

CONTACT POINT

Occupational allergic contact dermatitis to dibutyl maleate and dibutyl fumarate present in a safety shoe: A reason for concern?

Ingrid Siemund^{1,2} | Jakob Dahlin¹ 

¹Department of Occupational and Environmental Dermatology, Lund University, Skåne University Hospital, Malmö, Sweden

²Department of Dermatology and Venerology, Skåne University Hospital, Lund University, Lund, Sweden

Correspondence

Jakob Dahlin, Department of Occupational and Environmental Dermatology, Lund University, Skåne University Hospital, S-20502 Malmö, Sweden.

Email: jakob.dahlin@skane.se

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A few years ago, dimethyl fumarate was reported as a cause of allergic contact dermatitis (ACD) due to its use as an anti-mould agent in furniture exported from China.¹ Here we report ACD on the feet caused by two structurally related chemicals, dibutyl fumarate (DBF) and dibutyl maleate (DBM), present in the safety shoes the patient used at work.

CASE REPORT

A 28-year-old woman with no history of childhood eczema, rhinoconjunctivitis, or asthma was referred to our department with suspicion of contact allergy to her shoes in the spring 2021. She had been working at a bakery for 6 years. In autumn 2019 she began to use new safety shoes (Figure 1) at work. After a few months, she an

itchy erythematous rash began to appear on both feet. According to the pictures on her phone, a vesicular excoriated eczema was present on the dorsal sides and soles of both feet (Figure 1). She stopped using the safety shoes and was treated with a potent topical steroid. When she was seen by a dermatologist her feet were healed, and she did not show eczema elsewhere on her body.

The patient was patch tested with the Swedish baseline series, baseline addition used in Malmö, the shoe series, and with parts of the tongue of the shoe and the inner sole, “as is” and as acetone extracts.² Patch testing was performed using Finn Chambers Aqua (SmartPractice, Phoenix, Arizona). The occlusion time was 48 hours and test readings were performed on day (D) 3/4 and D7.^{3,4} On the first patch test reading, the patient had a doubtful reaction to dimethyl fumarate 0.1% pet. in the shoe series and strong reactions (+++) to the different parts of the shoe, tested “as is” and as extracts.

Analysis of the two extracts using gas chromatography–mass spectrometry⁵ showed that both samples contained DBM and DBF. The presence was confirmed by analysis of the pure substances. The amount of DBM and DBF in the tongue was about 410 ppm and 55 ppm, respectively. The inner sole contained about 5500 ppm DBM and 280 ppm DBF.

The patient was further patch tested with pet. preparations of DBF and DBM, concentrations 0.16% w/w (equimolar concentration to DMF 0.1% w/w) and 0.05% w/w. Positive reactions were registered for both DBF (+) and DBM (++) (Figure 2).

Control testing of DBF 0.05% pet. was performed in 20 patients. No positive reactions were registered (1/1 vs 0/20; $P < .048$, Fisher’s exact test, 2-sided). Control testing of DBM 5% pet. has previously been described.⁶



FIGURE 1 (A) The safety shoe and inner sole used by the patient. (B) Eczema on the dorsal side of the left foot

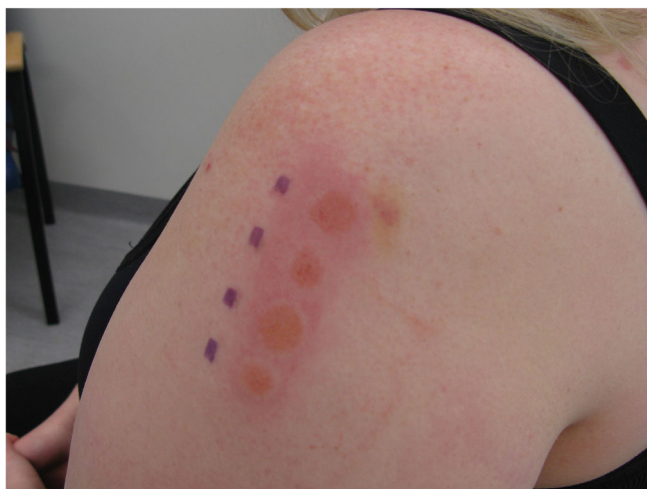


FIGURE 2 Patch test reactions to dibutyl fumarate (DBF) and dibutyl maleate (DBM) on day 3. Top to bottom: DBF 0.16% pet., DBF 0.05% pet., DBM 0.16% pet., DBM 0.05% pet

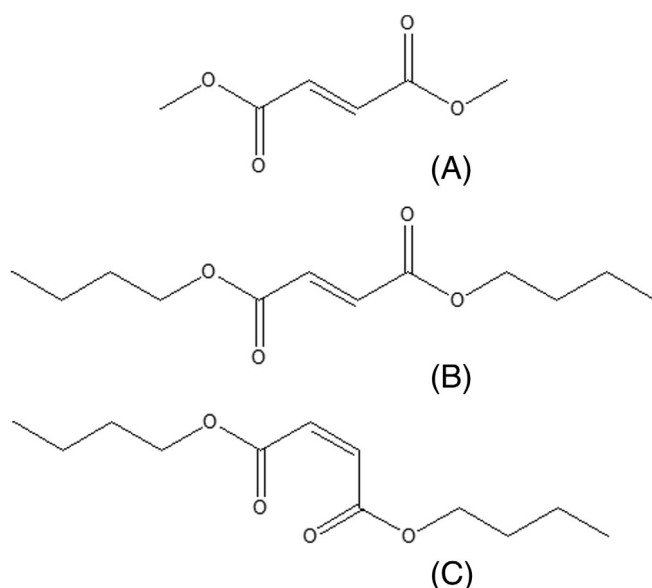


FIGURE 3 Chemical structures of (A) dimethyl fumarate, (B) dibutyl fumarate, (C) dibutyl maleate

DISCUSSION

DBM has previously been reported as a contact allergen present in glues^{6,7} and in the production of gelcoats.⁸ The presence of DBF and DBM in desiccant sachets and a rack covered with synthetic leather has also been reported.⁹ To the best of our knowledge, ACD to DBF has not previously been reported. Both DBM and DBF are reported as possible contact allergens by the European Chemicals Agency,^{10,11} however, the classification is not harmonized.

The weak reaction to dimethyl fumarate may be due to cross-reactivity caused by sensitization to DBM and DBF.¹ The

simultaneous reactions to DBF and DBM may be due to a common metabolite since the substances are stereoisomers (Figure 3).

The shoes (Figure 1) had a synthetic textile inner lining and a plastic inner sole covered with synthetic fabric. Analysis of extracts of different parts of the shoes (inner sole, lining, fabric covering tongue, foam inside tongue, fabric covering sole) showed that the foam inside the tongue and the inner sole contained the highest amounts of DBM and DBF. DBM and DBF may have been used as plasticizers in the production of the polymeric material in the shoe.

In the work of substitution of phthalate plasticizers, which are suspected to be endocrine-disrupting chemicals (but rarely causing contact dermatitis), DBF and DBM have been suggested as 'greener' alternatives.¹² Plasticizers that are blended into polymers do not react chemically with the polymer matrix and may leach from the polymer. Even though maleate and fumarate plasticizers may be more easily degraded in the environment, the risk of contact sensitization suggests that these substances should be avoided in polymers intended for close contact with human skin. DBF and DBM should be considered as additions to shoe series and plastic additive series.

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AUTHOR CONTRIBUTIONS

Ingrid Siemund: Conceptualization; investigation; writing-original draft.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

ORCID

Jakob Dahlin  <https://orcid.org/0000-0002-1058-1959>

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