

Routine patch testing with the sesquiterpene lactone mix in Europe: a 2-year experience

A multicentre study of the EECDRG

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To test the screening value of the sesquiterpene lactone (SL) mix in Europe today and describe epidemiological and clinical features of Compositae-sensitive patients, the SL mix 0.1% pet. was included in the standard patch test series in 11 European clinics. 10,695 patients were tested, and 106 (1%) had positive reactions, 74% of which were of current or old relevance. The prevalence of positive reactions varied between 0.1 and 2.7% in different centres. The median age of the 66 females was 51.5 years, and 55.2 in the 40 males. The 20 occupationally sensitized had a higher % of males and a median age of 43 years, whereas 7 UV-sensitive patients had a median age of 72 years. Garden plants were the major suspected sensitizers and the clinical patterns were partly, in accordance with plant dermatoses in general, involving hands, forearms and face, and partly widespread eczema in a large proportion of the patients. More than 1/3 were positive to perfume and/or colophony, possibly reflecting cross-reactivity. With only 1 case of active sensitization and no irritant reactions, the SL mix is a safe allergen and the overall prevalence of positive reactions supports its continued use in the standard patch test series.

Key words: allergic contact dermatitis; plants; Compositae; sesquiterpene lactone mix; occupational; colophony; fragrance © Munksgaard, 1999.

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The first large-scale patch test study with the sesquiterpene lactone (SL) mix emphasized its importance as a screening agent for allergy to Compositae and other SL-containing plants (1). However, based on a few case reports, the inadequacy of the SL mix in detecting all cases of Compositae sensitization was acknowledged from the beginning (1), and it has been further supported by subsequent studies (2–4). The aims of this investigation were to re-evaluate the SL mix in a larger European population today and to de-

scribe epidemiological and clinical features of the SL-sensitive patients.

Materials and Methods

The SL mix 0.1% pet. (Hermal, Reinbek, Germany), consisting of equimolar amounts of alantolactone, costunolide and dehydrocostus lactone, was included in the standard patch test series in 11 European clinics. The mixture was applied to the back for 2 days, using Finn or van der Bend Chambers[®] (1 clinic) on Scanpor[®] tape. Readings were made on day (D) 2–4 and possibly D 4–7 and

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Table 1. Results of patch tests with 0.1% SL mix in consecutively tested patients in 11 European centres in 1994 and 1995

Centre	Patients positive/tested		Total (% positive)		Relevance			
	1994	1995			c	o	d	i
Oulu, Finland	0/488	1/302	1/790	(0.1%)	1	–	–	–
Stockholm, Sweden	2/273	0/233	2/506	(0.4%)	2	–	–	–
Gentofte, Denmark	8/840	8/713	16/1553	(1.0%)	11	2	2	1
Odense, Denmark	18/527	9/467	27/994	(2.7%)	21	1	5	–
Amersham, UK	8/593	2/614	10/1207	(0.8%)	9	–	1	–
Dortmund, Germany	4/537	4/457	8/994	(0.8%)	1	–	4	3
Amsterdam, The Netherlands ^{a)}	8/519	11/589	19/1108	(1.7%)	12	1	6	–
Leuven, Belgium	6/619	2/690	8/1309	(0.6%)	4	1	3	–
Bologna, Italy ^{b)}	5/631	2/497	7/1128	(0.6%)	5	–	2	–
Bordeaux, France	5/435	2/435	7/870	(0.8%)	5	1	–	1
Almada, Portugal	1/110	0/126	1/236	(0.4%)	1	–	–	–
total	65/5572	41/5123	106/10,695	(1%)	72	6	23	5

c=current; o=old; d=don't know; i=irrelevant

^{a)} 1994 data from April to December only.

^{b)} 1994 data from March to December only.

D 10 (1 clinic) according to international guidelines (5). For each patient with a positive SL mix reaction, a documentation sheet, regarding clinical, epidemiological and patch test results on SL and fragrance mix, balsam of Peru and colophony, was filled in retrospectively.

Photopatch tests were performed with allergens in duplicate, irradiation of 1 set with most often 5 or 10 J/cm² UV-A (lower in patients with a reduced minimal erythema dose) on D 1–2 and second reading on D 3–4 and possibly D 7 (1 clinic), in accordance with the above-mentioned guidelines (5).

Associations between selected variables were tested with the χ^2 statistic with Yates' correction and the significance level was taken as 0.05.

Results

The major results are summarized in Table 1. In the 2-year period a total of 10,695 patients were tested with the SL mix, and 106 (1%) were positive. They comprised 66 females and 40 males, with a median age of 51.5 and 55.2 years, respectively (overall range 19–86). Most of the reactions were strongly positive and of current or old relevance (74%) (Table 2), 74% in females and 72% in males. There were no irritant reactions, but in 1 patient active sensitization was suspected because of a late (D 4–8) appearing ++ reaction. 1 clinic made readings on D 10: all patients had positive reactions to the SL mix on D 10, in 50% of the same strength as on D 4, in the rest slightly diminished compared to D 4.

60 persons were hobby gardeners, 56% of female and 57.5% of male. 58% of the 60 persons lived in the country or both country and city. Among hobby gardeners, 92% had current or old relevance

and 8% unknown or no relevance of their Compositae allergy ($p < 0.001$). Likewise, there was a correlation, though weaker, between residence and relevance of the reactions: 61% of those with current or old relevance lived in the country or both city and country, compared to only 33% of those with unknown or no relevance ($p < 0.05$). Correspondingly, suspected sources of sensitization were garden plants (in 61%), followed by weeds (33%), pot plants (21%), vegetables (14%) and pharmaceuticals (11%) in different combinations. Sensitization from pharmaceuticals alone, such as the bay leaf-containing Végébom[®] ointment (Laboratoire Jessel-Végébom SA, Paris, France) and chamomile cream, was suspected in 5 patients and was of current or old relevance. In 18 persons the source of sensitization was unknown. The most common pursuits of the nonoccupationally sensitized were pensioner (at least 38% retired from some kind of manual labour), housewife, office/administrative worker and health/child care worker.

Occupational sensitization to Compositae was seen in 20 (19%) patients, with a sex distribution of 9 females and 11 males and a median age of 43 years, 33 in females and 50 in males (overall range 21–72 years). The majority of patients came from 3 centres and their occupations and suspected

Table 2. Distribution of strength and relevance of positive SL mix reactions

Strength	Relevance			
	current	old	don't know	irrelevant
SL mix +	11	0	7	3
SL mix ++	37	6	14	2
SL mix +++	24	0	2	0

Table 3. Sex, age, occupation and suspected sensitizing Compositae plants in 20 occupationally sensitized patients

Centre	Patients occup. sens/positive	Sex/age (years)	Occupation	Compositae suspected
Stockholm, Sweden	1/2	F/59	gardening, service of gardening machines	garden plants, weeds
Gentofte, Denmark	1/16	F/72	former laboratory technician	garden plants
Odense, Denmark	3/27	F/29	gardener	pot plants
		F/21	gardener apprentice	pot plants
		F/24	gardener apprentice	pot plants
Amsterdam, the Netherlands	8/19	F/23	former work with <i>Cichorium endivia</i>	vegetable
		M/63	chrysanthemum grower	garden plants, pot plants
		F/34	flower shop	pot plants
		M/38	flower shop	pot plants
		M/55	farmer	weeds
		M/54	flower export	pot plants
		M/52	chrysanthemum grower	garden plants
		F/43	flower auction	pot plants, garden plants, weeds
Leuven, Belgium	1/8	M/50	veterinarian	garden plants, weeds
Bologna, Italy	2/7	M/30	joiner	unknown
		F/33	farmer	pot plants, garden plants, pharmaceut.
Bordeaux, France	4/7	M/33	cook	vegetables, pharmaceut.
		M/43	florist	pot plants, garden plants
		M/47	farmer	garden plants, weeds, vegetables
		M/55	forester	weeds

sources of sensitization are shown in Table 3. The number of occupationally sensitized is probably a minimum figure: there were 2 carpenters and 2 joiners among the patients and only 1 was considered to have a relevant Compositae allergy (Table 3), and likewise the origin of sensitization was unknown in 1 of 2 veterinarians. A postman with a strongly positive reaction to the SL mix was

suspected of occupational sensitization, but the relevance was registered as unknown.

72 of the patients had a chronic and 31 an acute eczema. In 3 patients, including 2 with leg ulcers, registration of eczema was not filled in, in the 2 last-mentioned because they were considered to have neither acute nor chronic eczema. Involvement of hands/fingers and face/other areas as well as widespread eczema was seen in the majority of the 72 patients with current relevance of the SL mix reactions (Table 4). Only 4 of the 26 atopic persons appear among the 17 with widespread eczema (Table 4). The same clinical patterns were seen in the occupationally sensitized patients (Table 4). 3 of the latter were atopics and 2 of them are included in the group with widespread eczema (Table 4). 9 patients had leg ulcers and only 2 of these had current relevance of the SL mix reactions, 1 of them due to use of Végébon[®].

48 persons (45%) had summer exacerbation of their eczema, and there was a statistically significant difference between the high prevalence of summer aggravation in those with current or old relevance of the allergy, compared to the low prevalence in those with unknown or no relevance ($p < 0.001$). On the other hand, there was no difference between the frequency of summer exacerbation between the occupationally and the non-occupationally sensitized.

13 patients, 5 female and 8 male, were photopatch and/or phototested. 2 persons, 1 female and

Table 4. Clinical patterns in patients with positive reactions to the SL mix

	Current relevance (including occupationally sensitized) (n=72)	Occupational Compositae dermatitis (n=20)
face/neck:	2	0
hands/fingers:	6	1
hands/fingers/forearm/arm:	3	1
face/neck and hands/fingers and/or forearm/arm:	22 ^{a)}	9 ^{e)}
hands/fingers and other areas:	17 ^{b)}	3
widespread eczema:	17 ^{c)}	4 ^{d)}
other eczema:	5 ^{d)}	2

^{a)} Including 4 atopics and 3 UV-sensitive patients.

^{b)} Including 5 atopics and 1 patient with chronic actinic dermatitis (CAD).

^{c)} Including 4 atopics, 2 UV-sensitive and 1 CAD patient

^{d)} Including 1 atopic.

^{e)} Including 1 atopic.

^{f)} Including 2 atopics.

Table 5. Distribution and relevance of positive reactions to fragrance mix, balsam of Peru and colophony in 106 Compositae-sensitive patients

	Reactions					Relevance			
	positive	doubtful positive	negative	IR	NT	current	old	don't know	irrelevant
fragrance mix	21	8	73	3	1	13	2	5	1
balsam of Peru	12	6	87	1	0	5	3	4	0
colophony	20	3	81	1	1	10	3	6	1

1 male, had a photocontact allergy to oxybenzone and *p*-aminobenzoic acid, respectively, and 7 persons, 3 females and 4 males, were UV-sensitive. The median age of the light-sensitive was 72 years, 72 in females and 63.5 in males. The results of patch testing with fragrance mix, balsam of Peru and colophony are shown in Table 5. 39 persons were positive to at least 1 of the allergens, and 6 persons had relevant reactions to 1 or more of these and unknown relevance of the SL mix reaction. Conversely, 10 persons with SL mix reactions of current or old relevance had perfume and/or colophony reactions of unknown relevance. 3 persons, included in the 16 last-mentioned, had both reactions of current/old and unknown relevance to the 3 allergens.

Discussion

An overall prevalence of 1% is high enough to emphasize the value of the SL mix as a screening mixture for Compositae allergy and justify its continued use. The considerable difference in the prevalence from centre to centre may reflect partly geographically determined variation in the flora, partly the frequency of gardening as hobby and floristry as a trade. The highest figures were seen in Amsterdam and Odense, both centres of the pot plant and/or cut flower industry. However, the prevalence of the occupationally sensitized in Odense was relatively low.

The sex ratio corresponds to that seen in more recent European studies (6, 7), with either an equal sex distribution or a preponderance of women. The age distribution is typical of patients with Compositae dermatitis and likewise the higher median age in the few patients with UV sensitivity is in accordance with the findings of Ross et al. (6) and du P. Menagé et al. (8) who reported mean ages of 64 to 69 years. A lower mean age in the occupationally sensitized is also characteristic, as shown by Hausen (9).

The strong association between being a hobby gardener and having a relevant Compositae allergy reflects the importance of direct plant contact, whereas the weaker association between part- or full-time residence in the country and a relevant

Compositae reaction may reflect other modes of sensitization, such as indirect or airborne, occurring more commonly in rural districts. However, it should be taken into account that 58% of the hobby gardeners lived in the country or both city and country.

Garden plants and weeds were, predictably, the most frequent sources of sensitization, except in the occupationally sensitized where pot plants were sensitizers in 1/2 of the patients. This is in accordance with the vast number of Compositae species, cultivated in herbaceous borders and growing wild, compared to the relatively few species, such as e.g. florists' chrysanthemum, *Gerbera*, marguerite daisy, cineraria and *Aster*, cultivated as potted plants. Sensitization to Compositae-containing pharmaceuticals was relatively rarely suspected and is probably not a major source of sensitization (10).

The prevalence of the occupationally sensitized is lower than the 28% found in a German study in an area with a large floristry industry, where patch testing was based on plant extracts (7), but higher than the 12% seen in an English study of routine SL mix testing (6). This may reflect a true difference in prevalence, but another possibility is that the plant extracts actually detect more of the occupationally sensitized than the SL mix. This is supported by a study on occupational dermatitis in Danish gardeners, where the Compositae mix detected about 2× as many as the SL mix on routine testing with both (11). This could also explain the low prevalence of the occupationally sensitized in Odense, despite a high general sensitization level. The sex distribution with a slight preponderance of males is quite different from that of the nonoccupationally sensitized, and probably reflects frequency of exposure. The clinical features were not different from those of plant dermatoses in general, with involvement of the hands, forearms and face in a large proportion of the patients. Contrary to previous investigations (1, 6, 12), localized eczemas were uncommon in both the occupationally and nonoccupationally sensitized: 2 had eczema of the face/neck and 7 of the hands/fingers as the only manifestation of Compositae dermatitis. Widespread eczema and eczema of the exposed skin of

the arms and face/neck were far more common and in accordance with the clinical pattern of classic Compositae dermatitis simulating (or initiating) photodermatitis.

Photopatch and photo testing were performed in only a few patients, but more than 1/2 of them were UV-sensitive, emphasizing the well-known association between Compositae dermatitis and light sensitivity/chronic actinic dermatitis (6, 8, 13).

More than 1/3 of the patients were positive to perfume and/or colophony. Even if separate or concomitant sensitization is likely, cross-reactivity between sesquiterpene lactones and terpenes of colophony (14), and potentially also fragrance/balsam of Peru (15, 16), is an intriguing possibility in the light of the divergence of relevance.

Most of the reactions to the SL mix were strongly positive. Weak (+) reactions were more often considered of unknown or no relevance, perhaps reflecting angry back reactions in some of the patients. No irritant reactions were recorded in this study, in contrast to the first where 0.1% of the reactions were considered irritant (1). Despite the strong reactions, the SL mix is still a safe allergen, with only 1 possible sensitization and no irritant reactions in 10,695 tests, and this combined with the overall prevalence of positive reactions supports its continued use in the standard patch test series in most places.

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