

Sesquiterpene lactone mix patch testing supplemented with dandelion extract in patients with allergic contact dermatitis, atopic dermatitis and non-allergic chronic inflammatory skin diseases

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We investigated the value of patch testing with dandelion (Compositae) extract in addition to sesquiterpene lactone (SL) mix in selected patients. After we detected a case of contact erythema multiforme after patch testing with dandelion and common chickweed (Caryophyllaceae), additional testing with common chickweed extract was performed. A total of 235 adults with a mean age of 52.3 years were tested. There were 66 men and 169 women: 53 consecutive patients with allergic contact dermatitis (ACD); 43 with atopic dermatitis (AD); 90 non-atopics suffering from non-allergic chronic inflammatory skin diseases; 49 healthy volunteers. All were tested with SL mix 0.1% petrolatum (pet.) and diethyl ether extracts from *Taraxacum officinale* (dandelion) 0.1 and 3.0% pet. and from *Stellaria media* (common chickweed) 0.1 and 3% pet. A total of 14 individuals (5.9%) showed allergic reaction (AR) to at least 1 of the plant allergens, 4 (28.6%) to common chickweed extract, and 11 (78.6%) to Compositae allergens. These 11 persons made the overall prevalence of 4.7%: 8 (3.4%) were SL-positive and 3 (1.3%) reacted to dandelion extract. 5 persons (45.5%) had AD, 2 had ACD, 2 had psoriasis and 2 were healthy controls. The Compositae allergy was relevant in 8 cases (72.7%). The highest frequency of SL mix sensitivity (9.3%) was among those with AD. Half the SL mix-sensitive individuals had AD. ARs to dandelion extract were obtained only among patients with eczema. A total of 9 irritant reactions (IRs) in 9 individuals (3.8%) were recorded, 8 to SL mix and 1 to common chickweed extract 3.0% pet. No IR was recorded to dandelion extract ($P = 0.007$). Among those with relevant Compositae allergy, 50.0% had AR to fragrance mix and balsam of Peru (Myroxylon pereirae resin) and colophonium. SLs were detected in dandelion but not in common chickweed. Our study confirmed the importance of 1 positive reaction for emerging, not fully established, Compositae allergy. In conclusion, the overall prevalence of 4.7% in our study represents a basal SL mix detection rate of 3.4% reinforced and safely supplemented by testing with the dandelion extract.

Key words: allergic contact dermatitis; atopic dermatitis; colophonium; Compositae; fragrance; irritant reaction; patch testing; plants; psoriasis; *Taraxacum officinale*. © Blackwell Munksgaard, 2004.

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The inadequacy of sesquiterpene lactone (SL) mix as a screening agent for Compositae dermatitis has partly been overcome by additional testing with Compositae extracts (1, 2). Additional testing with selected weeds has recently been proposed (2), particularly with dandelion, because this has become an important allergen in its own right in SL mix-negative patients (3–6). Testing with dandelion may detect most SL mix-negative, Compositae-sensitive persons (4, 5), though this

may vary between different geographical regions (2, 7). The significance of the weed as a sensitizer has not been clarified, though in the majority, the positive patch tests to dandelion extract were thought to be clinically relevant (2–5, 7–10). Dandelion (*Taraxacum officinale*, Compositae) is almost the commonest Compositae in our environment. The purpose of our study was to establish the value of testing with dandelion extract in addition to SL mix to detect Compositae contact

allergy in selected patients. Because we had previously detected a case of erythema multiforme that recurred after patch testing with dandelion and with common chickweed (*Stellaria media*, Caryophyllaceae) probably acting simultaneously (11), additional testing with extract of common chickweed was performed. Common chickweed is among the commonest weeds in our environment, but has not previously been recognized as cause of either sensitivity or irritancy. On the other side, despite its clinical importance, dandelion has been reported (by other authors) to be a weak sensitizer. Because weed extracts are capable of causing irritant reactions (IRs) on patch testing, it was interesting to assess the question of sensitivity as well as irritancy of extracts of these 2 common weeds, only 1 being Compositae, but both being compared in a selected group of patients.

Patients and Methods

Between January and July 2003, a total of 235 adult patients with a mean age of 52.3 (range 17–78) years were tested. There were 66 men and 169 women, classified into 4 groups. Group 1 included 53 consecutive patients with a patch test-verified allergic contact dermatitis (ACD). There were 4 men and 49 women. Their mean age was 50.3 (range 26–76) years.

Group 2 included 43 consecutive patients with atopic dermatitis (AD). There were 11 men and 32 women. Their mean age was 33.9 (range 17–72) years. All had skin and mucosal symptoms with respect to Hanifin and Rajka's diagnostic criteria, in addition to the positive skin tests and the presence of an elevated specific immunoglobulin (Ig)E serum level to common inhalant allergen(s) (12, 13).

Group 3 included 90 consecutive non-atopic patients suffering from non-allergic chronic inflammatory skin diseases, whom were diagnosed and treated at the Clinic for Dermatovenereologic diseases in Novi Sad. There were 50 psoriatics with all types of psoriasis except arthropathic and erythrodermal, 24 patients with acne vulgaris which affected about 20–25% of the body surface and 16 with leg ulcers. There were 44 men and 46 women with a mean age of 43.6 (range 17–78) years. Group 4 included 49 non-atopic volunteers, with no skin diseases. There were 7 men and 42 women, with a mean age of 35.1 (range 17–56) years.

This cohort of patients remained after exclusions were made because of lesions on the back, the use of cytotoxic or immunosuppressive agent such as methotrexate, cyclosporin, retinoids and UV-therapy for at least 6 months before, the

systemic use of corticosteroids, or the application of potent topical corticosteroids for at least 1 month before. Pregnant and lactating women were excluded.

Patch testing

Patch testing was performed after written consent from each patient was obtained. Patients were not patch tested if they had had sun exposure in the last month. The test area was weaned from other topical treatments for at least 3 days before testing, only emollients being allowed there.

All patients with contact dermatitis, patients with AD and those with non-allergic chronic inflammatory skin diseases were tested with the European standard series. Other specific series and allergens/plants were included when indicated by the patients' histories. Patch test allergens were mainly purchased from Hermal-Trolab[®] (Reinbek, Germany). All individuals were additionally tested with SL mix 0.1% petrolatum (pet.) (alantolactone 0.3%, dehydrocostus lactone 0.3% and costunolide 0.3%) supplied by Hermal-Trolab[®]; diethyl ether extracts from *T. officinale* 0.1 and 3.0% pet.; and diethyl ether extract from *S. media* 0.1 and 3% pet. All individuals with relevant allergic reaction (AR) to SL mix were additionally tested with Compositae mix 6% pet. (Trolab[®]) and its individual constituents, and extracts of arnica (*Arnica montana*) 0.5% pet., chamomile (*Chamomilla recutita*) 2.5% pet., tansy (*Tanacetum vulgare*) 1% pet., feverfew (*T. parthenium*) 1% pet. and yarrow (*Achillea millefolium*) 1% pet., all supplied from Trolab[®].

Patch tests were applied to the back for 2 days, using Curatest[®] (Lohman-Rauschen, Neuwied, Germany). Readings were made on day (D) 2 and D3, and whenever possible on D5–D8, according to the – to +++ scale recommended by the International Contact Dermatitis Research Group. Only reactions $\geq +$ were considered positive – AR. Doubtful reactions (DRs) ?+ were noted. Reactions recorded on D2 only were considered as IR. With regard to the scoring system suggested by Lachapelle (14, 15), the relevance of positive reactions was categorized as likely (R3), possible (R2) or doubtful (R1). Relevance of the Compositae mix positive reaction was based on 4 criteria: (i) the reaction being vesicular (++/+++); (ii) there being a good exposure history; (iii) improvement occurred after exposure reduction; and (iv) a $\geq +$ reaction to at least 1 ingredient of the Compositae mix. If 2 of 4 criteria were fulfilled, the reaction was considered to be truly relevant (16).

The protocol was approved by the Ministry for Science Technology and Development of the Republic of Serbia.

Plant material

T. officinale (Compositae) growing wild in Vojvodina (Serbia) was identified according to Gajić (17). Leaves, stems and flowers were harvested in May 2003, air dried at ambient temperature and stored until use. *S. media* (L) Vill. (Caryophyllaceae) growing wild in Vojvodina (Serbia) was identified as previously described (11). Leaves, stems and flowers were harvested in April 2003, air dried at ambient temperature and stored until use.

Plant extraction

200 g of powdered plant material was extracted with petroleum ether in Soxlet apparatus for 6 h (till the extract became colourless). The extract obtained was filtered, and the solvent was removed under reduced pressure.

Plant extract allergens for patch testing

Diethyl ether extracts from *T. officinale* and *S. media* were dried, evaporated and diluted 0.1 and 3.0% in pet. Pet. (100 g) was melted at 65°C, and volumes equivalent to 0.1 and 3 g of plant extracts were added drop-wise with vigorous stirring to yield a homogeneous 0.1 and 3.0% (w/v) suspension. The molten petrolatum suspension was cooled rapidly to maintain homogeneity (3).

Thin layer chromatography of crude T. officinale and S. media extracts

Thin layer chromatography (TLC) analysis of crude plant extract: 20 µl of 1% diethyl ether solution of each extract was developed on the 'Merck' silica gel GF₂₅₄ plates in the solvent system: chloroform : methanol (95:5), along with the commercial SL mix, as referent substances. After developing, plates were sprayed with vanillin-sulphuric acid reagent and heated at 100–105°C for 5–10 min, while under examination (18).

Intradermal tests

Intradermal testing was performed with common inhalant allergens (Torlak[®], Beograd, Serbia and Montenegro): *Dermatophagoides pteronyssinus*, house dust, mixed weed pollens, grass pollens, tree pollens, animal epithelia and feather. The mean wheal diameter was calculated for each allergen. The test was regarded as positive if the

mean diameter was greater than the negative control (normal saline) by more than: 5 mm (+); 5–10 mm (++); 10–15 mm (+++); or with pseudopodia (++++).

Determination of specific IgE level in serum

Phadiatop[®] EIA (Pharmacia AB, Uppsala, Sweden) was used as a method that provides differential determination of IgE antibodies specific to a mixture of inhalant allergens (*D. pteronyssinus*, *D. farinaceae*, cat, dog, horse, birch, timothy grass, mugwort, olive, *Cladosporium herbarum* and *Parietaria judaica*) in human serum. The specific IgE to common inhalant allergens were determined by the Phadezym RAST[®] or CAP according to the manufacturer's instruction (Pharmacia AB). The results were expressed in PRU/ml or in classes 1–4 and defined as positive when exceeding 0.35 PRU/ml (KUL/l) ($\geq$ class 1).

Statistical analysis

Statistical analysis was performed by using the statistical Software program M.1 for Windows. The chi-square test with Yates correction and the Fisher's exact test were used for the comparisons. Two-tailed *P* values less than 0.05 were regarded as statistically significant.

Results

A total of 14 individuals (7 with AD) of the 235 studied (5.9%) showed AR to at least 1 of the plant-related allergens, either to SL mix or to plant extracts. There were 3 men and 11 women, with a mean age of 45 (range 23–70) years. There were 4 individuals (28.6%) sensitive to common chickweed extract and 11 individuals (78.6%) sensitive to Compositae allergens. 8 persons (3.4%) were SL-positive and 3 (1.3%) reacted to dandelion extract (Table 1). In the group of 11 persons sensitive to Compositae allergens, there were 2 men and 9 women with a mean age of 48 (range 24–70) years. There were 5 patients (45.5%) with AD (Table 2), 2 patients (18.2%) with ACD (Table 3), 2 patients (18.2%) with psoriasis (Table 4) and 2 were healthy controls (18.2%) (Table 5). None of them showed AR to both the SL mix and the dandelion extract.

The SL mix-positive persons comprised 7 females (87.5%) and 1 male with a mean age of 43.8 (range 24–59) years. There were 4 patients with AD, 2 patients with psoriasis and 2 were healthy control persons. The highest frequency of SL mix sensitivity (9.3%) was found among those with AD (Table 1). Patients diagnosed with AD were sensitive to common inhalant

Table 1. Patch test results in 235 individuals tested with SL mix and dandelion extract

Allergen	Allergic contact dermatitis [n = 53 (22.6%)]		Atopic dermatitis [n = 43 (18.3%)]		Non-allergic skin diseases [n = 90 (38.3%)]		Healthy controls [n = 49 (20.9%)]		Total [n = 235 (100%)]	
	S	%	S	%	S	%	S	%	S	%
SL mix	0	0.00	4	9.3	2	2.2	2	4.1	8	3.4
Dandelion extract	2	3.8	1	2.3	0	0.0	0	0.0	3	1.3
Total	2	3.8	5	11.6	2	2.2	2	4.1	11	4.7

n = all tested; S = sensitive; SL mix = sesquiterpene lactone mix.

allergen(s). The most common allergens were *D. pteronyssinus* (86.7%), house dust (68.3%), mixed grass pollens (66.6%) and mixed weed pollens (43.3%). Allergic asthma and allergic rhinitis had occurred in 70% of these patients. The point prevalence of rhinitis was 65.0%. The point prevalence of asthma was 21.66%.

ARs to dandelion extract were obtained only among patients with eczema (Tables 2 and 6). A brief case history of the 3 subjects sensitive to dandelion extract is reviewed in Table 7.

The strength of the majority of reactions to the SL mix or dandelion extract was weak positive (+). The Compositae allergy was clinically relevant, current (CR) or past (PR), in 8 cases (72.7%). 7 of these 8 reactions, all 3 to dandelion and 4 to SL mix were considered to be CR3 (Tables 7 and 8). In 1 patient (AD2, Table 8), the relevance code for positive reaction to SL mix was CR2 (16). In order to improve the accuracy of relevance scores of positive patch test reactions to SL mix, we performed additional patch testing with Compositae allergens other than SL mix (Table 8). All 5 SL mix-positive patients with reactions coded CR3 or CR2 had at least 1 relevant positive patch test reaction. There were 4 patients with positive reactions to Compositae mix and 1 to *Chrysanthemum hortorum* in this group that turned out to be relevant.

A total of 15 DRs in 9 individuals (3.8%) were recorded. There were 2 patients with ACD, 2 patients with AD and 5 persons were healthy volunteers. 2 DRs were recorded to SL mix, 7 to dandelion extract (2 to 0.1% pet. and 5 to 3% pet.) and 6 to common chickweed extract (4 to 0.1% pet. and 2 to 3% pet.). Regarding IR, a total of 9 IRs (3.8%) were recorded, 8 to SL mix and 1 to common chickweed extract 3.0% pet. IRs to SL mix were recorded in 2 patients with AD (4.7%) and 6 healthy volunteers (12.3%). No IR was recorded to dandelion extract, the difference being significant ($\chi^2 = 6.23$ df = 1; $P < 0.05$) ($P = 0.007$, Fisher's exact test).

Regarding DRs and IRs among those sensitive to SL mix or to dandelion extract, only 1 with AD and sensitivity to dandelion extract showed IR to

SL mix (Table 2) and 1 SL mix-positive healthy control person DR to common chickweed extract 0.1 and 3.0% in pet. (Table 5).

Regarding other contact allergies, 3 SL mix-sensitive patients were sensitive to fragrance mix. Among those with relevant Compositae allergy, 4 were positive to fragrance mix and balsam of Peru (*Myroxylon pereirae* resin) and colophonium and 4 reacted to nickel.

TLC of crude *T. officinale* and *S. media* extracts

TLC analysis was carried out in order to detect SLs in crude petroleum ether extracts of examined plants. In *S. media* L, no SLs were detected. On the contrary, in the petroleum ether extract of *T. officinale*, a few dark blue spots were noticed on the chromatogram in the same region as in the standard SL mix.

Discussion

Routine screening with the SL mix in various geographical regions has shown prevalences between 0.7 and 1.8% (19–23). The high detection rate shown in our study is greater than that of the 2.8% reported in a recent Danish study (1). Our report is the first assessing the SL mix sensitivity rate in Serbia and Montenegro, and the first one that correlates this sensitivity with clinical manifestations of different skin diseases. Because the frequency of SL mix-positive reactions in our study was higher than 1%, it means that such a mix should be considered for the standard series of patch tests in our area (24).

Half the patients with SL mix sensitivity we have found among those with AD. The prevalence of atopy reported among Compositae-sensitive patients varies between 17 (25) and 28% (1). The high prevalence in our study is in accordance with recent reports (1, 26). Contrary to these, in Menz's and Winkelmann's study, the prevalence of atopy was low (17%) (25). Though controversy exists, in a large Danish study, a history of childhood eczema and hay fever were significant risk factors for occupational Compositae-related symptoms (27).

Table 2. Patch test results in patients with atopic dermatitis (AD)

Patch testing																				
Group		Patient no	Age (year)	Sex	Occupation	Other atopic diseases specific IgE	Positive intradermal test	Standard specific series	TE											
									SL mix			TE1			TE3			SME		
									D2	D3	D2	D3	D2	D3	D2	D3	D2	D3	D2	D3
AD	1	24	Female	Student	Phadiatop [®] ++		Dpt weed pollens grass pollens house dust	Nickel ++	-	+	-	-	-	-	-	-	-	-		
AD	2	34	Female	Housewife	AR Phadiatop [®] ++ Dpt RAST 4 Weed pollens RAST 4		grass pollens weed pollens Dpt house dust	Nickel + <i>O</i> -nitro p-phenylene diamine + ammonium persulphate + Amerchol [®] +	-	++	-	-	-	-	-	-	-	-		
AD	3	34	Male	Fireman	AR Dpt RAST 2		Dpt grass pollens tree pollens weed pollens	Butyl hydroxy toluene +	-	+	-	-	-	-	-	-	-	-		
AD	4	59	Female	Domestic	Phadiatop [®] ++		Weed pollens	Fragrance mix ++ benzocaine ++ +	+	+	-	-	-	-	-	-	-	-		
AD	5	54	Female	Hairstresser	AR Phadiatop [®] ++ + Dpt RAST 3		Dpt grass pollens weed pollens	Nickel + neomycin + cinnamic acid + benzoyl peroxide +	+	-	+	+	+	-	-	-	-	-		
AD	6	24	Male	Worker	AR AC Dpt RAST 2		Dpt	Chromate + sorbitan	-	-	-	-	-	-	-	++	-	++		
AD	7	55	Female	Clerk	AR AC Phadiatop [®] ++ +		Weed pollens tree pollens	sesquioleate + Fragrance mix +	-	-	-	-	-	-	-	-	+	+		
AD	8	34	Male	Clerk	AR AS Phadiatop [®] ++ + Dpt RAST 4		Dpt	Paraben mix + epoxy resin + thiuram mix + trolamine +	-	-	-	? +	-	? +	-	? +	+	-		
AD	9	70	Female	Housewife	AR Phadiatop [®] +		House dust feather weed pollens grass pollens tree pollens	chromate + nickel + cetearyl alcohol +	-	? +	-	-	-	-	-	-	-	-		
AD	10	47	Female	Clerk	AR AC AS Phadiatop [®] ++ + + Dpt RAST 3, grass pollens RAST 3 weed pollens RAST 3		Dpt grass pollens weed pollens	Ni ++ + chromate ++ + Amerchol [®] ++ + tween 40 ++ + tween 80 ++ + propolis ++ + sorbic acid ++ +	+	-	-	-	-	-	-	-	-	-		

AC = allergic conjunctivitis; AR = allergic rhinitis; AS = allergic asthma; D = day; Dpt = *Dermatophagoides pteronyssinus*; Phadiatop[®] = Phadiatop EIA-enzyme immunoassay; RAST 1-4 = RAST class 1-4; SL mix = sesquiterpene lactone mix 0.1% in petrolatum; SME = *Stellaria media* extract in petrolatum; SME1 = *S. media* extract 0.1% in petrolatum; SME3 = *S. media* extract 3% in petrolatum; TE = *Taraxacum officinale* extract in petrolatum; TE1 = *T. officinale* extract 0.1% in petrolatum. TE3 = *T. officinale* extract 3% in petrolatum; + = positive test; ++/+++ = strongly positive test; - = negative test; ?+ = questionable response, only on D3 or both on D2 and D3 refers a doubtful reaction.

Table 3. Patch test results in patients with allergic contact dermatitis (CD)

Group	Patient no	Age (year)	Sex	Occupation	Brief history	Standard specific series	Patch testing												
							SL mix	TE						SME					
								TE1	TE3										
										D2	D3	D2	D3	D2	D3	D2	D3		
CD	1	46	Female	Trader	15-year history of facial dermatitis with eyelid involvement	Colophonium +, bronopol + Enzymes in detergent ++	-	-	-	+	+	-	-	-	-	-	-		
CD	2	52	Female	Clerk	10-year history of periorcular dermatitis with eyelid redness	Nickel ++	-	-	-	-	+	+	-	-	-	-	-		
CD	3	45	Female	Professor	Episodic facial, hand and forearm swelling and redness. Urticarial eruption on the forearms after contact with kiwi fruit	Nickel +, formaldehyde + <i>p</i> -aminophenol +, kiwi pulp (after 20min) ++	-	-	-	?	?	+	+	?	+	?	+		
CD	4	43	Female	Bookbinder	8-year history of recurrent facial and hand dermatitis after contact with jewellery	Nickel ++, fragrance mix +	?	?	+	-	-	-	?	+	-	-	-		

CD = contact dermatitis; D = day; SL mix = sesquiterpene lactone mix 0.1% in petrolatum; SME = *Stellaria media* extract in petrolatum; SME1 = *S. media* extract 0.1% in petrolatum; SME3 = *S. media* extract 3% in petrolatum; TE = *Taraxacum officinale* extract in petrolatum; TE1 = *T. officinale* extract 0.1% in petrolatum; TE3 = *T. officinale* extract 3% in petrolatum; + = positive test; ++ = strongly positive test; - = negative test; ?+ = questionable response, on D3 only or both on D2 and D3 refers to a doubtful reaction.

Table 4. Patch test results in patients with non-allergic chronic inflammatory skin disease (NASD)

Group	Patient no	Age (year)	Sex	Occupation	Diagnosis	Standard specific series	Patch testing									
							TE						SME			
							SL mix		TE1		TE3		SME1		SME3	
							D2	D3	D2	D3	D2	D3	D2	D3	D2	D3
NASD	1	70	Male	Farmer	Stable plaque psoriasis	Peru balsam ++, fragrance mix ++	-	+	-	-	-	-	-	-	-	-
NASD	2	53	Female	Housewife	Stable plaque psoriasis	Fragrance mix ++	-	+	-	-	-	-	-	-	-	++

D = day; NASD = non-allergic chronic inflammatory skin disease; SL mix = sesquiterpene lactone mix 0.1% in petrolatum; SME = *Stellaria media* extract in petrolatum; SME1 = *S. media* extract 0.1% in petrolatum; SME3 = *S. media* extract 3% in petrolatum; TE = *Taraxacum officinale* extract in petrolatum; TE1 = *T. officinale* extract 0.1% in petrolatum; TE3 = *T. officinale* extract 3% in petrolatum; + = positive test; ++ = strongly positive test; - = negative test.

Among the patients suffering from non-allergic chronic skin diseases, a total of 2 patients sensitive to Compositae allergens were found, both having stable plaque psoriasis and both being SL mix-positive. We found no data regarding the prevalence of Compositae sensitivity among patients with psoriasis. Because a screening contact and atopic history may help in disclosing a subset of psoriatic patients who may benefit from a search for relevant contact allergies (28, 29), we think that the prevalence of 4% SL mix-sensitive among psoriatics detected in our study is worth reporting.

Recent studies have indicated an equal sex ratio (23), or majority of women of 62–78% (20, 22), making the percentage of females among the SL mix-sensitive persons in our relatively small study the highest reported. Generally, the sex distribution depends on the frequency of exposure,

changes in exposure thus having an important influence on female/male ratio (1).

Most of the reactions to SL mix were weakly positive. Relevance of these weak positive reactions to SL mix was found in 57.1% (4 reactions of 7), which was on a par with the 52.4% (11 reactions from 21) reported by Paulsen et al. (20). Adding strong positive reactions (++ and +++), the frequency of relevant ARs to SL mix rose to 62.5 and to 74%, respectively.

The overall frequency of IRs to SL mix was 3.4%, the highest ever reported. All IRs were weakly irritant. Allergens from the standard and additional series may produce in some patients mild erythematous IR. They occur at random and are probably related to skin hypersensitivity in these patients (15). This does occur during patch testing patients with active AD and is distinct from the 'angry back' syndrome (15). Both

Table 5. Patch test results in healthy control (C) persons

Group	Patient no	Age (year)	Sex	Occupation	Living place	Patch testing									
						TE						SME			
						SL mix		TE1		TE3		SME1		SME3	
						D2	D3	D2	D3	D2	D3	D2	D3	D2	D3
C	1	48	Female	Laboratory technician	Town	-	+	-	-	-	-	?+	?+	?+	?+
C	2	54	Female	Hospital cleaner	Village	-	+	-	-	-	-	-	-	-	-
C	3	23	Female	Student	Town	?+	-	-	-	-	-	-	?+	-	+
C	4	42	Female	Nurse	Town	-	-	-	-	-	?+	-	-	-	-
C	5	42	Female	Doctor	Town	+	-	-	-	-	?+	-	-	-	-
C	6	17	Female	Pupil	Town	-	-	-	-	-	-	?+	-	?+	-
C	7	39	Female	Doctor	Town	+	-	-	-	-	-	-	-	-	-
C	8	56	Male	Laboratory technician	Town	+	-	-	-	-	-	-	-	-	-
C	9	39	Female	Doctor	Town	+	-	-	-	-	-	-	-	-	-
C	10	47	Female	Chef	Town	+	-	-	-	-	-	-	-	-	-

D = day; SL mix = sesquiterpene lactone mix 0.1% in petrolatum; SME = *Stellaria media* extract in petrolatum; SME1 = *S. media* extract 0.1% in petrolatum; SME3 = *S. media* extract 3% in petrolatum; TE = *Taraxacum officinale* extract in petrolatum; TE1 = *T. officinale* extract 0.1% in petrolatum; TE3 = *T. officinale* extract 3% in petrolatum; + = positive test; - = negative test; ?+ = questionable response, on D3 only or both on D2 and D3 refers to a doubtful reaction.

Table 6. Patch test results in subjects sensitive to dandelion extract

Group	Patient no	Age (year)	Sex	Occupation	Living place	Patch testing													
												TE				SME			
						SL mix		TE1		TE3		SME1		SME3					
						D2	D3	D2	D3	D2	D3	D2	D3	D2	D3				
CD	1	46	Female	Trader	Town	–	–	–	+	–	+	–	–	–	–				
CD	2	52	Female	Clerk	Town	–	–	–	–	–	+	–	–	–	–				
AD	5	54	Female	Hairdresser	Town	+	–	+	+	+	+	–	–	–	–				

AD = atopic dermatitis; CD = contact dermatitis; D = day; SL mix = sesquiterpene lactone mix 0.1% in petrolatum; SME = *Stellaria media* extract in petrolatum; SME1 = *S. media* extract 0.1% in petrolatum; SME3 = *S. media* extract 3% in petrolatum; TE = *Taraxacum officinale* extract in petrolatum; TE1 = *T. officinale* extract 0.1% in petrolatum; TE3 = *T. officinale* extract 3% in petrolatum; + = positive test; – = negative test.

our patients with AD and IR to SL mix were free from any current dermatitis during patch testing. Only 1 of them (Table 2, patient AD10) had strongly positive +++ patch test reactions to nickel and chromate. This might produce 'angry back' syndrome but, when retested, this patient exhibited the same IR to SL mix. Patch tests were read not immediately but 20–30 min after removal of the tape. This was performed in order to eliminate transient false-positive erythematous reactions caused by the occlusive effects of allergens and tapes (15).

Literature data regarding IR to SL mix are scarce. Paulsen et al. (1) reported very few IRs. Routine screening has shown the prevalence of IR to SL mix between 0.0 (16, 20) and 0.1% (24). In their original report, Ducombs et al. (24) found the SL mix 0.1% pet., to be much less irritant compared to 1% pet., with only 0.1% IR versus 0.97%. Interestingly, in that multicentre study, all 5 IRs were recorded in the same centre, High Wycombe, UK., where 461 patients were tested (24). Nevertheless, no IR was recorded to dandelion extract in our study, the difference being significant ($P = 0.007$).

Extraction of SL from fresh (30) or air-dried (3) plants using purified diethyl ether has previously been described. The reported concentration of dandelion extract used for patch testing varies among different studies from 1 (3) to 10% pet. (8) and 10% alcohol (2, 7, 9). The recommended concentration is 2.5% pet. (Chemotechnique Diagnostics AB, Malmo, Sweden-plant series) (2, 4–6). Our own extracts were prepared from local supplies. An initial concentration of 0.1% pet. was used, because patch test with 'non-standard' contactants should begin with 0.1%. The concentration was increased to 3% pet., in order to test whether this slight increase (compared with 2.5% pet.) would produce an irritant response. For the many allergens that are also irritants, the concentration necessary to elicit an AR may differ little from that producing an irritant response. We did not expect such a response, because up to now no data on irritation produced by dandelion or common chickweed have been published in the English language literature.

Because none of 235 individuals showed any IR to dandelion extract 0.1 or 3% pet., nor was there any delayed reaction suggesting active

Table 7. Brief case history of the 3 subjects sensitive to dandelion extract

Group	Patient no	Age (year)	Sex	Brief history
CD	1	46	Female	15-year history of episodic facial dermatitis. Every spring and autumn she developed periorcular redness and swelling. The eruption involved eyelids. She particularly suspected cosmetics and 'airborne particles' such as pollens. She had lots of dandelions in her lawn, though she avoided direct contact.
CD	2	52	Female	10-year history of periorcular facial dermatitis with eyelid redness. Tending to clear in the winter, the eruption was worse during weekends after gardening when she avoided cosmetics.
AD	5	54	Female	She had worked as a hairdresser for the previous 20 years. She had an atopic history with chronic allergic rhinitis, and was convinced that her vesicular hand eczema was connected with her work. When she retired, the eruption had not improved. She noticed a flare after weeding in her own garden.

AD = atopic dermatitis; CD = contact dermatitis.

Table 8. Patch test reactions to Compositae plants/extracts in 5 SL mix-sensitive persons with relevant Compositae allergy

Group	Patient no	Living place	Involvement	Summer aggravation	Positive to plant/extract	Source of sensitization
AD	1	Town	Face Eyelids Neck	Yes	Compositae mix ++ Arnica 0.5% petrolatum +++ Tansy 1% petrolatum + Wild chamomile 2.5% petrolatum +	Arnica-containing cosmetics
AD	2	Village	Face Neck	Yes	Compositae mix ++ Arnica 0.5% petrolatum ++ Wild chamomile 2.5% petrolatum +	Herbal cosmetics, Weeding
AD	4	Village	Face Hands	Yes	<i>Chrysanthemum hortorum</i> as is ++ Compositae mix + Arnica 0.5% petrolatum + Tansy 1% petrolatum + Feverfew 1% petrolatum +	Gardening
NASD	1	Village	Hands	Yes	Compositae mix +++ Feverfew 1% petrolatum +++ Tansy 1% petrolatum ++	Farming
NASD	2	Village	Ears Auditory meatus	No	Arnica 0.5% petrolatum + Arnica 0.5% petrolatum ++	Arnica-containing shampoo

SL mix, sesquiterpene lactone mix 0.1% in petrolatum; AD = atopic dermatitis; Compositae mix = ether extract mixture 6% in petrolatum of arnica; 0.5%, wild chamomile 2.5%, tansy 1%, feverfew 1%, yarrow 1% supplied by Trolab®; NASD = non-allergic chronic inflammatory skin disease; + = positive test; ++/+++ = strongly positive-vesicular reaction.

sensitization, the prevalence of dandelion sensitivity of 1.3% is high enough to emphasize the value of dandelion extract 3% pet. as a constituent of the screening plant series for Compositae allergy in our area (24).

All dandelion extract positive reactions were of likely current relevance (CR3) (15), which is in agreement with previous reports (2, 5, 7–10). All dandelion-sensitive patients in our study were SL mix-negative. Similarly, in Nettis's study (31) of contact allergy to Compositae in patients with AD, all 5 patients (6.3%) with positive patch tests to plant extract and allergen were SL mix-negative, while 2 of them were positive to dandelion extract (2.5% pet.). Moreover, the SL mix failed to detect 38% of Compositae-sensitive patients in 1 series, while testing with dandelion extract (2.5% pet.) alone detected 73% of these SL mix-negative patients (4), and in Thomson's and Wilkinson's (6) study, among 4 patients reacting to Compositae but not to SL mix, 3 were allergic to dandelion extract (2.5% pet.). Likewise, Lovell and Rowan (3) reported 7 dandelion-sensitive subjects, all of whom were positive to dandelion extract (1% pet.), though only 2 reacted to SL mix. The failure of SL mix to detect dandelion allergy might be due the presence of the glucose residue on the dandelion antigen. The allergen in dandelion has been identified as taraxinic acid 1'-O- β -glucopyranoside, an eudesmanolide SL, linked to β -glucose via an ester linkage. On the other hand, plant extracts have generally been claimed to contain more allergens, such as polyacetylenes, thiophenes and

epoxythymol diesters. These compounds do not cross-react with SLs but may contribute actively to the development of Compositae dermatitis (26). In addition, lower detection rates of dried plant extracts compared to fresh plant extracts (these sometimes being slightly irritant), as well as different exposure patterns (e.g. via herbal remedies), should also be considered (2).

Despite its clinical importance, dandelion has been reported to be a weak sensitizer, some of the reactions probably being cross-reactions (2). Thus, in a recent Danish study, 39% tested positive to dandelion (as is and oleoresin 1:10 w:v alcohol and ether extract 2.5% pet.), but contrary to previous studies, almost all were positive to both Compositae mix and SL mix (2). Similarly, in another British study, 23% of the patients with photosensitivity dermatitis and actinic reticuloid syndrome were dandelion extract (1:10 alcohol) and SL mix-positive (7).

Because only 1 among 235 individuals showed any IR to common chickweed extract 0.1 or 3% pet., nor was there any reported case of active sensitization, the prevalence of sensitivity of 1.7% means that such an extract 3% pet. should be considered for the plant series in our area.

More than 1/3 of the SL mix-sensitive persons were positive to perfume, which was on a par with that reported by Paulsen et al. (20). Among those with relevant Compositae allergy, 37.5% had AR to fragrance mix and balsam of Peru that was even higher than the 24% reported by Paulsen et al. (1); adding positive colophonium reaction, the percentage rose to 50.0 and 38.5. Thus,

fragrance allergy was on a par with nickel allergy. A similar finding was also found in 2 recent Danish and 1 German study (1, 20, 32).

Conclusion

Though not all of our patients with weak positive reactions to SL mix had relevant Compositae allergy, our study confirmed the importance of inclusion of these reactions not only for limited sensitization or cross-reactivity but also for emerging, not fully established, Compositae allergy. In conclusion, the overall prevalence of 4.7% Compositae sensitivity in our study represents a basal SL mix detection rate of 3.4% reinforced and safely supplemented by testing with the dandelion extract.

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