitization to the other compounds cannot totally be excluded. The patients reacted neither to epoxy resin nor to any other epoxy compounds tested. Cross-reactions between EPTMAC and these compounds do not occur. They have no other structural similarities except the epoxide group (2).

The process men had mainly worked with the non-reactive CS, and patch tests with all CS samples from the drying process were negative. Skin contact with EPTMAC chemical and additional cationizing chemicals in the process was also possible, e.g., in the case of pipe blockages, although the whole manufacturing system was closed (2, 14). The skin symptoms of the present patients developed more slowly, after some years' rather than some months' work, compared to our previous patients (1–3), suggesting that contamination of work sites and gloves with EPTMAC was the main reason for their sensitization and recurrence of their dermatitis. Contamination with process chemicals, including EPTMAC, was probable because all 18 workers had free access to all places in the factory; the workers involved in the drying process of CS could reach their work site only through the cationizing department, and protective gloves were not in personal use, as everyone used anyone's gloves. The regular use of dirty gloves might even have promoted the sensitization of patient nos. 1 and 2 (Table 1).

Their additional sensitization to Kathon® LX (15), possibly caused by sampling of CS as water solution, probably explains the long duration of their recurrent dermatitis. 2 commercial antimicrobials were used as preservatives, one containing glutaraldehyde and the other Kathon® LX. Kathon® LX is a strong sensitizer that contains the same isothiazolinones as Kathon® CG but at a 10-fold concentration. We have previously reported (16) a worker who was sensitized to Kathon® LX as the result of a splash of concentrated solution of the chemical from a single accidental exposure. Kathon® LX has many industrial applications, including polymer and latex solutions, dispersed organic pigments, adhesives and tackifiers,

textile processing fluids, inks and printing fluids. It is not recommended to be used in products intended for direct human contact such as cosmetics and toiletries. It must not be used in pharmaceuticals, human or animal food, or agricultural and horticultural applications (15).

Patch testing with glove materials (Table 2) revealed a false-positive test reaction. Retesting and appropriate control tests, at least, are necessary before a glove reaction can be considered to be truly allergic. Testing with the ingredients of a suspected glove should also be done whenever possible.

All 3 process men continued working on the drying of CS, but avoided contact with all process chemicals, and adopted a more careful hand-care system and use of personal protective gloves of the same types as earlier. Also, the other workers were informed about the sensitizing risks of process chemicals and their careful handling. 2 months later during retestings, patient no. 2 had only mild dermatitis on one hand, and 6 months after the examinations, patient nos. 1 and 3 were symptomless.

EPTMAC, as well as Kathon® LX used as a preservative in the starch modification process, were causes of dermatitis, but not CS. In the case of long-standing (years) recurrent dermatitis, the re-examination of patients with verified exposure history and skin tests is necessary. In line with our previous study (1–3), contamination of work sites and gloves, performing maintenance tasks, and sampling of process materials, caused sensitization. The results also confirm that EPTMAC is a strong human sensitizer and should be regarded as sensitizing by skin contact. EPTMAC 0.2%–0.5% pure chemical in pet. seems to be the optimal patch test concentration.

In processes where reactive allergenic chemicals are used, contaminated gloves carry an extra risk of sensitization (17). Disposable polymer gloves are therefore recommended. If the gloves are not disposable, all workers need personal gloves. Dirty gloves should be discarded immediately. Repeated information on sensitizing chemicals and their careful handling, as well as on the correct use and care of protective gloves, is also necessary to all potentially exposed workers.

References

1. Estlander T, Jolanki R, Kanerva L. Occupational allergic contact dermatitis from a quaternary ammonium compound containing an epoxy group (2,3-epoxypropyl trimethyl ammonium chloride). In: *XV Nordiska Kongressen i Allergologi*, Åbo, Finland, 5–8 June 1984, abstr. no. 34.
2. Estlander T, Jolanki R, Kanerva L. Occupational dermatitis to 2,3-epoxypropyl trimethyl ammonium chloride. *Contact Dermatitis* 1986; 14: 49–52.
3. Jolanki R. Occupational skin diseases from epoxy compounds. Epoxy resin compounds, epoxy acrylates and 2,3-epoxypropyl trimethyl ammonium chloride. *Acta Dermatovenereologica* 1991; suppl 159: 1–80.
4. Bergqvist-Karlsson A. Contact allergy to glycidyl trimethyl ammonium chloride. *Contact Dermatitis* 1985; 12: 61–62.
5. Estlander T. Occupational skin disease in Finland. Observations made during 1974–1988 at the Institute of Occupational Health, Helsinki. *Acta Dermatovenereologica* 1990; suppl 155: 1–85.
6. Kanerva L, Jolanki R, Estlander T. Allergic contact dermatitis from epoxy resin hardeners. *Am J Cont Derm* 1991; 2: 89–97.
7. Jolanki R, Tarvainen K, Tatar T, Estlander T, Henriks-Eckerman M-L, Mustakallio KK, Kanerva L. Occupational dermatoses from exposure to epoxy resin compounds in a ski factory. *Contact Dermatitis* 1996; 34: 390–396.
8. Turjanmaa K, Reunala T, Räsänen L. Comparison of diagnostics methods in latex surgical glove urticaria. *Contact Dermatitis* 1988; 19: 241–7.
9. Schrell A, Russ W H, Huber B. *Amination of cellulosic synthetic fibers for dyeing with anionic reactive dyes*. Hoechst A.-G. Germany, Patent no. EP-683251 A1, 1995 Nov 22.
10. Marschner W, Hoppe M. *Dyeing cellulosic and cellulosic blend fabrics with metal complex dyes for wash-out effect*. Bayer A.-G, Germany. Patent no. DE4410866 A1, 1995 Oct 5.
11. Weuthen M, Kahre J, Hensen H, Tesman H. *Cationic surfactants prepared from alkyl and/or alkenyl oligoglucosides*. Henkel K.-G.a.A, Germany. Patent no DE4413686 A1, 1995 Oct 26.
12. Nakajima T, Watanabe Y, Saka N. *Preparation of cationized hydroxyalkyl galactomannans as cosmetic bases*. Nippon Starch Refining, Japan. Patent no. JP07173028, 1995 Jul 11.
13. Saraumi N. *Adsorbents for removal of dyes from wastewater, and their manufacture*. Daisow Co Ltd, Japan. Patent no. JP07100372 A2, 1995 Apr 18.
14. Fregert S. Possibilities of skin contact in automatic processes. *Contact Dermatitis* 1980; 6: 23.
15. Rohm and Haas Nordiska AB. Kathon LX polymer latex preservative, safety guidelines, August 1990.
16. Kanerva L, Tarvainen K, Pinola A, Leino T, Granlund H, Estlander T, Jolanki R, Förström L. A single accidental exposure may result in a chemical burn, primary sensitization and allergic contact dermatitis. *Contact Dermatitis* 1994; 31: 229–235.
17. Estlander T, Jolanki R. How to protect the hands. *Dermatol Clin* 1988; 5: 105–114.

Address:

Tuula Estlander
Section of Dermatology
Finnish Institute of Occupational Health
Topeliuksenkatu 41 aA
FIN-00250 Helsinki
Finland

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.