

Contact dermatitis to a rubber allergen with both dithiocarbamate and benzothiazole structure

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Contact dermatitis to rubber products are often caused by additives used during manufacture, and diagnosed from patch test with established rubber allergen series. In these series the compounds are divided into separate groups such as thiurams, dithiocarbamates and mercaptobenzothiazoles. The objectives were to investigate the substances with allergenic structures present in a diving mask giving rise to facial dermatitis, also those substances including structures from different groups of rubber chemicals. The rubber material was analysed by high-performance liquid chromatography and diode-array detector. The patient was tested by epicutaneous tests using pure substances, extracts and authentic rubber material. 2-Benzothiazolyl-*N,N*-diethylthiocarbamylsulfide, was found in the diving mask and the patient showed positive reaction to the pure compound and to extracts of the diving mask. This compound has structures of both mercaptobenzothiazole and thiuram/dithiocarbamate in its formulae. Besides the established groups of rubber accelerators, uncommon allergens with structures from more than one group can be formed or added at vulcanization. Chemical analysis of the product is needed to find these allergens.

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Allergic contact dermatitis to rubber compounds is one of the most common occupational dermatoses (1, 2). Accelerators added at vulcanization are known to be the cause of most of these cases of dermatitis. The accelerators are traditionally divided into groups of substances with similar structures and reactivities. Thiurams, dithiocarbamates and mercaptobenzothiazoles are the three main groups of allergenic rubber accelerators (3). Because of the chemical reactivity of these substances, new compounds can easily be formed when different allergens are mixed, and especially as a result of the elevated temperatures used at vulcanization.

In this paper we report on a patient with an allergic reaction to 2-benzothiazolyl-*N,N*-diethylthiocarbamylsulfide (BT-DEC), a substance with structures from two different groups of accelerators, i.e. thiurams and mercaptobenzothiazoles (Fig. 1). We have found that a similar compound – 2-benzothiazolyl-*N,N*-dimethylthiocarbamylsulfide (BT-DMC) – is formed at vulcanization in a pilot plant where thiurams and mercaptobenzothiazoles are used as accelerators.

Case Report

An 18-year-old man with a history of rhinoconjunctivitis and asthma but essentially without earlier skin disease was referred to our clinic because of a facial dermatitis. He was an eager player of underwater rugby. During these activities he used a diving mask with close waterproof contact to the skin. He had used this diving mask for a long time without any problem. For 3 months he had been having a red, itching, squamous dermatitis in the face at the contact area of the diving mask. He was recommended to stop using the diving mask and he healed completely.

Epicutaneous testing was performed using the standard series (TRUE test, 2 panels) and a rubber series. We also added tests with the diving mask as is and as an acetone extract. BT-DEC was added as an extra test after chemical analysis of the diving mask. Positive patch tests were registered for the diving mask as is and for the acetone extract of the diving mask (Table 1). We also found positive test reactions for thiuram mix, tetramethylthiuram monosulfide (TMTM) and BT-DEC. No reaction was registered for any of the mercaptobenzothiazol (MBT) tests.

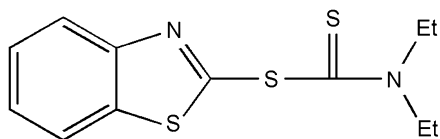


Fig. 1. Chemical structure of 2-benzothiazolyl-*N,N*-diethylthiocarbamylsulfide (BT-DEC), CAS no: 95-30-7.

Table 1. Rubber allergens giving positive patch test reactions [only readings at day 3 (D3) are presented]

Allergen	Concentration	D3
Thiuram mix	0.025 mg/cm ²	++
Tetramethylthiuram monosulfide	1% pet.	++
BT-DEC	1% pet.	++
Diving mask	As is	+++
Diving mask	Extract	++

BT-DEC, 2-benzothiazolyl-*N,N*-diethylthiocarbamylsulfide; pet., petrolatum.

A chemical analysis of the diving mask was performed by extracting 0.5 g of the diving mask with 5 ml acetone (4). The extract was analysed by high-performance liquid chromatography using a non-metal column, all according to a procedure presented earlier (4, 5). In the extract, we found MBT but also BT-DEC, an unusual accelerator with the trade names Nocceler 64 or Ethylac.

Discussion

The categorization of rubber compounds into separate groups based on the chemical structures has been the basis of all evaluations of rubber allergy. In a multicentre study performed by the North American Contact Dermatitis Group, it was shown that less positive reactions were obtained by using TRUE test compared to the Finn Chamber patch test technique (6). Our patient showed a positive reaction to the thiuram mix in the TRUE test panel. All compounds in the thiuram mix were tested as separate tests in our rubber series using the Finn Chamber technique and petrolatum as vehicle. TMTM was the only positive test found. Our patient showed no reaction to tetramethylthiuram disulfide (TETD) or zinc diethyldithiocarbamate (ZDEC) but to TMTM. BT-DEC has ethyl groups on the nitrogen like TETD and ZDEC, but unlike TMTM, which has methyl groups on the nitrogen. For this reason, we do not think that the reaction to BT-DEC represents a cross-reaction to thiurams or dithiocarbamates but is a genuine allergy to a new group of rubber allergens. In a previous paper, a positive test to BT-DEC could be correlated to a cross-reaction to MBT (7). However, our patient showed no reaction to any of the MBT derivatives.

We have performed pilot-scale vulcanization studies with commonly used mixtures of thiurams and mercaptobenzothiazoles (Bergendorff O, Persson C, Lüdtke A, Hansson C, submitted for publication). In these experiments simulating industrial conditions, BT-DMC is formed, which is a compound analogous to the allergen studied in this paper. This case shows that new compounds, which can be formed under the hard conditions present at vulcanization of rubber, can give allergic contact dermatitis. Thiurams and dithiocarbamates, where the substituents on the nitrogen atom differ (methyl, ethyl, butyl, etc.) will, therefore, give rise to a series of new substances that probably are new allergens waiting to be presented in coming case reports.

Allergic contact dermatitis to rubber chemicals is a major cause of occupational skin disease. In some patients, we registered positive patch test reactions to the rubber as is or to an extract of it, but no positive patch test to any added substance can be found. The case described here points to a group of uncommon allergenic additives that is not found among commercial patch test preparations. Whether BT-DEC is added as an accelerator in the production of the diving mask or has been formed during vulcanization could not be determined in our case because no information could be obtained from the manufacturer. However, we have found (Bergendorff O, Persson C, Lüdtke A, Hansson C, submitted for publication) that this type of benzothiazole-dithiocarbamate adducts are formed at vulcanization of rubber using mercaptobenzothiazoles and thiurams as accelerators. So, also when information is available from the manufacturer one cannot be sure of the allergens present in the vulcanized product. The only way to identify the allergens present in the vulcanized product is to perform a chemical analysis. The analyses of thiurams and mercaptobenzothiazoles have been established for several years (8, 9). However, there has been a lack of suitable methods for analyses of dithiocarbamates. A newly published work, which has been optimized in our laboratory, has opened the field of dithiocarbamate analyses concomitant to thiuram and MBT analyses (4, 5). The present work shows that, among rubber-sensitive patients, there are probably several missed contact allergies to allergens formed during vulcanization.

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