

Contact allergy to 1,2-benzisothiazolin-3-one

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1,2-Benzisothiazolin-3-one (BIT) (CAS no. 2634-33-5) is a biocide and fungicide that is widely used in paint and varnishes, but also in household cleaning products such as laundry detergents, and in agriculture pesticide formulations. BIT is the most frequently used isothiazolinone on the Danish market, followed by methylisothiazolinone (MI) and methylchloroisothiazolinone (MCI)/MI (1). A Danish study found 985 registered products on the Danish market containing BIT (1). BIT is a well-known contact allergen, and can also cause airborne and systemic contact dermatitis (2). BIT was found to be not safe for use in cosmetic products in 2012 (3), and most published cases are therefore occupational (4–11).

The Allergen Bank is a service established in 1992 for dermatologists in practice in Denmark, where, on a subscription basis, they can gain access to extra contact allergens, for example BIT, as supplements to the baseline series for case-by-case testing of individual patients (12). BIT (0.05% and 0.1% pet.) has been available from the Allergen Bank since 2001, and is found in the shoe series and a cooling lubricant series, but can also be ordered as an individual allergen.

Methods and Results

Patch test results from eczema patients from 2002 to 2015 tested with BIT (0.1% and 0.05% pet.) at the department of dermatology and in the dermatology offices were reviewed. At the department of dermatology, Odense University Hospital, benzisothiazolinone (0.1% and 0.05% pet.; Trolab[®], SmartPractice, Phoenix, AZ,

USA) was tested in Finn Chambers[®] on Scanpor[®] tape (SmartPractice), applying 20 mg. For dermatologists subscribing to the service, 30 mg of benzisothiazolinone in pet. (0.1% and/or 0.05%) was sent to the office in IQ Ultra Chambers[®] (Chemotechnique Diagnostics, Vellinge, Sweden). Patch tests were read on day (D)3/D4 and D7 at the department according to ESCD recommendations (13). In the dermatology offices tests were performed according to their clinical routines. The Allergen Bank had 55 subscribers in 2015. It was up to the individual clinician to decide which concentration of BIT to use for testing, or whether to use both concentrations.

Three hundred and ninety-two patients were tested with 0.05% BIT and 183 with 0.1% BIT; 27 patients had positive patch test reactions to BIT (0.05% and/or 0.1%). Nearly 2.5 times more patients were tested in private practice than in the dermatology department, so more positive reactions to BIT were diagnosed in private practice (Table 1). Most patch test reactions were weak or moderate (+ or ++) on D3/D4, and only one negative patch test reaction turned positive on D5/D7. No doubtful or irritant reactions were found. Eight patients were patch tested simultaneously with both 0.05% and 0.1% BIT; 4 had positive reactions to both, and 4 had negative reactions to 0.05% BIT and + reactions to 0.1% BIT (Table 2). Of the patients with positive patch test reactions to BIT, 85% were men, and 67% had hand eczema; 63% of cases were occupationally related. However, we have no detailed information about occupations. Current relevance was reported for 4 cases from the dermatology department and for less than half of the patients tested in private practice (Table 1). Two of 4 of the patients from the department had concomitant reactions to MCI/MI (data not shown). However, data on concomitant reactions between isothiazolinones for patients tested in private practice were not available.

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Klaus E. Andersen established the Allergen Bank service in Denmark.

Table 1. Patch test reactions to 1,2-benzisothiazolin-3-one in private practice and at the department of dermatology from 2001 to 2015

	Dermatology offices		Department of dermatology	
	D3/D4 0.05 pet.	0.1 pet.	D3/D4 0.05 pet.	0.1 pet.
?+	0	0	0	0
+	8	3	0	1
++	8	3	2	2
+++	3	1	0	0
No. of additional positive reactions only on D5/D7	1	–	–	–
No. of tested patients	283	124	109	59
No. of positive reactions (%)	20 (7)	7 (6)	2 (2)	3 (5)
Clinical relevance, no. (%)	10 (50)	2 (29)	2 (100)	3 (100)

Table 2. Patch test results on D3/D4 of patients tested simultaneously with 1,2-benzisothiazolin-3-one 0.1% and 0.05%

Patient no	0.05 pet.	0.1 pet.
1	Negative	++
2	Negative	+
3	Negative	+
4	Negative	+
5	++	++
6	++	++
7	++	++
8	+++	+++

Discussion

Almost all publications on contact allergy to BIT are case reports. BIT is considered to be a weak to moderate contact allergen and less sensitizing than MI (3, 14, 15). In this study of aimed testing, 5.5% of 183 patients tested with BIT 0.1% pet. had positive reactions, and 5.6% of 392 tested with BIT 0.05% pet. had positive reactions. In a large central European study, 8728 patients were tested (aimed testing) and 141 (1.6%) had positive patch test reactions to BIT 0.1% pet. (16). Lundov et al. found a prevalence of 0.2% positive patch test reactions among 2411 patients tested consecutively with 0.1% BIT aq., and BIT is therefore considered to be a rare allergen, despite its frequent use in water-based paints (17, 18).

BIT has been used for patch testing in a variety of concentrations and vehicles (eth., aq., and pet.), and Chew and Maibach concluded in 1997 that BIT 0.1% pet. was irritant, in contrast to Andersen and Rycroft, who suggested patch testing with BIT 0.1% pet., and commented that BIT 0.1% aq. was not irritant and that aq. could be used as test vehicle as well (19, 20). There are no solid data showing the optimal test concentration and vehicle for BIT. No irritant reactions were recorded for either concentration. As BIT is a widely used preservative, the occurrence of allergic contact dermatitis caused by BIT may be underestimated, and dermatologists should increase their awareness of this allergen. The data in this study were collected retrospectively, and this is an important limitation, as information about occupation and specific products is unavailable. However, BIT was used for aimed testing, and was most often ordered as a single allergen after exposure analysis. Perhaps the clinical relevance is underreported from private practice, but we do not know whether this is the case. Cross-reactivity between different isothiazolinones has been discussed previously, as have concomitant sensitizations, and this may explain some of the missing relevance in certain patients, but this was not specifically investigated in this study (16). A study is needed to establish the optimal patch test concentration of BIT.

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