

Sorbitan sesquioleate; a rare cause of contact allergy in consecutively patch tested dermatitis patients

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Summary

Background. Sorbitan sesquioleate (SSO) has been added to fragrance mix I (FM I) as an emulsifier since the 1990s. Being a contact allergen itself, SSO has the potential to cause false-positive reactions to FM I. Recent results obtained with selected FM I-positive patients have shown that 5% have concomitant positive reactions to SSO.

Objectives. To investigate the 5-year prevalence of contact allergy to SSO and evaluate the importance of SSO allergy when patch test results for FM I are interpreted.

Methods. This was a retrospective database study of consecutively patch tested eczema patients (n = 4637) from 2010 to 2014. All patients were tested with our baseline series including FM I and SSO 20% in pet.

Results. Sensitization to SSO was identified in 9 (0.2%) patients. The proportion of FM I-positive patients with concomitant positive reactions to SSO was 1.4%.

Conclusions. SSO is a rare cause of contact allergy, with a 5-year prevalence of 0.2% in consecutively tested patients. Contact allergy to the emulsifier does not play a major role when the overall frequency of contact allergy to FM I is evaluated. However, to correctly diagnose individual patients, concomitant patch testing with FM I and SSO is encouraged.

Key words: clinical relevance; concomitant reactions; contact allergy; emulsifier; fragrances; fragrance mix I; sorbitan sesquioleate.

Sorbitan sesquioleate (SSO) is a mixture of monoesters and diesters of oleic acid and anhydride products derived from sorbitol (1). Since the 1990s, SSO at a concentration of 5% has been added as an emulsifier to fragrance mix I (FM I) in order to ensure satisfactory dispersion of the eight constituents of the mix in the petrolatum vehicle (2). Furthermore, the addition of SSO to the single constituents of FM I in breakdown testing increases the frequency of positive allergic reactions (2, 3).

SSO is a frequently used emulsifier, and is found in topical steroids (4), wound dressings (5), and various other

consumer products, including diapers, toothpastes, and creams (6). However, being an established contact allergen itself (7), SSO has the potential to cause false-positive reactions to FM I. For traditional reasons, testing for specific contact allergy to SSO is performed with a 20% concentration in pet (8). Whereas initial results on specific contact allergy to SSO in consecutively tested dermatitis patients showed a prevalence of 0.5–0.7% (2, 7, 8), a recent US study found a prevalence as high as 3.2% (9). In a subgroup of FM I-positive patients, concomitant positive reactions to SSO 20% pet. have recently been reported in 5.2% of patients, and the need for inclusion of SSO in baseline series testing has been highlighted to ensure correct interpretation of patch test reactions to FM I (10, 11).

This aim of this study was to determine the prevalence of specific contact allergy to SSO determined with routine patch testing at our facility in a 5-year period, and to assess whether SSO allergy poses an actual diagnostic pitfall when patch test results to FM I are interpreted.

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Materials and Methods

Data for this retrospective study were obtained from the clinical database on contact allergy at the Department of Dermatology and Allergology, Copenhagen University Hospital Herlev-Gentofte, Denmark (12). Consecutive patients who were suspected of suffering from allergic contact dermatitis, and who had been tested with our baseline patch test series between January 2010 and December 2014, were included. Baseline patch testing at our department is performed with the European baseline series, an extended patch test series, and our fragrance series including SSO (all materials obtained from Almirall Hermal GmbH, Reinbek, Germany). FM I (8% pet.) contains 5% SSO, whereas the single constituents of FM I (1% pet.) all contain SSO 1%, except for oakmoss (*Evernia prunastri*) absolute, which contains SSO 5%. SSO as an individual allergen is patch tested 20% pet. Patients with positive reactions to SSO 20% pet. were further evaluated with perfume mix 6% pet. (Chemotechnique Diagnostics, Vellinge, Sweden) as part of the department's standard procedure during the study period. Perfume mix 6% pet. contains the same single constituents as FM I, excluding amyl cinnamal and oak moss absolute, all at a 1% concentration, and does not contain SSO.

Patch testing was performed according to international guidelines (13), by the use of Finn Chambers®, with allergen application on the upper back for 48 h. Readings were performed at day (D)2, D3–D4, and D5–D7; the maximum reactions are presented here. Grading of positive reactions (+, ++, and +++) was performed according to international recommendations (13), and an irritant reaction (IR), doubtful reaction (?+) or negative reading was interpreted as a negative response.

Owing to prior testing and known sensitivity, not all patients were tested with the complete baseline series according to the department's standard procedure. These patients are reported separately where relevant. All data were handled anonymously.

Data management and statistical analyses were performed with SPSS™ version 22. Significance testing for contingency tables was performed with Fisher's exact test, and a two-sided *p*-value of <0.05 was considered to be statistically significant. Confidence intervals (CIs) for binomial proportions were calculated with the Wilson score test (<http://www.openepi.com>).

Results

A total of 4637 patients were patch tested with our complete baseline series during the 5-year period. Maximum reactions to SSO 20% pet. are shown in Table 1. Nine

Table 1. Maximum reactions to sorbitan sesquioleate 20% pet., *n* = 4637

Reaction	% (n)
+++	0
++	0.06 (3)
+	0.13 (6)
NT-S	0.02 (1)
IR	0.43 (20)
?+	1.5 (70)
Negative	97.8 (4537)

IR, irritant reaction; NT-S, not tested, sensitized; ?+, doubtful reaction.

Table 2. MOAHLFA index for sorbitan sesquioleate (SSO)-positive patients as compared with sorbitan sesquioleate-negative patients

	SSO patch test		<i>p</i> -value
	Positive, <i>n</i> = 9 % (n)	Negative, <i>n</i> = 4537 % (n)	
Male sex	55.7 (5)	30.7 (1392)	0.14
Occupational dermatitis	0	20.5 (932)	0.22
Atopy	44.4 (4)	19.2 (870)	0.08
Hand dermatitis	33.3 (3)	38.2 (1734)	1.00
Leg dermatitis	11.1 (1)	1.7 (78)	0.15
Facial dermatitis	55.6 (5)	27.5 (1249)	0.13
Age ≥ 40 years	66.7 (6)	66.5 (3015)	1.00

p-Values calculated with Fisher's exact test.

[0.2% (95%CI: 0.1–0.4)] patients had positive reactions to SSO, and 1 patient had previously been shown to be sensitized. According to a chart review, contact allergy to SSO was of current relevance in 3 patients, owing to the use of leave-on cosmetic products (*n* = 2) and a topical steroid ointment (*n* = 1). One patient had past relevance of exposure, whereas the remaining 5 patients had unknown relevance of their positive patch test reactions to SSO 20% pet.

For the 9 patients with positive reactions to SSO 20% pet., baseline characteristics at the time of testing, defined according to the MOAHLFA index, are shown in Table 2, and compared with those of SSO-negative patients (not including patients with IR and ?+ responses). SSO-positive patients were more likely to be male (56% versus 31%), have a history of atopic dermatitis (44% versus 19%), and suffer from leg dermatitis (11% versus 2%) and facial dermatitis (56% versus 28%). Only the difference in history of atopic dermatitis approached statistical significance when the groups were compared.

Concomitant patch test reactions to SSO 20% pet. and FM I are shown in Table 3. During the study period, 4595

Table 3. Cross-tabulation of concomitant reactions to fragrance mix I (FM I) and sorbitan sesquioleate (SSO) for patients tested with both allergens, n = 4595

FM I (n)	SSO 20% (n)				Total
	Negative	?+	IR	+ / ++	
Negative	3342	40	12	0	3394
?+	671	12	3	2	688
IR	83	2	2	0	87
+ / ++ / +++	403	15	2	6	426
Total	4499	69	19	8	4595

IR, irritant reaction.

Thirty-eight patients (including 1 SSO-positive patient) were not tested with FM I, owing to known sensitivity.

Four patients (all SSO-negative) were not tested with FM I, for unknown reasons.

patients were tested concomitantly with both allergens. A total of 426 patients [9.3% (95%CI: 8.5–10.1)] had positive reactions to FM I. Of these FM I-positive patients, 6 [1.4% (95%CI: 0.6–3.0)] had concomitant positive reactions to SSO 20% pet. Three of the 6 patients with concomitant positive reactions to SSO and FM I had no positive reactions to any of the eight single constituents of FM I. The remaining 3 patients had three or more positive reactions to the single constituents of the mix (data not shown). The results of breakdown tests with FM I in SSO-negative patients will be presented in a separate article.

The 8 SSO-positive patients with either concomitant positive or doubtful reactions to FM I were further evaluated with the perfume mix 6% pet. Six (75%) of 8 patients had negative reactions to perfume mix 6% pet., and 2 patients with ++ reactions to FM I had doubtful reactions to the perfume mix not containing SSO (data not shown).

Discussion

The data from this study shows that contact allergy to SSO is rare, with only 0.2% (95%CI: 0.1–0.4%) of consecutively patch tested dermatitis patients in a 5-year period having positive reactions to the emulsifier. To our knowledge, these results represent the largest number of consecutively patch tested patients for whom SSO has been included in standard baseline patch testing. Our results are in line with the earliest reports on the frequency of contact allergy to SSO in consecutively tested patients (2, 7), and we cannot confirm any increasing prevalence as otherwise reported in the United States (6, 9). Among patients with positive reactions to FM I, we found that only 1.4% (95%CI: 0.6–3.0) had concomitant positive reactions to SSO, which is also a lower frequency

than recently reported (10, 11). This discrepancy could be attributable to Geier et al. performing breakdown testing, including testing for specific SSO contact allergy, in <25% of FM I-positive patients. Owing to the low number of patients with concomitant positive reactions to SSO and FM I, we did not further evaluate patterns of reactions to the single constituents of FM I in these patients.

Contact allergy to SSO has previously been shown in case series of patients with chronic leg ulcers (5, 14, 15). Obviously, no conclusions regarding clinical characteristics can be drawn on the basis of only 9 patients with positive patch test reactions to SSO in our study. However, we found that >40% of SSO-positive patients had a history of atopic dermatitis. Although this did not reach statistical significance relative to SSO-negative patients, this tendency could be attributable to increased exposure to SSO as an emulsifier in topical steroid preparations for recurrent eczema (16, 17). Genetically impaired skin barrier function, such as loss-of-function mutations in the filaggrin gene, could also be of relevance for the risk of developing contact allergy to SSO, as recently shown in a case report from our department (18).

In the past, we have used perfume mix 6% pet. to evaluate patients with positive patch test reactions to SSO 20% pet. and positive or doubtful reactions to FM I for an underlying fragrance contact allergy. The perfume mix does not contain two of the eight fragrance ingredients in FM I (amyl cinnamal and oakmoss absolute), so false-negative reactions may occur. However, this has been the only way to perform an additional assessment, as co-sensitization, at least from a theoretical point of view, to both SSO and a fragrance ingredient may be present. Until 2013, perfume mix 6% pet. did not contain SSO; however, beginning in 2014, SSO at a concentration of 1% was added to the mix by the manufacturer (personal correspondence). This did not affect the results presented here (only 1 patient was tested with the mix in 2014, and had a negative reaction), but obviously limits the utility of perfume mix 6% pet. in the future.

In summary, SSO is a rare cause of contact allergy, with a 5-year prevalence of 0.2% in consecutively patch tested dermatitis patients. We conclude that contact allergy to the emulsifier does not seem to play a major role when the overall frequency of contact allergy to FM I is evaluated, with only 1.4% of FM I-positive patients having concomitant positive reactions to SSO in this study. However, in order to correctly diagnose the individual patient, concomitant patch testing with FM I and SSO should be performed, and baseline testing with SSO will remain part of the standard procedure at our department.

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