

Allergic contact dermatitis caused by topical herbal remedies: importance of patch testing with the patients' own products

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Summary

Background. Natural ingredients have variable compositions, so their allergenic potencies may differ.

Objectives. To retrospectively analyse subjects reacting to herbal remedies over the past 27 years, with the aim of (i) evaluating demographic characteristics and lesion locations, (ii) describing the frequencies of positive patch test reactions, (iii) identifying sensitization sources, and (iv) studying concomitant sensitivity.

Patients and Methods. In total, 15980 patients were patch tested between 1990 and 2016 with the European baseline series and/or other series, product(s) used, and, whenever possible, the respective ingredients.

Results. Altogether, 8942 (56%) of 15 980 patients presented with at least one positive reaction. Reactions to topical herbal medicines, most often applied to treat an eczematous condition, leg ulcers, or other wounds, were seen in 125 (0.8%), that is, 1.4% of the contact-allergic subjects. Hands, legs and feet were the most frequently affected body sites. Twenty-one botanical allergens were identified, the commonest being *Myroxylon pereirae* (balsam of Peru), Compositae plants, and tincture of benzoin. Many patients presented with multiple positive test reactions, and some did not react to the commercial allergens but only to the products used.

Conclusions. Topical herbal remedies should not be applied on damaged skin, as multiple sensitization may develop. Moreover, patch testing with the culprit products is important for the diagnosis.

Key words: allergic contact dermatitis; batch variations; botanicals; concomitant reactions; herbal medicine; iatrogenic; medicinal plants; natural; phytodermatitis; topical drugs.

Topical herbal remedies are used to (self-)treat various diseases such as common colds, muscle pain, and

rheumatism (1), but most commonly skin eruptions such as acne, skin burns, alopecia, warts, fungal infections, and wounds (2). They are often claimed to contain 'only natural ingredients', which patients seem to relate to safety, so many of them might not reveal their use, or might even deny it (3). Adverse reactions such as irritant contact dermatitis, phototoxic reactions, contact urticaria and, particularly, allergic contact dermatitis have been reported, but their frequency seems to be underestimated (4). In some rare cases, even systemic hypersensitivity reactions have occurred (5, 6).

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Table 1. MOAHLEA index for the total population (n = 15 980) and for the study population, i.e. patients with positive patch test reaction(s) to a topical herbal remedy (n = 125)

	%						
	M	O	A	H	L	F	A
Total population	34	16	23	38	3	35	50
Study population	27	4	21	29	14	14	64

M, male sex; O, occupational; A, atopic dermatitis; H, hand dermatitis; L, leg ulcer/stasis dermatitis; F, facial dermatitis; A, age ≥ 40 years.

Table 2. Age distribution of the patients with positive patch test reaction(s) to topical herbal remedies

	Age (years)								Total
	< 20	20–29	30–39	40–49	50–59	60–69	70–79	> 79	
Men	3	3	5	4	5	6	6	2	34
Women	3	18	10	19	16	18	4	3	91
Total	6	21	15	23	21	24	10	5	125

We performed a retrospective analysis of patients who had attended our patch test clinic (a tertiary referral centre) between 1990 and 2016, and analysed the data of those suffering from allergic contact dermatitis caused by topical herbal medicines, with the aim of (i) evaluating demographic characteristics and lesion locations, (ii) describing the frequencies of positive patch test reactions to botanical ingredients, (iii) identifying sensitization sources, and (iv) studying concomitant sensitivity.

Methods

All data were retrieved from, and evaluated with, a patient database developed in-house in the Contact Allergy Unit of the University Hospitals of KU Leuven (7). This database contains socio-demographic variables, the medical history and the results of all contact allergy investigations for patients suspected of having allergic contact dermatitis, or patients with other diseases such as irritant dermatitis or other forms of eczema for which an allergenic cause needed to be excluded. Moreover, for each allergen identified, the respective sensitization source (causal factor) can be retrieved.

During the 27-year period from 1 January 1990 to 15 November 2016, 15 980 patients presenting with an eczematous dermatosis were patch tested with a modified European baseline series and/or other series, the products used, and, whenever possible, the respective ingredients. The test substances were obtained from Trolab® Allergens (previously Almirall Hermal, Reinbek, Germany; now SmartPractice Europe®, Barsbüttel, Germany) and/or Chemotechnique Diagnostics

(Vellinge, Sweden), or self-prepared according to the concentrations proposed by de Groot (8), and stored at 4°C. The patch tests were applied on the patient's back with Van der Bend® patch test chambers (Van der Bend, Brielle, The Netherlands) applied to Micropore® (3M Health Care, Borken, Germany), and later with IQ Ultra chambers® (Chemotechnique); they were fixed initially with Fixomull® (Beiersdorf, Hamburg, Germany) and later with Mefix® (Mölnlycke Health Care, Göteborg, Sweden). The patch test readings were performed according to ESCD guidelines (9) on day (D) 2, D3 (exceptionally), and D4, and often also later. A +, ++ or +++ reaction at either reading was recorded as an allergic patch test reaction; an irritant reaction, doubtful reaction or no response was recorded as a negative result.

All patients who presented with a positive patch test reaction to a herbal medicine and/or botanical ingredient present in such a topical preparation were considered in this study, including (over-the-counter) pharmaceuticals, preparations by the pharmacist, and 'paramedical' products (medical devices). All specific sensitization sources were evaluated; positive patch test reactions to botanicals used for purposes other than pharmacological activity, for example *Cananga odorata* (ylang-ylang) or rose oil, that is, essential oils being used as fragrance components (10), were omitted. Also, these have been extensively studied and reported on in the past (11).

Differences in the characteristics and lesion locations are presented in 2×2 contingency tables, and were statistically tested with the χ^2 test in an Excel® (Microsoft®) spreadsheet, with p -values of ≤ 0.05 being considered to be significant. The study was approved by the ethical research committee of our hospital.

Table 3. Lesion locations of the patients with positive patch test reaction(s) to topical herbal remedies

	Arms	Body folds	Eyes	Face	Feet	Generalised	Genitals	Hands	Legs	Lips	Trunk
Men	1	0	0	4	10	0	3	10	10	2	1
Women	4	1	2	10	17	6	4	24	22	5	7
Total	5	1	2	14	27	6	7	34	32	7	8

Table 4. Botanical active principles in medicinal herbal preparations yielding relevant positive patch test reactions, ordered alphabetically by their common name (allergens marked with an asterisk are the commercialized patch test preparations)

Allergen	Test concentration	Men		Women		Total	
		Positive	Patch tested	Positive	Patch tested	Positive	Patch tested
Arnica plant/flower extract*	0.5% pet.	1	44	7	149	8	193
Balsam of Peru*	25% pet.	9	5263	21	10 372	30	15 635
Benzoin, tincture	10% eth.	7	55	14	105	21	160
Calendula flower extract	10% eth.	2	126	9	378	11	504
Camphor	2% and 10% pet.	0	63	1	121	1	184
<i>Centella asiatica</i>	5% pet.	0	9	4	25	4	34
Echinacea	10% eth.	0	13	1	31	1	44
Escine	1% pet.	0	3	1	5	1	8
Eucalyptus oil	2% pet.	1	70	4	168	5	238
Geranium oil*	2% pet.	2	84	7	180	9	264
Guaiaculene	2% pet.	0	7	1	20	1	27
Hamamelis (distilled witch hazel)	5% aq.	0	45	1	103	1	148
Laurel leaf oil*	2% pet.	3	37	2	47	5	84
Lavender oil*	2% pet.	2	238	18	595	20	833
Menthol*	2% pet.	0	197	2	468	2	665
Niaouli oil*	2% pet.	0	15	2	24	2	39
Pine oil	2% and 5% pet.	0	40	1	81	1	121
Propolis*	10% pet.	4	43	9	104	13	147
Roman chamomile*	1.0% pet.	2	117	4	430	6	547
Tea tree oil, oxidized*	1% and 5% pet.	4	27	7	78	11	105
Thyme oil	5% eth.	1	15	2	27	3	42

eth., ethanol.

Results

Among the 15 980 patients investigated for contact allergy, 5387 (34%) were men and 10 593 (66%) were women; the mean age was 41 years in both subgroups. Of these patients, 8942 (56%) showed a positive reaction to at least one of the allergens tested. In 125 patients (0.8%), 34 men and 91 women, a topical herbal remedy was the cause of dermatitis; this represents 1.4% of the contact-allergic patients. The mean age in this group was 47 years: 46 years for women, and 51 years for men. The MOAHLFA index and age distribution of the total population and the study group are shown in Tables 1 and 2, respectively. Twenty-six patients (8 men and 18 women) had atopic eczema. Seventeen patients suffered from leg ulcer(s) and/or stasis dermatitis. As summarized in Table 3, the hands ($n = 34$), legs ($n = 32$) and feet ($n = 27$) were the most commonly affected body areas, some of the patients presenting with several lesion locations. The 21 botanicals yielding relevant positive reactions, and their

patch test concentrations and vehicles, are summarized in Table 4. As these concern pharmaceutical ingredients, we preferred not to use the INCI nomenclature as for cosmetics.

Table S1 lists all patients who reacted to herbal topical remedies, the indications for use, the positive patch test reaction(s) to the products used, and/or the relevant botanical ingredients, along with concomitant reactions to related substances, apparently without clinical relevance, owing to common or similar ingredients, or resulting from (pseudo)-cross-sensitivity (12).

The most frequent sensitization sources were preparations to treat atopic, contact or other eczema ($n = 43$), among which 19 were on the hands, leg ulcers ($n = 20$), to treat wounds ($n = 11$), to degrease the skin ($n = 9$), to treat dry lips ($n = 8$), to treat anal/perianal lesions ($n = 7$), and and to treat pain (6) (Table S1). Most patients presented with multiple reactions, the mean number of positive patch test reactions being seven per person. Figure 1

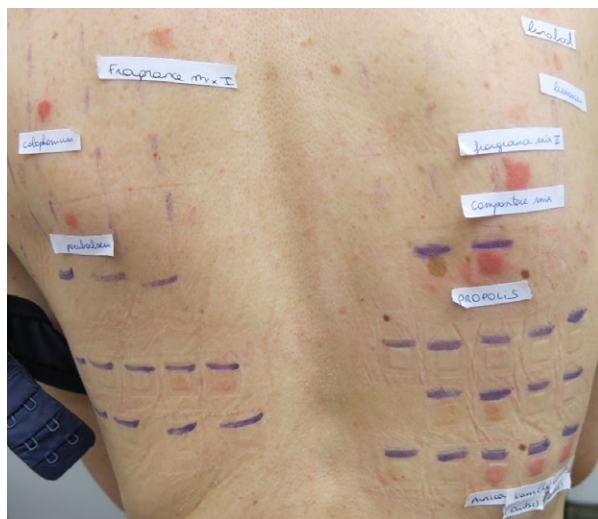


Fig. 1. Patient sensitized following the use of a propolis lotion to treat a wart, who presented with multiple positive patch test reactions to propolis, fragrance mixes I and II, colophonium, *Myroxylon pereirae* (balsam of Peru), hydroperoxides of linalool and limonene, Compositae mix, arnica, and both German and Roman chamomile.

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Discussion

Patient characteristics

The fact that 56% the total population had at least one positive patch test reaction is related to our department being a tertiary referral centre; that is, many patients were prediagnosed with, or highly suspected of having, allergic contact dermatitis; 1.4% of the positive reactions were caused by botanical active principles. The majority of these patients were women; however, the proportion did not differ significantly from the total population tested ($p=0.1$), as for the patients with atopic eczema ($p=0.6$). The percentage of patients aged >40 years was significantly higher in the study group ($p=0.002$). Accordingly, the mean age was 47 years as compared with 41 years in the total group. Differences were also seen concerning the proportion of patients suffering from leg ulcer(s) and/stasis dermatitis ($p<0.001$). The latter is definitely considered to be a risk factor for iatrogenic skin sensitization, which is explained by local inflammation, a

damaged skin barrier, and the use of occlusive bandages favouring skin penetration (13).

Allergens with sensitization sources

The highest frequencies of positive patch test reactions were obtained with *M. pereirae* (balsam of Peru; $n=30$), Compositae plant extracts ($n=26$), and tincture of benzoin ($n=21$). Balsam of Peru (*M. pereirae* resin), a natural balm consisting of essential oil and resin (oleoresin) (14), was previously often present in dermatological preparations, especially hand and lip balms, as well as in preparations for the treatment of haemorrhoids, because of its wound-healing and antimicrobial effects. Nowadays, these preparations are only rarely used in Belgium; indeed, the majority of the positive reactions were observed before the year 2000, and only six during the last 10 years. This is in contrast to the many positive reactions to balsam of Peru as a fragrance allergy marker in the baseline series; in total, between 1990 and 2016, 987 of 15 635 (6%) patch tested patients reacted positively.

Tincture of benzoin, an oleoresin obtained from *Styrax benzoin* and other species of *Styrax* (11), diluted 10% in ethanol, is often applied to the skin as an antiseptic, but also as a degreaser to increase the adherence of surgical tape or other adhesive bandages (15). The latter was the case for 8 of 21 sensitized patients. Thirteen showed simultaneous reactions to balsam of Peru, 14 to fragrance mix I, and 6 to colophonium. These concomitant reactions are known from the literature, and are explained by similarities in chemical structure of some of the ingredients (16).

Propolis (bee glue), the resinous substance that honeybees collect from living plants for the construction of their nests (17), is used for its antibacterial, antifungal and antiviral properties, and hence to treat burns, leg ulcers, psoriasis, warts, herpes labialis, and many other dermatoses. Its chemical composition is highly variable, depending on the plant species from which the bees collect the exudate; however, the most widely used 'poplar-type' propolis contains mainly phenolics. The esters of caffeic acid seem to be particularly strong sensitizers, with routinely tested subjects showing reaction frequencies of 2%, and sometimes even >3%. Therefore, in some countries, it is included in the baseline series [for example, it is included in the British Contact Dermatitis Society baseline series (18)]. In general, about 43% of the patients also react to balsam of Peru, because of either cross-reactivity with other cinnamic derivatives, or pseudo-cross-reactivity (the presence of common allergens, such as benzoic acid, caffeic acid, benzyl benzoate, and benzyl cinnamate). Other frequently reported

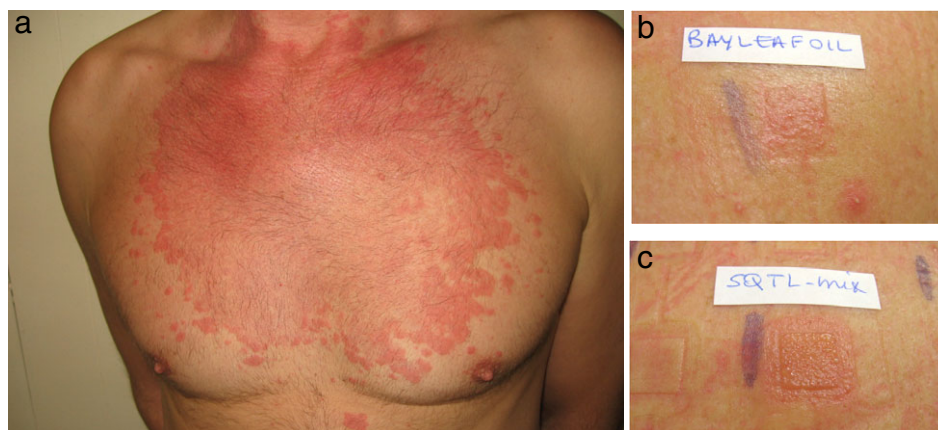


Fig. 2. Allergic contact dermatitis following the use of an inhalant ointment to treat a common cold (a), with positive patch test reactions (day 2) to laurel oil (+) (b) and sesquiterpene lactone (SQTL) mix (++) (c).

concomitant reactions are those to fragrance mix I, colophonium, beeswax, certain essential oils, such as clove oil, coriander oil, and peppermint oil, and certain plants, such as arnica and calendula. Of 13 patients in this study, 10 also reacted to balsam of Peru, 6 to fragrance mix I, 5 to colophonium, 4 to lavender oil, 3 to arnica, and 2 to Roman chamomile.

The Compositae (Asteraceae) family is probably the most important skin-sensitizing plant family in Europe (19). *Calendula officinalis*, also known as marigold, is used for the symptomatic treatment of minor inflammations of the skin, such as sunburn, as well as to promote healing of minor wounds. Its anti-inflammatory activity has been ascribed to triterpenoids present in the flowers. Not all of the allergens have yet been identified (20). *Arnica montana* is used in various topical preparations, most frequently as an ethanol-based tincture, because of its anti-inflammatory and experimentally proven wound-healing effects. It has a strongly sensitizing capacity, with sesquiterpene lactones (SQTLS) being the most important allergens; Austrian researchers previously reported an overall arnica sensitivity of 1.1% (21). Roman chamomile (*Chamaemelum nobile*), used for its wound-healing and anti-inflammatory effects (19), caused positive reactions in 6 patients, in 1 following the use of a self-made facial dressing. In contrast, we did not find relevant positive reactions to German chamomile. *Echinacea purpurea*, or purple coneflower, is traditionally used for the external treatment of small superficial wounds, because of its immunostimulant activity (22). One patient presented with a severe reaction following the use of an echinacea tincture to treat a sprained ankle, with generalized secondary spread. He had a +++ positive

patch test reaction to echinacea, and also to Compositae mix, arnica, and fragrance mix I.

As described in the literature, patients often cross-reacted or co-reacted to other Compositae species (19); for example, 2 more patients had positive patch test reactions to both arnica and calendula, and 2 other patients had positive patch test reactions to both arnica and Roman chamomile. Concomitant reactions to other allergens, that is, fragrance allergens, balsam of Peru, colophonium, and tea tree oil, also occurred, mainly because of the presence of common terpenes (12). Twenty-two patients in our study reacted positively to at least one botanical of the Compositae family, with only 4 of them being identified by the SQTL mix alone, and 3 additional cases being identified by the Compositae mix (unfortunately, this was tested in only 14 of 22 patients). The SQTL mix in the baseline series does not seem to be an adequate screening agent for identifying all contact-allergic cases (23), so, in 2010, we started to routinely test with Compositae mix, which has been suggested to be a more sensitive (24), although still not 'perfect', marker. Indeed, Reider et al. assumed that this was attributable to differences in the chemical composition of the SQTL used, which varies remarkably with the origin and provenance of the plants used for extraction (21); therefore, they suggested a commercial Compositae mix to be adjusted to regional conditions.

Interestingly, we observed a clear case of photoaggravation with photopatch testing, showing a + reaction to Compositae mix on the non-irradiated side as compared with a ++ reactions on the irradiated side. Initial contact sensitization to SQTL may indeed lead to generalized photosensitivity (25, 26), and Lepoittevin et al. showed

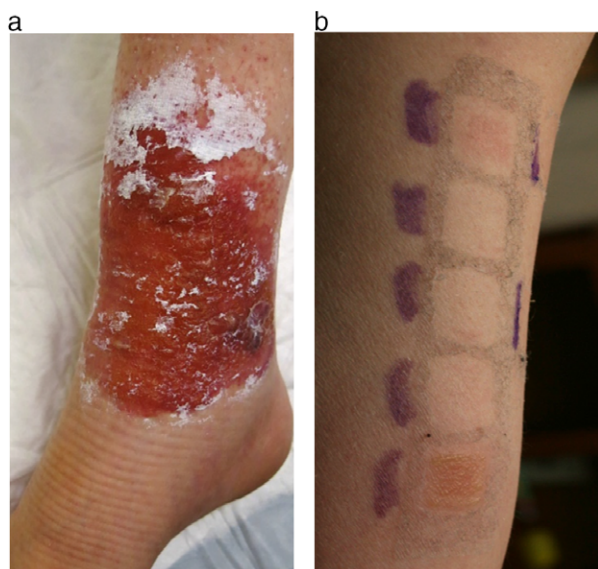


Fig. 3. Severe allergic contact dermatitis of the lower leg following the use of arnica tincture (a). Patch testing with the compounds showed positive reactions to the arnica extract used in the preparation from the pharmacist (day 2, +; day 4, ++) (b, lower test site), but not to the commercial arnica patch test preparation.

photoreactivity of these molecules (27). Unfortunately, we did not photopatch test with the SQTL mix.

Twenty patients reacted positively to lavender oil, which is obtained by steam distillation of the flowering tops of *Lavandula angustifolia*, and is traditionally used for local massage in cases of rheumatism, gout, neuralgia, sciatica, and scabies, because of its pain-relieving properties (22). Other essential oils are also used for their pharmacological activities, that is, bactericidal, antiviral, antifungal, anti-inflammatory, and insecticidal (28). Tea tree oil, obtained from the *Melaleuca alternifolia* tree, and used to treat skin diseases, such as acne, eczema, skin infections, wounds, burns, and mycoses, has been frequently reported to be an allergen (29). In our study population, 11 patients showed positive patch test reactions. Six of them had applied the pure oil: 4 for the treatment of tinea pedis, resulting in dermatitis at the site of application; in 2, dermatitis spread all over the body. Geranium oil (*Pelargonium graveolens* flower oil), used to treat chronic wounds and leg ulcers because of its anti-inflammatory properties (30), caused positive reactions in 9 patients, 2 of whom also reacted to lavender oil, which contains similar terpenes.

Several essential oils are also used for their antibacterial properties, for example in wound dressings, and these were identified as the cause of contact dermatitis in 3 patients who applied thyme and niaouli oil (the

essential oils of *Thymus vulgaris* and *Melaleuca viridiflora*, respectively); however, they are also present in inhalant ointments for respiratory tract infections. One of the patients thus developed allergic contact dermatitis following the use of Vicks Vaporub® (Procter & Gamble Europe, Strombeek-Bever, Belgium) to treat a common cold, with positive patch test reactions to the product itself and its ingredients eucalyptus oil and camphor (obtained from *Eucalyptus globulus* and *Cinnamomum camphora*, respectively). A similar case has been previously reported (31). Figure 2 shows a case of allergic contact dermatitis caused by an inhalant ointment (bought in Turkey, company unknown), with positive patch test reactions to laurel oil (bay leaf oil, obtained from *Laurus nobilis*). This patient also reacted to SQTL mix; these allergens are also found in plants of the Lauraceae family (32, 33).

Most of the causal herbal preparations (Table S1) were used for the treatment of pre-existing eczematous lesions, many on the hands, leg ulcers and other wounds, and other inflammatory diseases. Hence, such preparations should indeed be avoided in patients suffering from leg ulcers and/or stasis dermatitis (34), but also in patients with any other condition involving damaged skin, particularly in view of the risk of multiple sensitizations.

Problems encountered with botanicals

A particular problem when patch testing is performed with natural ingredients is that these are complex mixtures of variable composition, the chemical natures of which, and hence the allergenic potencies, may vary from batch to batch according to their origin. Moreover, many chemicals are also susceptible to autoxidation and skin metabolism (35). This makes standardization of patch testing with natural ingredients very difficult. As these particularities also apply to commercialized allergens, it is of the utmost importance to always test with the patients' own product(s). Figure 3 shows a patient with allergic contact dermatitis caused by arnica tincture used to treat an insect bite on her leg (Fig. 3a), with a positive patch test reaction only to the gel preparation (tested 'as is'; D2, +; D4, +++), the commercial patch test preparation (*Arnica montana* extract, 0.5% pet.; Chemotechnique) giving a negative result. Patch testing with the compounds of the gel (Fig. 3b, test below), obtained from the pharmacist, showed a positive reaction only to the arnica extract used in the preparation (D2, +; D4, ++). SQTL mix and Compositae mix did not cause reactions either. This sensitization would thus have been overlooked if the extract itself had not been tested. Furthermore, 3 other patients reacted to the botanical preparations as such, and not to the respective commercial allergens, that is, arnica, tea tree oil, and propolis.

Moreover, the nomenclature of botanical ingredients is confusing. EU legislation requires the clear labelling of herbal preparations (36); however, some manufacturers try to bypass this legislation by registering their products as 'medical devices'. Additionally, given the variability of plant extracts, it is not always clear which plant extracts are actually used. Patients sensitized through the use of herbal medicines should also be able to avoid cosmetic products containing similar allergens. However, the plant extracts used probably differ in composition, and are also given as INCI names, that is, Latinized names that are often based on obsolete botanical names, and are thus not easy to understand for consumers or the medical community. Moreover, not all essential oils used as fragrances are labelled on the cosmetic packaging. Last, but not least, sensitized patients should also be warned that the same allergens may appear in food and drinks, and as dietary supplements. Hence, systemic reactions may also occur.

Limitations of the study

Mainly because of its retrospective nature, this study has several limitations. Herbal preparations are not standardized, and neither are the patch tests, implying that results are not comparable with those from other centres. Moreover, not all patients who reacted to a botanical allergen were systematically tested with related allergens; for example, Compositae mix was not tested in all patients who reacted to individual members of this plant family. The study population considered was selective, as it comprised patients consulting our tertiary referral centre; hence, we assume that the prevalence of allergic contact dermatitis caused by herbal remedies is substantially underestimated. Indeed, patients often self-manage these reactions without consulting a dermatologist.

Furthermore, even when sensitization had occurred, contact allergy could not always be confirmed.

Conclusion

Herbal remedies should be avoided in the treatment of damaged skin, as most patients develop multiple contact sensitivity, with simultaneous reactions being, in most cases, attributable to the presence of common ingredients. Natural ingredients are complex mixtures of variable composition, which makes standardization of patch testing almost impossible. Hence, it is important to test with the patients' own product(s) and the respective ingredients, as contact-allergic reactions may be missed if only commercial patch test allergens are tested.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. The patients who reacted to herbal topical remedies, the indications for use, the positive patch test reaction(s) to the products used, and/or the relevant botanical ingredients, along with concomitant reactions to related substances, apparently without clinical relevance, owing to common or similar ingredients, or resulting from (pseudo)-cross-sensitivity.

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Table S1. The patients who reacted to herbal topical remedies, the indications for use, the positive patch test(s) to the products used, and/or the relevant botanical ingredients, along with concomitant reactions to related substances, apparently without clinical relevance, due to common or similar ingredients, or resulting from (pseudo)cross-sensitivity.

Patient			Causative herbal product			Purpose of use	Patients' own product	Arnica	Balsam of Peru	Benzoin, tincture	Calendula	Camphor	Centella asiatica	Echinacea	Escine	Eucalyptus oil	Geranium oil	Guaiaculene	Hamamelis	Laurel oil	Lavender oil	Menthol	Niaouli oil	Pine (needle) oil	Propolis	Roman chamomille	Tea tree oil	Thyme oil	FM1, FM2 or components	Colophonium	Limonene hydroperoxide	Linalool hydroperoxide	Wood tar	Compositae mix	Sesquiterpene lactone mix	Total positive patch tests
1	F	67	Arnica ointment			Shoe dermatitis		x																								nt		5		
2	F	83	Herbal ointment			Atopic dermatitis		x												x						x						nt	x	9		
3	M	59	Herbal ointment, propolis talk			Contact dermatitis		x	x															x								nt		10		
4	F	42	Calendula cream			Atopic dermatitis	x	x								x					x		i									x	nt		12	
5	F	27	Herbal ointment; Vickx vaporub®			Generalized eczema; common cold		x	i			x				x							i		x	x							x		16	
6	F	23	Hand cream			Occupational hand dermatitis		x																											4	
7	F	46	Arnica ointment			Sprained ankle	x	x	i		x											i												p	17	
8	F	75	Herbal ointment			Ulcer on amputation stump		x	x		x																								40	
9	F	24	Arnica cream			Head wound	x																												7	
10	F	49	Arnica tincture			Tendinitis of the wrist	x																												3	
11	F	71	Herbal ointment			Hand eczema			x																									nt		7
12	M	23	Lipbalm			Lipcare			x																										nt	3
13	F	69	Ointment prepared by the pharmacist			handeczema, fissures			x																										nt	2
14	F	61	Anal ointment			Pruritus ani			x																										nt	8
15	M	36	Anal ointment			Pruritus ani			x																										nt	6
16	F	48	Lipbalm			Lipcare			x	i															i										nt	9
17	F	63	Ointment prepared by the pharmacist; herbal balsam			Atopic dermatitis			x																										nt	2
18	F	42	Ointment prepared by the pharmacist			Woundhealing			x	i																									nt	3
19	F	60	Herbal balsam			Eczema			x	i																									nt	11
20	F	58	Herbal ointment			Rosacea			x																										nt	1
21	F	68	Ointment prepared by the pharmacist			Woundhealing			x	i																									nt	9
22	F	24	Hand ointment			Handeczema, fissures			x	i															i										nt	10
23	F	56	Lipbalm			Daily hydration of the lips			x																i										nt	5
24	M	60	Anal ointment			Pruritus ani			x																										nt	2
25	M	35	Handcream			Chronic handeczema			x																										nt	2
26	F	21	Herbal ointment			Woundhealing			x																										nt	4
27	M	63	Balsam of Peru			Fissures			x																										nt	10
28	F	51	Lipbalm			Lipcare			x																										nt	4
29	F	41	Lipbalm			Lipcare			x																										nt	1
30	F	51	Herbal ointment			Handeczema			x																										nt	5
31	F	36	Herbal ointment			Atopic dermatitis			x																										nt	8
32	F	40	Ointment prepared by the pharmacist			Handeczema, fissures			x																										nt	3
33	F	44	Herbal ointment			Scars			x																										nt	13
34	M	65	Anal ointment			Hemorrhoids			x																										nt	1
35	M	47	Udder cream			Daily hydration hands and feet			x																										nt	1
36	F	64	Ointment prepared by the pharmacist			Eczema and fissures on the foot			x																											15
37	M	53	Herbal ointment			Handeczema, fissures			x																	i										4
38	M	38	Herbal ointment			Woundhealing			i	x																									nt	7
39	F	25	Lipbalm			Cheilitis			i	x																									nt	11
40	M	70	Hand ointment			Handeczema			i	x																										6
41	M	53	Degreaser			Before application of an ankle plaster				x																									nt	14
42	F	41	Degreaser			Before application of a wound dressing			i	x																									nt	4
43	F	28	Herbal ointment; tincture of benzoin			Fissures	x			x																									nt	3
44	M	85	Herbal ointment			Atopic dermatitis			i	x																									nt	6

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101	F	37	Wound dressing	Hand surgery																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																
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