

Allergic contact dermatitis from octylisothiazolinone

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Summary

Background. Octylisothiazolinone is a biocide that has been reported as a moderate, but rare contact allergen.

Objectives. To investigate the occurrence of octylisothiazolinone contact allergy and allergic contact dermatitis diagnosed and registered in the Allergen Bank at Odense University Hospital during the past 20 years. Octylisothiazolinone has been used for targeted testing only.

Method. All octylisothiazolinone-patch test results registered in the Allergen Bank between January 1992 and February 2012 were analyzed.

Results. A total of 20 out of 648 patients patch tested with octylisothiazolinone had positive reactions. The majority of the patients (90%) with relevant sensitizations to octylisothiazolinone had been exposed in occupational settings and most patients were painters.

Conclusions. Octylisothiazolinone is a relevant sensitizer.

Key words: antimicrobial; biocide; contact allergy; isothiazolinone; octylisothiazolinone; paint; preservative.

Octylisothiazolinone (OIT) is a contact allergen of moderate potency (1). It is a biocide and preservative, marketed for use in a range of industrial products such as polishes, paints, cleaners and metalworking fluids for some 30 years (2). Accordingly, most cases of reported allergic contact dermatitis from OIT are of occupational origin (1–5). However, a Swedish investigation reported that 3% of detergents on the Swedish market contained OIT (6). OIT is also registered as an antimicrobial agent in the European Commission database (CosIng) with information on cosmetic substances and ingredients with the INCI-name octylisothiazolinone. However, it may not be used in cosmetic products in the EU and does not appear

among the listed preservatives used in the United States and Canada (7) Fig. 1.

OIT shares similar chemical characteristics with other isothiazolinones, but differs in potency of sensitization: methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) > benzylisothiazolinone (BIT) > OIT (8). Differences in the frequency of sensitization is also partly explained by the similar order in the extent of use (9).

The literature on contact allergy from OIT consists mainly of case reports and only a few register-based studies (1–5, 10, 11). The objective of this study was to investigate the occurrence of allergic contact dermatitis from OIT registered in the Danish Allergen Bank. The study covers a total of 20 years of patch test data.

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Materials and Methods

The outcome of targeted diagnostic patch testing with OIT in contact dermatitis patients registered in the Allergen Bank database from January 1992 to February 2012 were reviewed retrospectively. The medical records for patients

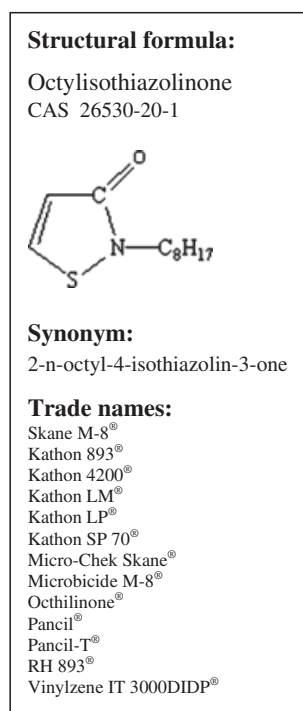


Fig. 1. Structural formula, synonyms and trade names for octylisothiazolinone.

with positive patch tests to OIT at the department were examined and for the patients tested positive by private practice dermatologists a questionnaire was sent to the dermatologists with questions asking for information about the patient's dermatitis, the patient's exposure to OIT and the long-term consequences of the alleged OIT-contact allergy.

The patch test material was 2-n-octyl-4-isothiazolin-3-one 0.1% in petrolatum (Chemotechnique®, Vellinge, Sweden). At the department patch tests were applied using Finn Chamber® technique to the upper back and remained occluded for 2 days. Readings were performed on day 3/4 and day 5/7. In dermatology practice local patch test procedures were followed. Scoring of test reactions was done according to the recommendations of the International Contact Dermatitis Research Group (ICDRG) (12). The clinical relevance was determined by the doctor's evaluation of the patient's history, dermatitis pattern and through exposure analysis.

Patch test results of patients tested with other isothiazolinones, methylchloroisothiazolinone-/methylisothiazolinone (MCI/MI) and benzisothiazolinone (BIT), in addition to OIT were also reviewed with regards to co-sensitization or cross-reactivity.

Results

From January 1992 to February 2012 a total of 10 844 patients were tested at the hospital department and 11 123 patients were tested by dermatologists in private practice with contact allergens ordered from the Allergen Bank. A total of 648 patients (3%) had aimed patch tests with OIT, and 20 (3.1%) had a positive patch test reaction to OIT. The male to female ratio was 2:1. The youngest patient was 18 years of age and the oldest 66 years with an average age for the group in total of 44 years.

Three patient cases were excluded from the study due to lack of follow-up information. Of the remaining 17 patients, 2 were diagnosed at the department and 15 patients were retrieved from 9 dermatology practices. Supplementary information for 13 patients was obtained by means of the questionnaires that were answered by the private practice dermatologists. Five of the 13 patients in practice were tested with a shoe series containing OIT. The other eight were tested with a selection of biocides. No information is obtained about test reactions to the baseline series used in the different practices.

Relevant exposure to OIT was found in 10 of the 15 cases (67%) explaining the positive reactions. Paints proved to be the most frequent cause of sensitization ($n = 6$). Other causes were cooling fluids ($n = 2$), shoes ($n = 1$) and textiles ($n = 1$) (Table 1).

A total of 36 doubtful and 5 irritant reactions (6%) were recorded in addition to the 20 positive patch test reactions to OIT suggesting that the patch test material is also a marginal irritant and a lowering of the test concentration may be considered.

Concomitant or cross-reactivity to MCI/MI and BIT is shown in Table 2.

Four patients had recurrent/chronic dermatitis and in four other patients their eczema had healed (Table 1) after the patients had changed their jobs. Relevant exposures to OIT in the patients' work-environments were found in three of these cases.

Discussion

This is a large retrospective register-based study of OIT contact allergy and allergic contact dermatitis. Twenty patients were registered with positive patch test to OIT in the Allergen Bank between January 1992 and February 2012 and at least ten of these had clear clinical relevance. The Allergen Bank is a service for private practice dermatologists in Denmark where they can subscribe to extra contact allergens to supplement the baseline series (13). The occurrence of OIT contact allergy in Denmark is probably much larger than found in this study, since the diagnosis requires that the dermatologist has access

Table 1. Results from the questionnaires and the patients' medical records

Case	Sex	Age	Location of eczema	Occupation	Exposure	Relevance	Occupational
Tested at the department							
1	F	18	Hands, arms, legs	Painter apprentice	Paint	Yes	Yes
2	F	43	Hands, lower arms	Textile worker	Textiles	Yes	Yes
Tested in private practice							
3	M	32	Face, hands	Painter	Paint	Yes	Yes
4	F	54	Face, hands	Painter	Paint	Yes	Yes
5	M	43	Hands	Painter	Paint	Yes	Yes
6	M	54	Hands, lower arms and legs, torso	Painter	Glues, wood preservatives	Yes	Yes
7	M	47	Face, neck, hands, arm	Painter	Paint	Yes	Yes
8	F	59	Feet	?	?	?	?
9	M	50	Hands	Fireman	Cooling fluids	Yes	?
10	M	28	Hands	Automechanic	Cooling fluids, oils	Yes	Yes
11	M	46	Feet	IT-employed	Shoes?	?	No
12	F	66	Hands, armpit, buttock, groin	Metal-worker	?	?	?
13	M	40	Feet	Chef	Shoes	Yes	No
14	M	19	Feet, lower legs	Student	?	?	No
15	M	58	Hands	Mechanic	Cutting oil	Yes	Yes

M, male; F, female; ?, information not available.

Table 2. Patch test results registered in the Allergen Bank

Case	OIT reaction		MCI/MI reaction		BIT reaction	
	D3/4	D5/7	D3/4	D5/7	D3/4	D5/7
1	+	+	IR	IR	–	–
2	++	–	–	–	IR	–
3	+	–	+	–	++	–
4	++	–	–	–	NT	–
5	++	–	++	–	++	–
6	++	–	+	–	NT	–
7	+++	–	+	–	NT	–
8	+	–	–	–	NT	–
9	++	–	NT	–	–	–
10	+	+	NT	–	NT	–
11	++	–	–	–	NT	–
12	++	–	–	–	NT	–
13	+	–	–	–	NT	–
14	+	+	–	–	NT	–
15	+	+	NT	–	–	–

BIT, benzoisothiazolinone; MCI, methylchloroisothiazolinone; MI, methylisothiazolinone; NT, not tested; OIT, octylisothiazolinone; IR, irritant reaction; –, no reaction/not read.

to the allergen and suspicion of exposure in the individual contact dermatitis patient. Further, some of the doubtful ($n = 36$) or irritant ($n = 5$) reactions may in fact be weak, but relevant allergic reactions (14).

The most frequent cause of sensitization was water-based paints. This is in line with previous reports of contact allergy to OIT (1–4, 8, 10, 15–17). The other causes of sensitization (cooling fluids, shoes and textiles) have all also been reported in the literature formerly (4, 10, 11, 18).

Interestingly, nine out of the ten relevant exposures were of occupational origin. The results also revealed that three patients with relevant, work-related allergic reactions to OIT had changed jobs to avoid exposure. Only then had their eczema healed. Consequently, their contact allergy to OIT had negative life-changing consequences.

It has been suggested that the isothiazolinones, given the similarities in the chemical structures, may exhibit cross-reactions between these compounds (19). Another publication reported that simultaneous reactions to the three isothiazolinones are extremely rare (8). However, they tested OIT in a concentration of 0.025% in petrolatum. In contrast, four of the patients with contact allergy to OIT 0.1% in petrolatum in this study also reacted to MCI/MI and two to BIT. Only 12 patients were tested with MCI/MI and 6 patients with BIT in addition to OIT. It is noteworthy though, that all patients with concomitant positive patch tests to OIT and BIT and/or MCI/MI were painters. This supports the idea of co-sensitization rather than cross-reactivity, since the painters are very well likely to have been exposed to all of the before mentioned isothiazolinones (MCI/MI, OIT and BIT), which is frequently used as preservatives in paints.

In conclusion, OIT is a relevant sensitizer as demonstrated by the results in this retrospective study. However, in the individual case of contact allergy to OIT it is important that the allergy is diagnosed due to the risk of severe implications on the patients' job-situation and ultimately quality of life. Suspicion of contact allergy to OIT should especially come to mind when the patient is a painter.

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References

- Mathias C G, Andersen K E, Hamann K. Allergic contact dermatitis from 2-n-octyl-4-isothiazolin-3-one, a paint mildewcide. *Contact Dermatitis* 1983; **9**: 507–509.
- Thormann J. Contact dermatitis to a new fungicide, 2-n-octyl-4-isothiazolin-3-one. *Contact Dermatitis* 1982; **8**: 204.
- Reyes Balaguer J, Martin Herrera A, De la Cuadra Oyanguren J, Hernandez Fernandez de Rojas D. Occupational allergic contact dermatitis to 2-N-octyl-4-isothiazolin-3-one. *J Investig Allergol Clin Immunol* 2008; **18**: 76–77.
- Aalto-Korte K, Alanko K, Henriks-Eckerman M L, Kuuliala O, Jolanki R. Occupational allergic contact dermatitis from 2-N-octyl-4-isothiazolin-3-one. *Contact Dermatitis* 2007; **56**: 160–163.
- Young H S, Ferguson J E, Beck M H. Contact dermatitis from 2-n-octyl-4-isothiazolin-3-one in a PhD student. *Contact Dermatitis* 2004; **50**: 47–48.
- Yazar K, Johnsson S, Lind M L, Boman A, Lidén C. Preservatives and fragrances in selected consumer-available cosmetics and detergents. *Contact Dermatitis* 2011; **64**: 265–272.
- Steinberg D. 2010 frequency of preservative use. *Cosmet Toilet Mag* 2010; **125**: 46–51.
- Geier J, Schnuch A. No cross-sensitization between MCI/MI, benzisothiazolinone and octylisothiazolinone. *Contact Dermatitis* 1996; **34**: 148–149.
- Alexander B R. An assessment of the comparative sensitization potential of some common isothiazolinones. *Contact Dermatitis* 2002; **46**: 191–196.
- Oleaga J M, Aguirre A, Landa N, Gonzalez M, Diaz-Perez J L. Allergic contact dermatitis from Kathon 893. *Contact Dermatitis* 1992; **27**: 345–346.
- Fukunaga A, Nishiyama S, Shimizu H et al. Non-occupational allergic contact dermatitis from 2-N-octyl-4-isothiazolin-3-one in a Japanese mattress gel-sheet used for cooling. *Contact Dermatitis* 2010; **62**: 317–318.
- Wilkinson D S, Fregert S, Magnusson B et al. Terminology of contact dermatitis. *Acta Derm Venereol* 1970; **50**: 287–292.
- Andersen K E, Rastogi S C, Carlsen L. The Allergen Bank: a source of extra contact allergens for the dermatologist in practice. *Acta Derm Venereol* 1996; **76**: 136–140.
- Duus Johansen J, Frosch P J, Lepoittevin J-P. *Contact Dermatitis*: Berlin, Springer-Verlag, 2011.
- Fischer T, Bohlin S, Edling C, Rystedt I, Wieslander G. Skin disease and contact sensitivity in house painters using water-based paints, glues and putties. *Contact Dermatitis* 1995; **32**: 39–45.
- Jee S H, Chao K Y, Sun C C, Wang J D. Outbreak of contact dermatitis related to acticide EP paste in a paint manufacturing factory. *J Formos Med Assoc* 1996; **95**: 628–631.
- Mose A P, Lundov M D, Zachariae C et al. Occupational contact dermatitis in painters - an analysis of patch test data from the Danish Contact Dermatitis Group. *Contact Dermatitis* 2012; **67**: 293–297.
- Geier J, Lessmann H, Dickel H et al. Patch test results with the metalworking fluid series of the German Contact Dermatitis Research Group (DKG). *Contact Dermatitis* 2004; **51**: 118–130.
- Bruze M, Fregert S, Gruvberger B, Persson K. Contact allergy to the active ingredients of Kathon CG in the guinea pig. *Acta Derm Venereol* 1987; **67**: 315–320.