

Contact allergy to herbal teas derived from Asteraceae plants

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Contact allergy to herbal teas derived from the Asteraceae plant family was investigated in patients allergic to sesquiterpene lactones (SLs). 20 patients with a known contact allergy to SLs were recalled and patch tested with aqueous extracts of 8 different herbal teas based on Asteraceae plants as well as with parthenolide and other SLs. In 18 of 20 patients with SL allergy, there were positive test reactions to the Asteraceae teas, mainly to those based on German chamomile, dandelion and wormwood. Among the SLs, parthenolide was the most frequent co-reactor. Obviously, most patients with a contact allergy to SLs are allergic to commercial teas derived from the Asteraceae plant family as well.

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The plant family Asteraceae (Compositae) is widely spread, occurring as wild and cultivated plants. Herbal remedies as well as skin care and cosmetic products based on Asteraceae plants are used because of allegedly health-promoting properties (1). Human skin contact with the plants is common not only during leisure activities but also in some occupations. Also oral intake of Asteraceae-derived products is frequent, e.g. salads, herbal teas and remedies. All these exposures may result in allergic reactions, mainly of 2 different types: as allergic rhinoconjunctivitis or allergic asthma mediated by pollen allergens and as allergic contact dermatitis, including systemic contact dermatitis, mediated by sesquiterpene lactones (SLs), important allergens present in different parts of the plant (2).

SL mix as included in our standard patch test series gives rise to 1%–2% positive reactions among dermatitis patients. At our departments, we have had some patients reporting a worsening of their hand eczema after the ingestion of herbal teas. Therefore, as a first step, we found it warranted to study our patients with SL allergy with regard to the allergenic potential of different herbal teas as shown by patch testing.

Materials and Methods

Patients

Patients previously patch tested with the European standard series because of suspected contact allergy and found positive to SL mix (containing alantolactone, costunolide and dehydrocostuslactone) were recalled for examination and patch testing. There were 20 patients, aged 35–75 years (mean 56 years), 13 women and 7 men.

18 patients had been patch tested because of long-standing hand eczema, of pompholyx type in 17 cases. 1 patient had had a face and eyelid dermatitis, and 1 patient had been tested because of eczema after using adhesive plaster.

When previously tested, all patients had been found to be patch test positive to other contact allergens besides SL mix. The 3 most frequent contact allergies among these 20 patients were nickel (11), cobalt (11) and colophony (4).

In accordance to the patients' records, atopic disease including atopic dermatitis, allergic rhinoconjunctivitis and/or asthma occurred in 9 of the patients.

1 of the 20 patients had had occupational contact with SL-containing plants.

As controls, 31 consecutive patients with dermatitis, negative to SL mix, were patch tested with the herbal teas. Among the controls, the most frequent contact allergies were nickel (6), fragrance mix (3) and colophony (1).

The study was approved by the Ethics Committee at Lund University Medical Faculty. Informed consent was obtained from each patient.

Patch test material

The 20 patients were tested with the following 6 petrolatum (pet.) preparations: SL mix 0.1% w/w, the separate SL alantolactone 0.033% w/w and the combination of costunolide and dehydrocostuslactone, each at 0.033% w/w. They were also tested with the SL parthenolide 0.1% w/w and pet. preparations of Roman chamomile (*Chamaemelum nobile*) 1.0% w/w and German chamomile (*Matricaria recutita*) 2.5% w/w.

The SL mix, the pet. preparation of Roman chamomile (*C. nobile*), alantolactone and costunolide combined with dehydrocostuslactone were supplied by Chemotechnique Diagnostics, Tygelsjö, Sweden. They did not contain any emulsifier.

The pet. preparation of German chamomile (*M. recutita* 2.5% with sorbitan sesquiolate 5% as emulsifier) originated from Trolab (Hermal, Reinbeck, Germany). Sorbitan sesquiolate 20% in pet. obtained from Chemotechnique Diagnostics was tested in 8 patients.

All patients and controls were tested with water extracts of 8 different herbal teas from the plant family Asteraceae. The herbal teas were acquired in 1 and the same health-food shop (teas originating from identical brands could not be ascertained). The chamomile tea was labelled to contain German chamomile (*M. recutita*). The other teas were golden rod (*Solidago virgaurea*), wormwood (*Artemisia absinthium*), marigold (*Calendula officinalis*), milfoil (*Achillea millefolium*) and dandelion (*Taraxacum officinale*). There were 2 different kinds of German chamomile and milfoil tea (I and II).

Test preparation of herbal teas

The process of making test preparations of the herbal teas is shown in Fig. 1.



Fig. 1. The procedure to make patch test solutions of herbal teas.

A water extract was prepared as follows: 50 ml boiling water was added to 1.5 g dried herbs in a glass beaker. After 10 min, the tea was filtrated through filter paper no. 3 (Munktell Filter AB, Grycksbo, Sweden). The water was evaporated in a rotary evaporator. To the almost dry residue in the glass jar, 1 ml of water was added, and this solution then constituted the stock solution for patch testing. The stock solution (100% w/v) was tested together with 2 aqueous dilutions (10% and 1% w/v).

Also ethanol and acetone solutions of evaporated water extracts were prepared, i.e. 2 water extracts were prepared as above. To the almost dry residues, 1.0 ml of ethanol and 1.0 ml of acetone, respectively, were added. However, not all of the residue could be dissolved neither in ethanol nor in acetone.

All the patients were also tested with these 2 solutions.

Patch testing

The pet. test preparations and test solutions, 15 µl of each solution, were applied on the back with Finn chambers (Epitest OY, Tuusula, Finland) on Scanpor tape (Norgesplaster A/S, Vennelesla, Norway) and removed after 48 hr.

The test reactions were read on D3 and D7 according to the International Contact Dermatitis Research Group (3). 9 patients were read also on D10.

Results

The results of patch testing with SLs and the water extracts of herbal teas in the patients are summarized in Table 1.

Of the 20 patients originally positive to SLs, 1 (no. 12) was entirely test negative (Table 1). Of the remaining 19 patients, 17 were positive to SL mix and all 19 to parthenolide.

All 17 patients hypersensitive to SL mix tested positively to 1 or more herbal teas (Table 1).

Most positive reactions were observed with chamomile tea, followed by wormwood and dandelion tea. 3 of the patients had positive reactions to all 6 different kinds of tea. 5 patients were positive to all teas except marigold. 1 patient was positive only to chamomile and dandelion tea. 1 patient was positive to milfoil tea alone.

Table 1. Positive test reactions (at least on 1 reading occasion) in the 20 sesquiterpene lactone (SL)-positive patients to petrolatum (pet.) preparations of SL mix, individual SLs and Roman and German chamomiles as well as to water extracts of different herbal teas

Test preparations	Patient	1	2	3	4	5	6	7*	8	9	10	11	12	13*	14*	15*	16*	17*	18*	19*	20*
SL mix	0.1 % pet.	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alantolactone	0.033% pet.					+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Costunolide + dehydrocostuslactone	0.067% pet.	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parthenolide	0.1% pet.	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Roman chamomile	1% pet.													+	+						
German chamomile	2.5% pet.					+	+		+		+	+	+	+			+	+	+	+	+
Germ chamomile tea I	100% aq.			+	+	+	+				+	+	+	+			+	+	+	+	+
	10% aq.				+		+				+	+	+	+							
	1% aq.						+							+							
Germ chamomile tea II	100% aq.			+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+
	10% aq.						+				+	+	+	+							
	1% aq.													+							
Golden rod tea	100% aq.					+						+		+	+		+	+			
	10% aq.													+							
	1% aq.													+							
Wormwood tea	100% aq.	+	+	+	+	+	+		+		+	+	+	+	+		+	+	+	+	+
	10% aq.						+							+							
	1% aq.													+							
Marigold tea	100% aq.				+						+			+	+						
	10% aq.													+							
	1% aq.													+							
Milfoil tea I	100% aq.				+		+				+			+	+			+	+	+	+
	10% aq.													+							
	1% aq.													+							
Milfoil tea II	100% aq.				+	+	+	+	+		+	+	+	+		+		+	+	+	+
	10% aq.					+	+				+	+	+	+				+	+		
	1% aq.												+	+							
Dandelion tea	100% aq.	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+
	10% aq.				+	+	+	+	+				+	+			+				
	1% aq.						+						+	+		+					

*Read also on D10.

11 patients tested positively to the pet. preparation of German chamomile while only 2 patients had a positive reaction to that of Roman chamomile.

None of the 8 patients tested with sorbitan sesquioleate showed a positive reaction.

Among the 31 controls, formerly shown to be negative to SL mix, 2 were positive to 2 and 3 herbal teas, respectively. All 17 patients hypersensitive to SL mix (Table 1) tested positively to 1 or more herbal teas. 2 of 31 SL-negative controls versus 17 of 17 SL-positive patients had a positive reaction to 1 or more herbal teas ($P < 0.001$, Fisher's exact test, 2-sided).

Positive test reactions to the aqueous extracts of the 8 teas were found to a similar degree with water and alcohol solutions (100% stock solution of each) (totally 81 reactions with each solution). Acetone solutions had the lowest number ($n = 60$) of positive reactions.

Some of the reactions did not turn positive until D7 (Table 2). There was a difference mainly between different patients but also between different teas and preparations. Milfoil tea had the largest number of late reactions. In 3 cases, milfoil tea showed a positive reaction for the first time on D7 and in three on D10.

Discussion

The present study shows a strong correlation between contact allergy to SL and several herbal teas. This is not surprising, because all herbal teas in the study were based on plants from the family Asteraceae, known to contain this group of chemicals (4, 5).

Tea made from German chamomile, often used as a herbal remedy, rendered the largest number of positive reactions. Also, it was a clear difference in frequency of positive test reactions

between the preparations of German and Roman chamomiles. Whether this difference depends on difference in the concentration of test preparations or reflects a true difference in prevalence of contact allergy to Roman and German chamomiles cannot be determined. There is, however, also a geographic difference because the Roman chamomile only grows in middle and southern Europe, while the German chamomile grows wild also in northern Europe. Therefore, in the patch test plant series used in our area, German chamomile should be present together with Roman chamomile.

Although closely related by name, Roman and German chamomiles represent different species indicating that they contain different SLs (5). Interestingly, one of the patients hypersensitive to Roman chamomile did not test positively to the German chamomile.

Usually, allergenic chemicals are extracted by using organic solvents, such as ether, ethanol or acetone. In the present study, we chose to extract with boiling water in order to simulate the ordinary process of making tea. For the final solution, when preparing test material, we used water, ethanol and acetone. It was found that acetone as a test solvent gave fewer positive test reactions than the other 2.

1 patient (no.7) contacted us on D10 and showed a positive reaction for milfoil. Therefore, we decided to read the remaining 8 patients also on D10.

Table 2 summarizes the day of appearance of positive patch tests without indicating peak intensity of the allergic reaction. Only 1 of 26 (approximately 4%) positive test reactions to the 2 German chamomile teas appeared on D7 or later while the corresponding figures for the 2 milfoil teas were 6 of 19 (approximately 32%).

Table 2. Number of patients tested positively on various days

	D3	D7	D10	Total
Sesquiterpene lactone mix 0.1% petrolatum (pet.)	15	2		17
Alantolactone 0.033% pet.	4		1	5
Costunolide + Dehydrocostuslactone 0.067% pet.	14	2		16
Parthenolide 0.1% pet.	18	1		19
Roman chamomile 1.0% pet.	1	1		2
German chamomile 2.5% pet.	8	1	2	11
German chamomile tea I (<i>Matricaria recutita</i>)	10		1	11
German chamomile tea II (<i>M. recutita</i>)	11	4		15
Golden rod tea (<i>Solidago virgaurea</i>)	5	4		9
Wormwood tea (<i>Artemisia absinthium</i>)	12		1	13
Marigold tea (<i>Calendula officinalis</i>)	2	1		3
Milfoil tea I (<i>Achillea millefolium</i>)	5	1	1	8
Milfoil tea II (<i>A. millefolium</i>)	7		2	11
Dandelion tea (<i>Taraxacum officinale</i>)	11	1		12

Furthermore, positive reactions appearing on D7 or later were also registered for the pet. preparations of German chamomile (3 of 11 = 27%). Whether this difference for the German chamomile test preparations (pet. and water extracts) reflects differences in penetrations for various vehicles, indicates different allergenic constituents of the test preparations or depends on the formation of allergenic metabolites is not currently known.

These results imply that a late test reading has to be recommended when working with SL-containing plant extracts.

The 7 positive reactions in 4 patients to alantolactone, German chamomile, German chamomile tea I, Milfoil tea I and Milfoil tea II appearing after D7 and registered on D10 may be interpreted as patch test sensitization. Theoretically, patch test sensitization is one explanation to reactions registered on D10. However, a more likely explanation is late-appearing reactions in pre-sensitized individuals. 2 facts speak in favour of this explanation: (i) the patients were known to be hypersensitive to SL and SL-containing plants and (ii) it has been proven that patch test reactions can appear after D7 without being an example of patch test sensitization (6).

Hand eczema of the pompholyx type is common among patients with SL allergy (7, 8). Pompholyx has also been reported to be frequent in individuals with nickel allergy (9) and atopic dermatitis (10), although not supported by the results of a recent Danish study (11).

Interestingly, both nickel allergy and atopy were overrepresented in the present material.

Of the 18 patients with hand eczema, 6 experienced a change for the worse during the patch test procedure including increased itching and appearance of new palmar vesicles.

This might at least theoretically be explained by a percutaneous absorption of the allergens from the patch test area (12–14).

1 patient (no. 12) (Table 1) with a previous contact allergy to SL mix was now found entirely test negative to all preparations and extracts. This may be explained by a recent sun exposure at the Mediterranean (15).

Among the 31 controls, all negative to SLs, 2 were positive to 2 and 3 herbal teas, respectively. There is a statistically significant difference in the number of positive reactions to herbal teas between those with and without contact allergy to SL mix demonstrating an allergic capacity of the herbal teas. The morphology of the herbal tea reactions in the controls was consistent with allergic reactions. As the SL mix does not trace

all contact allergy to Asteraceae plants (16), additional patch testing of the 2 controls with our plant series was performed resulting in positive reactions in the 2 controls testing positively to herbal teas; in both cases, the patch test was positive to *T. officinale*. Thus, the conclusion is that it is more likely that the test result of SL mix in the 2 controls was 'false negative' rather than that the test result of herbal teas was 'false positive'.

The mode of sensitization to allergens contained in herbal teas can only be hypothesized.

A large number of patients have contact with Asteraceae plants in leisure activities such as gardening. In the present material, only 1 patient had had occupational contact with this plant family.

The present study corroborates that the herbal teas contain SLs. It also shows that the process of making tea by using boiling water yields a beverage which contain a sufficient amount of sensitizers to elicit contact allergic reactions in patients hypersensitive to SLs.

Whether this principle also holds true for ingestion of herbal teas remains to be investigated.

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