

# Patch test with sorbitan sesquioleate in Italian consecutive patients: a one-year multicenter SIDAPA study

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Sorbitan sesquioleate (SSO) is an oil-soluble and non-ionic surfactant derived from sorbitol and oleic acid. It is used as a water-dispersible emulsifier in several cosmetics and pharmaceutical preparations, including moisturizers, personal care products, nail treatments, toothpastes and topical medications such as corticosteroids, antibiotics, and antifungals.<sup>1,2</sup> Moreover, SSO has been added in the 1990s at a concentration of 5% to fragrance mix I (FM I) as emulsifier for the eight constituents of FM I.<sup>3,4</sup> However, as SSO is a well-known contact allergen, it could cause false-positive patch test reactions to FM I.<sup>5</sup> Recently, de Groot et al raised the question if the addition of SSO to the European baseline series is necessary, reasonable, or unavoidable.<sup>6</sup> The prevalence of positive patch test reactions to SSO and the concomitant reactions to FMI in the Italian population were thus studied.

## Methods

In eleven clinics homogeneously distributed across Italy, 5336 consecutive patients (1702 men, 3634 women; mean age 46.1 years) were patch tested for contact dermatitis between January and December 2018. Patch testing was performed with the SIDAPA (Società Italiana Dermatologia Allergologica Professionale Ambientale) baseline series<sup>7</sup> containing SSO 20% pet. since 2016 and FM I 8% pet. including 5% SSO. Haye's Test Chambers (Haye's Service, Alphen aan den Rijn, The Netherlands) on Soffix tape (Artsana, Grandate, Italy) were used with allergens from FIRMA Diagent (Florence, Italy). Readings were performed on day (D)2, D4, and D7 according to ESCD recommendations; patients were asked to return in case of late reactions. Irritant and doubtful reactions were not considered.

## Results

Among the 5336 patients tested, 27 (0.5%) showed positive reactions to SSO, 12 males (0.6%) and 15 females (0.4%). In 59.3% (16/27) of these patients we observed strong (++) and extreme (+++) positive reactions, more commonly in females (66.7%) than in males (50.0%) (Table 1). Clinical relevance was observed in 19 of 27 SSO-positive patients (70.4%), and ++ and +++ reactions were

more frequent in subjects with clinical relevance (68.4%) than in patients without clinical relevance (37.5%) (Online supplemental Table 1).

All relevant positive reactions to SSO were observed in patients with non-occupational sources of exposure to this emulsifier. Particularly, relevant positive reactions to SSO were induced by cosmetics in 10 patients (52.7%) (7 by leave-on and 3 by rinse-off cosmetics), by topical corticosteroids in 4 (21.0%), and by other topical medications in 5 patients (26.3%). The latter were had leg ulcers treated for many years with pharmaceutical preparations containing SSO. Involved sites of allergic contact dermatitis induced by SSO included: hands in 8 patients (42.1%), upper extremities in 3 (15.8%), face in 3 (15.8%), feet in 2 (10.5%), lower extremities in 2 (10.5%); a generalized eruption was seen in 2 patients (10.5%). Concomitant patch test results to SSO and FM I are reported in Table 2. Among all patch tested patients, 226 (4.2%) reacted to FM I; of these, 14 (6.2%) showed positive patch test to SSO.

## Discussion

The data from 5336 patients consecutively patch tested in Italy during a 1-year period showed a prevalence of 0.5%, meeting the threshold of 0.5-1.0% for inclusion in the baseline series.<sup>8</sup> The prevalences reported in other European countries range from 0.2% in Denmark (4637 patients patch tested from 2010 to 2014)<sup>1</sup> to 2.7% in The Netherlands (in 395 children and adolescents from 1996 to 2013).<sup>9</sup> Moreover, among the non-European countries, a retrospective study conducted in the USA in 591 patch tested patients in 2008-2010 showed an higher prevalence (2.9%),<sup>5</sup> probably due to a higher exposure to SSO.

We underline that ++ and +++ positive reactions to SSO were observed in the majority of our patients, above all in females, probably due to the source of exposure (often cosmetics). All patients with clinically relevant reactions to SSO had non-occupational sources of sensitization, and in 52.7% of these patients cosmetic products, particularly leave-on cosmetics, were responsible for SSO sensitivity, as previously reported.<sup>1</sup> The remaining patients (47.3%) with relevant positive reactions to SSO were sensitized through corticosteroid ointments and other

topical medications, confirming previously published data.<sup>5</sup> In fact, SSO is contained in many topical corticosteroids,<sup>4</sup> as well as in topical dressings for leg ulcers.<sup>10</sup>

Regarding concomitant reactions to FM I, 6.2% of patients sensitized to FM I were positive to SSO (Table 2). This frequency is similar to that reported by the IVDK study in 1669 patients (5.5%)<sup>7</sup> and higher than that reported in Denmark in 426 patients (1.4%).<sup>1</sup> Without patch testing SSO, these patients could be wrongly diagnosed as allergic to FM I. This supports continued testing of SSO in the baseline series for a longer period to better study its prevalence. Conversely, in patients sensitized to SSO, 51.9% also reacted to FM I. This frequency is 13 times higher than in SSO negative patients (4.0%, 212/5309), higher than recently reported,<sup>6</sup> probably due to the lower prevalence of FM I sensitivity in our Italian patients (4.2%).

## References

1. Bennike NH, Johansen JD. Sorbitan sesquioleate; a rare cause of contact allergy in consecutively patch tested dermatitis patients. *Contact Dermatitis*. 2016;74:242-245.
2. Castanedo-Tardan MP, Jacob SE. Allergic contact dermatitis to sorbitan sesquioleate in children. *Contact Dermatitis*. 2008;58:171-172.
3. Frosch PJ, Pilz B, Burrows D, et al. Testing with fragrance mix. Is the addition of sorbitan sesquioleate to the constituents useful? *Contact Dermatitis*. 1995;32:266-272.
4. Asarch A, Scheinman PL. Sorbitan sesquioleate, a common emulsifier in topical corticosteroids, is an important contact allergen. *Dermatitis*. 2008;19:323-327.
5. Cressey BD, Kumar N, Scheinman PL. Contact allergy to sorbitans: a follow-up study. *Dermatitis*. 2012;23:158-161.
6. de Groot A, Gilissen L, Geier J, Orton D, Goossens A. Adding sorbitan sesquioleate to the European baseline series: Necessary, reasonable, or unavoidable? *Contact Dermatitis*. 2019; doi: 10.1111/cod.13332. [Epub ahead of print].
7. Stingeni L, Bianchi L, Hansel K, et al. Italian Guidelines in Patch Testing - adapted from the European Society of Contact Dermatitis (ESCD). *G Ital Dermatol Venereol*. 2019;154:227-253.

8. Bruze M, Condé-Salazar L, Goossens A, et al. Thoughts on sensitizers in a standard patch test series. The European Society of Contact Dermatitis. *Contact Dermatitis*. 1999;41:241-250.
9. Lubbes S, Rustemeyer T, Sillevs Smitt JH, et al. Contact sensitization in Dutch children and adolescents with and without atopic dermatitis - a retrospective analysis. *Contact Dermatitis*. 2017;76:151-159.
10. Pasche-Koo F, Piletta PA, Hunziker N, Hauser C. High sensitization rate to emulsifiers in patients with chronic leg ulcers. *Contact Dermatitis*. 1994;31:226-228.

**Table 1** Concomitant and non-concomitant reactivity between sorbitan sesquioleate 20% pet. (SSO) and fragrance mix I (FM I) in 5336 consecutively patch tested patients

	FMI positive patients (+/++/+++) (%)	FMI negative patients (%)	Total (%)
SSO positive patients (+/++/+++)	14 (6.2)	13 (0.3)	27 (0.5)
SSO negative patients	212 (93.8)	5097 (99.7)	5309 (95.5)
Total	226 (100)	5110 (100)	5336 (100)