

Review Article

Contact sensitization from Compositae-containing herbal remedies and cosmetics

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The Compositae (Asteraceae) family of plants is currently an important cause of allergic plant contact dermatitis in Europe. The family comprises some of the oldest and most valued medicinal plants, and the increasing popularity of herbal medicine and cosmetics may theoretically result in a growing number of Compositae sensitizations from these sources. According to the literature at least 15 species, including among others arnica (*Arnica montana*), German and Roman chamomile (*Chamomilla recutita* and *Chamaemelum nobile*), marigold (*Calendula officinalis*), *Echinacea* and elecampane (*Inula helenium*), have been suspected of sensitization or elicitation of Compositae dermatitis. Epidemiological data are available for 2 species only, arnica and German chamomile, the rest of the evidence being anecdotal. Based on this, sensitization seems to occur relatively frequently with a few species such as arnica and elecampane, and occurs rarely with the majority, especially the widely used German chamomile. Sesquiterpene lactones are the most important allergens, but there are a few cases of sensitization from a coumarin, a sesquiterpene alcohol and a thiophene. The risk of elicitation of dermatitis by using Compositae-containing products in Compositae-sensitive individuals is by-and-large unknown.

Key words: allergic contact dermatitis; Arnica; Asteraceae; Compositae; dandelion; Echinacea; elecampane; feverfew; German chamomile; great burdock; herbal cosmetics; herbal remedies; marigold; phytomedicine; plant dermatitis, Roman chamomile; sesquiterpene lactones; topical treatment. © Blackwell Munksgaard, 2002. © Blackwell Munksgaard, 2002.

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The use of herbal remedies and cosmetics has increased considerably in Western societies in recent years (1). The rise has been followed by a growing number of reports of adverse effects, including allergic contact dermatitis, from plant constituents of these preparations such as, e.g. tea tree oil and other essential oils (1).

The daisy family (Asteraceae, Compositae), with its numerous and widespread sesquiterpene lactones (SLs), is probably the most important allergenic plant family in Europe today (2, 3). At the same time it comprises some of the oldest and most valued medicinal plants, notably German chamomile and arnica (4). These and other species are also widely used in cosmetic formulations, and patients with Compositae contact sensitivity are routinely warned of applying such products (4). A recent British study reported a high prevalence of positive reactions to plant extracts in patients with cosmetic dermatitis, most frequently to tea tree oil followed by Compositae (5). While the relevance of the tea tree oil reactions was obvious in most of

the patients, the association between use of Compositae-containing cosmetic products and Compositae sensitization was less clear (5).

The aim of this review is to assess the evidence of sensitization or exacerbation of Compositae dermatitis from the use of Compositae-containing herbal remedies and/or cosmetic preparations.

The plant species involved are listed alphabetically, primarily by botanical name, followed by vernacular name. For plants used as ingredients in cosmetics, the INCI (International Nomenclature of Cosmetic Ingredients) names are added.

***Achillea millefolium* L.**

(milfoil, yarrow; INCI name *Achillea millefolium*)

Milfoil is an old medicinal plant and the whole plant (*Herba millefolii*) as well as the flowers (*Floris millefolii*) are officinal (4). Traditionally, milfoil preparations have been used both externally and internally: the names knight's milfoil and soldier's woundwort refer to the wound-healing effects of

the plant (4); the tea is recommended for wounds while a decoction has been used as a compress in skin diseases. Because of a spasmolytic effect, the drug is used for indigestion and liver diseases besides a variety of other conditions in traditional medicine (4). Furthermore, today milfoil extracts are used in 'natural' cosmetics as a 'biological additive' and a recent report states that it was used in 65 cosmetic formulations in the US in 1998 (6). A short ether extract of the whole plant is one of the constituents of the Compositae mix, and positive reactions to a 1% petrolatum milfoil extract are positive in 40–50% of Compositae mix-sensitive patients (2, 7). Nevertheless, few cases of sensitization/exacerbation from herbal medicaments or cosmetics have been published. Hausen refers to at least 2 cases of milfoil-induced 'skin lesions' in a book on medicament side-effects from 1899, and in his 1996 report on Compositae mix testing, he states that 10 of 118 Compositae-allergic patients were sensitized by herbal remedies or cosmetics, though milfoil is not specifically mentioned (2, 8). Generalized dermatitis after drinking milfoil tea has been reported twice, and according to Hausen milfoil tea contains SLs (9–11). The most important SL allergen in milfoil is α -peroxyachifolid (8, 12). SLs are contained in the essential oil of milfoil, but due to its presumably low water-solubility it is not known whether the reaction to the tea was caused by small amounts of SLs or some other allergen such as, e.g., a flavonoid (6). Sensitization from a plant-based massage liniment containing bay leaf and 3 Compositae species, including milfoil, was ascribed to elecampane without patch testing all constituents (13).

The dermatitis-inducing capacity of cosmetic formulations with milfoil seems to be low based on clinical testing, where products containing 0.1–0.5% of a 2% extract were generally non-irritant and nonsensitizing (6).

***Arctium lappa* L.**

(great burdock; INCI name *Arctium lappa*)

Great burdock has been used as a medicinal plant since antiquity (4, 14). Some of the purported effects of the leaves and root and the root oil (*Oleum Bardanae*) are antiseptic, diuretic, hair-growth stimulating and anti-inflammatory (4, 14, 15). The last-mentioned effect has been put to use in infusions and plasters and is probably the reason why it is recommended as a skin wash for psoriasis and acne (14, 15). Even though a dermatitis-inducing potential is ascribed to burdock leaves and the root oil, few cases have been reported (4, 10). Dreyer described a case of dermatitis after long use of the root oil (16). More recently, Rodriguez et

al. reported 3 cases of exudative allergic contact dermatitis after application of burdock plasters for various injuries/tendonitis (14). A dilution series of an aqueous burdock root infusion elicited + + + reactions in all 3 patients, but was negative in 20 controls. Patch tests with the SL mix were not carried out, but a probable allergen is the SL arctiopicrin (4). Great burdock was another of the plant ingredients in the contact dermatitis-inducing massage liniment mentioned above, where elecampane was considered the primary sensitizer (13).

***Arnica montana* L.**

(arnica; INCI name *Arnica montana*)

Arnica is one of the most important European medicinal plants (17). It was first used as a folk remedy, the quinine of the poor, later – from the 18th century – also officinally, and, furthermore, today it is found in homoeopathic preparations and herbal cosmetics (17). In the USA, where other arnica species are officinal, Arnica Montana Extract was thus used in 97 cosmetic formulations according to the data submitted to the FDA in 1998, and in Germany extracts of arnica flowers were constituents of more than 200 commercial phytomedicinal products in the 1980s (17–19). The anti-inflammatory and experimentally proved wound-healing effects have been made use of in a variety of preparations for external application, especially the ethanol-based tincture of arnica and various healing ointments (4, 17). Both the weed, the commercially available drug and the single SLs have a strongly sensitizing – and irritant – capacity: important SL allergens include helenalin and xanthalongin (4, 17). It is therefore not surprising that, in his survey of arnica allergy, Hausen lists more than 100 reported cases between 1844 and 1977 (17). The majority of these were ascribed to the use of the – often inexpediently undiluted – SL-containing tincture of arnica (17). Among 3 more recent reports on positive patch test reactions to tincture of arnica, only 1 was due to sensitization from the tincture; the others were ascribed to cross-reactivity which may occur with sunflower, chrysanthemum and other Compositae species (4, 19–22). A 0.5% petrolatum (pet.) short ether extract of arnica is 1* of the constituents of the Compositae mix, and the fact that 10 of 44 arnica-positive patients were mono-sensitized in a large German study probably reflects the widespread use of tincture of arnica (2). The overall arnica sensitivity in this study is on a par with that of a recent Austrian investigation where 5 of 443 consecutive patients (1.13%) tested positive to arnica; 3 of the 5 remembered using arnica as a topical remedy, but the sensitizing products are not described further

(23). Occupational sensitization from arnica-based massage oils has been seen in Germany and Denmark (7, 17).

On the other hand, Hörmann & Korting state that sensitization from arnica ointments rarely occurs (19). Bruynzeel et al. indeed found 3 cases of positive patch tests to an arnica-containing ointment (Table 1), but 2 of the patients were positive to a constituent of the ointment base and none of the 3 were tested with arnica (24). A patient sensitized to an arnica-containing jogging cream tested positive to, among others, a 5% pet. arnica extract and thus irritation cannot be ruled out (Table 1) (25). Furthermore, in a European multicentre study on allergic contact reactions to cosmetics in 475 patients, only 1 was positive to arnica, and in another study resinoid of arnica, a perfume material, was patch test negative in Compositae-sensitive patients (26, 27). This is in accordance with human studies of the sensitizing potential of a face cream and a skin cream, both containing 1% of a mixture of Arnica Montana Extract and sunflower seed oil: none of them were sensitizers (18). Some patients, however, may react to arnica-containing cosmetics, even in rinse-off products: Hausen reports 1 case of dermatitis in the auditory meatus due to the use of an arnica-containing shampoo (2).

***Artemisia vulgaris* L.**

(mugwort; INCI name *Artemisia vulgaris*)

Mugwort has been used both officinally and in folk medicine as, e.g., an antiepileptic and anthelmintic (4, 28). The SLs psilostachyin and psilostachyin-C are weak sensitizers and furthermore their concentration in mugwort of Northern Europe is low, so few cases are reported (4, 22, 29). Only 1 of these was due to medicinal use of the plant: a 44-year-old Japanese male treated his Rhus dermatitis with mugwort 'as is' and a brew made from the plant (30). After drinking some of the brew as a tea a widespread bullous dermatitis with mucosal involvement, most consistent with erythema multiforme, developed and the reaction was considered to be an 'internal/external' allergy (30). Patch testing was not performed due to the severity of the symptoms (30).

***Calendula officinalis* L.**

(marigold; INCI name *Calendula officinalis*)

As indicated by the botanical name, marigold has been used as a medicinal plant for hundreds of years and the drug, Flores Calendulae, is still used officinally in some countries today (4). The main indications are treatment of wounds and skin diseases, and recently it has been reintroduced and

become extremely popular in herbal cosmetics (4). A recent report mentions that it was used in 178 cosmetic products in the US in 1998 (31). Experimentally, the plant extract is weakly sensitizing and this is supported by the scarcity of case reports until recently (4, 9). Sensitization may occur from growing and harvesting marigold used for production of a beauty cream or possibly from the use of plant-based cosmetics (4, 32). However, clinical testing of a cosmetic formulation with a 1% Calendula extract showed a low irritant and a non-detectable sensitizing potential (31). Likewise, a commercial perfume material, absolute of Calendula, was patch test negative in Compositae-allergic patients (27).

The diagnosis of Calendula allergy is doubtful in the studies of Underwood and Gaul and Bruynzeel et al.: the former saw 4 patients with positive patch tests to Calendula, but details of patch test concentration and relevance are lacking (33). Likewise, Bruynzeel et al. found that 1 of 2 patients with positive patch tests to an ointment containing 10% Calendula tincture (Table 1) was also positive to wool fat, and further testing with plant ingredients was not carried out (24).

These findings contrast markedly with those of a recent Austrian study (23): Reider et al. found that 9 of 443 consecutive patients were sensitized to marigold (10% pet.), and the reactions were of possible relevance in 4 and certain relevance in 2 (23). The allergens of marigold are unknown.

Chamomile

As pointed out by Hausen in his extensive 1984 review the vernacular name 'chamomile' has been used interchangeably for at least 3 different species, namely German chamomile [*Chamomilla recutita* (L.) Rauschert], Roman chamomile [*Chamaemelum nobile* (L.) All.] and dog fennel [*Anthemis cotula* L.] (34). German and Roman chamomile are both important medicinal plants, and despite their allegedly similar properties, they differ chemically (4, 35).

***Chamomilla recutita* (L.) Rauschert (German chamomile; INCI name *Chamomilla recutita*)**

The sweet-scented German chamomile has been used as a medicinal herb worldwide for thousands of years and has become increasingly popular in recent decades (34, 36). Chamomile has experimentally supported effects as an anti-inflammatory, spasmolytic, wound-healing and sedative/anxiolytic agent and is also widely used in 'natural' cosmetics today (4, 36). The active constituents are contained in the essential oil of chamomile, which

Table 1. Compositae-containing commercial products eliciting positive patch test reactions

Name of product	Plant extract	Patch test results	Comments	Reference
Arniflor™ ointment (VSM, Alkmaar, The Netherlands)	Arnica tincture 10% (<i>Arnica montana</i>)	3 positive Arniflor™, 2 of whom were positive to wool fat (ointment constituent)	NT with arnica extract	24
Jogging cream (Asepia, Monaco)	Arnica extract	1 positive cream as is, lipacide-cas, palmitoyl hydrolysed milk protein, palmitoyl collagen amino acids, arnica extract 5%, negative to 27 other ingredients	Tested with arnica 5% pet. (irritant?)	25
Calendula™ ointment (VSM, Alkmaar, The Netherlands)	Calendula tincture 10% (<i>Calendula officinalis</i>)	2 positive Calendula™, 1 of whom was positive to wool fat (ointment constituent)	NT with Calendula extract	24
Kamillosan™ ointment (Homburg, Diemen, The Netherlands)	Chamomile extract 4% (<i>Matricaria chamomilla</i>)	5 positive Kamillosan™, 2 of whom were positive to Matricaria leaf and 2 to wool fat (ointment constituent)	3 NT with Matricaria leaf	24
Kamillosan® ointment and lotion	Probably as above	1 patient positive to Kamillosan® ointment and lotion, alcoholic and chloroform extracts of German and Roman chamomile as well as plant as is and chamomile tea		48
Kamillosan® cream (Asta-Pharma AG, Frankfurt, Germany)	Extract of SLs-free chamomile cultivar 'Degumille'	1 positive to 2 ointment base constituents and 'Degumille' concentrate; 230 patients patch test negative to Kamillosan® cream		49
Kamillosan® concentrate (ASTA Medica, Dresden, Germany)	Water/alcohol extract of SLs-free chamomile cultivars 'Degumille' and 'Manzana'	1 positive to Kamillosan® concentrate, negative to diluted Kamillosan® concentrate (= use concentration)		37
Kamillosan® solution (= use concentration) (ASTA Medica, Dresden, Germany)	As above	1 person positive to the solution out of 830 tested	152 patients patch test negative to Kamillosan® ointment and cream	50, 51
Kamillosan® ointment (UK) (suppliers Norgine Limited)	Extracts and oils of Roman chamomile 10.5% (<i>Chamaemelum nobile</i>)	1 person positive to Kamillosan® ointment, chamomile oil 0.1% pet. and negative to other ingredients; another person positive to chamomile oil 0.1% pet. (negative to other ingredients) and positive to cinnamic alcohol, cinnamic aldehyde and balsam of Peru		60
Echinacea™ ointment (VSM, Alkmaar, The Netherlands)	Echinacea tincture 10% (<i>Echinacea angustifolia</i>)	2 persons positive to Echinacea™ ointment, negative to ingredients	NT with Echinacea extract	24
Eudan® (breath refresher)	<i>Inula helenium</i>	1 person positive to <i>Inula helenium</i> 1% and 10% alcohol	Patch test concentrations may irritate	69

NT = not tested.

comprises, e.g., anti-inflammatory and spasmolytic sesquiterpene alcohols such as α -bisabolol, the blue chamazulene with a weaker anti-inflammatory effect, farnesene, polyenes and several flavonoids. From a dermatological point of view the content of sensitizing SLs such as anthecotulide is especially important. However, the composition of

the drug, *Matricariae flos*, depends on country of origin. Chamomile imported from Argentina may contain larger amounts of the strongly allergenic sesquiterpene lactone anthecotulide, and in addition may be contaminated with the morphologically similar dog fennel (*Anthemis cotula* L.), which contains up to 7.3% anthecotulide, whereas

chamomile of European origin contains only traces (4, 34). Common medicinal preparations of chamomile include essential oil, hot-water extract (tea) and a water/alcohol extract (37). Due to its poor water solubility, only 30–45% of the essential oil will be present in chamomile tea, but according to Hausen the tea actually contains SLs (11).

A 2.5% pet. extract of German chamomile is one of the constituents of the *Compositae* mix, and recent European studies have shown a high prevalence of chamomile sensitivity in *Compositae*-allergic persons (2, 7). However, the prevalence of adverse reactions to chamomile in herbal preparations is unknown. In a German study of 1000 cases of contact dermatitis, 33.8% were iatrogenically acquired and chamomile preparations were among the most frequently sensitizing substances (38). There is a lack of information, however, on both details of patch test results to rule out reactions to other constituents of the preparations, and on botanical identification of the chamomile used, though it was most likely German chamomile (34, 38). This prevalence was opposed by the findings in another German study: Beetz et al. tested 200 non-selected patients with, among other things, 11 chamomile-containing products and extracts of (probably German) chamomile (34, 39). Of 21 (10.5%) persons with positive reactions to the chamomile herbal preparations, 3 tested positive to a chamomile extract and only 1 reaction was considered relevant due to previous reaction to a chamomile ointment (39). This study demonstrates that contact allergy to chamomile-containing topical remedies is rarely due to genuine chamomile allergy, and this conclusion is in accordance with some previous German studies and a later European study on cosmetic allergy (26, 39).

The risk involved in using the SL-containing oil of chamomile has been addressed by Rudzki et al. in their extensive study on sensitization from essential oils (40). They tested 200 consecutive patients and 50 balsam-allergic persons with 35 essential oils and calculated an index of sensitization based on kilograms of oil used annually in the Polish cosmetics industry per patient positive to that oil. German chamomile oil was first on this list, possibly due to frequent use of chamomile compresses in Poland (40). A later case report describes a combined and clinically relevant Type I and Type IV allergy to chamomile oil in a female patient with chronic recurrent urticaria (41).

Despite an increasing number of case reports on contact dermatitis due to essential oils used in aromatherapy (42–44), only 1 case with a positive reaction to (probably German) chamomile oil has been published in this group of patients (45).

Another commercial preparation is Kamillos-

an®, which in its continental version is based on a standardized water/alcohol extract of SL-free German chamomile cultivars 'Degumille' and 'Manzana' (37, 46). Furthermore, the extract is filtered to avoid pollens in the final product (37). The allergenic potential of Kamillosan®, which seems to be anti-inflammatory (47), has been studied by several groups: in a Dutch multicentre study, 5 of 1032 patients tested positive to Kamillosan® (Homburg, Diemen, the Netherlands) (Table 1) and, while the reaction in 2 of the patients probably was caused by wool fat in the ointment base, 2 other persons actually tested positive to chamomile leaf (24). Testing with constituents was not performed in another Dutch patient with positive reactions to Kamillosan® ointment and lotion, chamomile tea and extracts of German and Roman chamomile, and thus reactions to ingredient(s) of the ointment cannot be ruled out (48). Klaschka & Patzelt-Wenczler tested 231 patients with contact dermatitis and only 1 was positive to both a 'Degumille' concentrate and 2 constituents of the Kamillosan® cream base (Asta-Pharma AG, Frankfurt, Germany) (Table 1) (49). Likewise, Polish studies of a large series of patients tested with diluted/undiluted Kamillosan® solution or Kamillosan® cream/ointment (ASTA Medica, Dresden, Germany) found only 1 positive reaction to the standard dilution (= use concentration) in 830 patients tested and 1 positive reaction to undiluted, but not diluted, Kamillosan® in 28 patients tested (Table 1) (37, 50, 51). The fact that the latter patient tolerated Kamillosan®, diluted according to the manufacturer's recommendation, despite her strong chamomile allergy, also to aqueous preparations, supported the main conclusion of Rudzki & Jablonska: Kamillosan® is safe even in chamomile-allergic persons (51).

Other possible allergens in chamomile could be coumarins such as herniarin or flavonoids (4). Furthermore, bisabolol or one of its oxidation products has been reported as allergenic (52).

Local and systemic contact dermatitis from chamomile tea have been reported in 2 cases from Portugal and Spain (53, 54). Both patients were SL mix-positive and positive to chamomile tea, indicating that even the presumed small amounts of SLs in the tea may be responsible (53, 54). Another possible allergen in chamomile tea is pollen, which is found in large amounts in commercially available teas (55). Immediate-type reactions from contact urticaria to more severe systemic reactions after topical use or ingestion have been reported by several groups (55–57). Reider et al. (57) concluded that the incidence and risk of Type I allergy to chamomile may be underestimated and recently the well-known serological cross-reactivity between

chamomile and mugwort (*Artemisia vulgaris*) was shown to have a clinical equivalent: sensitization to mugwort could be a primary risk factor for developing symptoms after ingestion of chamomile infusions (58).

In conclusion, even though type IV allergy to chamomile is found in > 50% of Compositae-sensitive patients in larger European studies (2, 7) and even though chamomile extracts are widely used in herbal remedies and cosmetics, the risk of sensitization/elicitation of dermatitis seems to be low based on published reports. Both chamomile oil, chamomile tea and extracts of SL-free chamomile cultivars may be allergenic. The risk involved in using these preparations in Compositae-allergic patients is unknown.

Chamaemelum nobile (L.) All. (Roman chamomile; INCI name *Anthemis nobilis*)

The drug, Flores Anthemidis, has anti-inflammatory and spasmolytic properties like German chamomile and is used for the same purposes: medicinal teas, wet compresses, herbal remedies and a host of 'natural' cosmetics (4, 10, 59). Roman chamomile contains, among other things, several SLs, the most abundant of which is nobilin, flavonoids, the allergenic α -pinene and limonene, and also bisabolol (4, 35, 52).

Roman chamomile has been a popular medicinal plant since the Middle Ages, especially in England, France and Belgium (4). 2 cases of contact-allergic nipple eczemas in breastfeeding women were reported from England: both women had applied Kamilloosan® ointment (suppliers Norgine Limited), which in the UK version contains extracts and oil of Roman chamomile instead of German chamomile, and both patients had a ++ + reaction to chamomile oil 0.1% pet. and negative reactions to other ingredients (Table 1) (60). Sensitization from compresses containing Roman chamomile has been reported in 2 SL mix-positive patients from Belgium and Portugal, whereas a French patient sensitized from both compresses of Roman chamomile and a homoeopathic preparation containing Roman chamomile oil was negative to SL mix (53, 59, 61). Presumably, cases of sensitization are primarily caused by SLs, but prolonged or repeated topical application seems necessary to sensitize with the tea because of its lower content of allergens (53). 3 of these 5 patients reported had weakly positive reactions to fragrance allergens and 2 to balsam of Peru (*Myroxylon Pereirae*), which may reflect cross-reactions to the above-mentioned terpenes that represent another group of possible allergens (59–61).

Anthemis cotula L. (dog fennel)

This plant has been used as a folk remedy like German chamomile, but not officinally (4). Dog fennel is both strongly sensitizing and irritant, but among more recent reports only 1 was possibly caused by the use of an *Anthemis cotula*-containing hand cream (51).

***Echinacea purpurea* (L.) Moench. (purple coneflower; INCI name *Echinacea purpurea*)**

Originally a medicinal plant to the North American Plains Indians, *Echinacea* has now become a very popular herb in both the USA, Australia and Europe (36, 62). It is mainly used internally and documented effects of this purported immunostimulant include prevention and treatment of upper respiratory tract infections and recurrent genital candidiasis (28, 36, 63, 64). Topical use may be indicated because of several experimentally proved wound-healing mechanisms (36). Side-effects are rare, but there is a risk of severe allergic reactions, including anaphylaxis (after oral administration), and contact dermatitis in atopic patients, especially if they are Compositae-sensitive (62, 63, 65). Underwood & Gaul found 4 patients with positive patch tests to *Echinacea*, but the plant may not be the primary sensitizer (33). Bruynzeel et al. saw 2 patients with positive patch test reactions to an ointment containing 10% *Echinacea* tincture (Table 1), and even though they were patch test negative to components of the ointment base, testing with plant extract was not performed, making the diagnosis of *Echinacea* allergy uncertain (24).

***Inula helenium* L.
(elecampane; INCI name *Inula helenium*)**

Elecampane is one of the oldest medicinal plants, used since Roman times and considered a panacea in the Middle Ages (4, 10). Both the root (*Radix Inulae/Radix Helenii*) and the leaves (*Folia Inulae*) are used medicinally, and according to Hausen the former is still used for diseases of the respiratory organs, as a vermifuge and as a stomachicum (4). Furthermore, helenin, which is a commercially available mixture of 3 SLs from elecampane, has been used as a parenteral anticatarrh medicine in Spain (66). The former topical use for skin diseases has been largely abandoned, but there seems to be a renewed interest in elecampane as a constituent of herbal cosmetics (4). Elecampane contains at least 17 SLs, the most important of which are the strongly sensitizing alantolactone as well as isoalantolactone (4). Even a 1% petrolatum extract of the plant may sensitize (67). External use of el-

ecampane is therefore associated with the greatest risk of not only contact dermatitis, but also more widespread immunological responses such as erythema multiforme-like eruptions (13, 68–70). Kim et al. reported a case of ulcerous contact stomatitis from a breath freshener widely used in Korea (Table 1) (69). The allergens were licorice root (*Glycyrrhiza uralensis*) and probably elecampane, though the use of high patch test concentrations of elecampane extracts introduced an element of possible irritation (69). Gil Mateo et al. reported a case of acute eczema due to a 'herbal bag', and Pazzaglia et al. another case of dermatitis due to a herbal massage liniment (13, 70). Both patients were positive to the SL mix and alantolactone; the latter patient may also have been sensitized to burdock milfoil or bay leaf present in the massage liniment, but was not tested with these (13). Bay leaf from another plant family (Lauraceae) contains both costunolide and dehydrocostus lactone, which together with alantolactone are the constituents of the SL mix (11).

***Inula viscosa* Aiton (sticky elecampane)**

Sticky elecampane is a folk remedy of Southern Spain and the only case reported is that of a young woman who treated her haemorrhoids with an infusion of the plant and quickly developed anal itching and a vesicular dermatitis of the hands and forearms (71). She was strongly patch test positive to 2 fractions of an ether extract of the plant as well as to the related elecampane, alantolactone and isoalantolactone (71). The 2 fractions may represent the formerly isolated SLs 2-desacetoxyxanthinin and inuviscolide (71).

***Saussurea lappa* Clarke (costus)**

Costus root oil was formerly used in the fragrance industry, but due to its content of the allergenic SLs costunolide and dehydrocostus lactone, the International Fragrance Association in 1982 advised against its use as a fragrance raw material (4). The allergy is thus mostly of historical interest though costus root oil is still commercially available (4).

***Tagetes patula* L. (French marigold)**

French marigold is first of all known for its content of the phototoxic and allergenic α -terthienyl (4, 72). Bilsland and Strong reported the 1st – and so far only – case of sensitization due to use of a herbal remedy containing this plant: an aromatherapist with intermittent vesicular hand eczema tested positive to a 1.5% (working) dilution of French marigold essential oil in grapeseed oil and

negative to both the last-mentioned and 8 other essential oils (73). The patch test reaction combined with a flare of her hand eczema and negative reactions in 7 controls points to the almost certain allergic nature of the dermatitis.

***Tanacetum parthenium* (L.) Schulz-Bip. (feverfew, motherherb; INCI name *Chrysanthemum parthenium*)**

This old medicinal plant, originally used, among other things, for fever, headache, stomach-ache and various gynaecological and obstetrical conditions, has become very popular as a lay remedy with a documented effect in migraine prevention (74–76). Commercial preparations of the leaves or fresh leaves are taken orally and in some patients the latter may cause severe inflammation of the mucous membranes of mouth and tongue with swelling of the lips (77). This could be an allergic contact stomatitis that should not be confused with mouth ulcers, which are one of the most common, but presumably systemically induced, side-effects (77). A 1% pet. extract of feverfew is one of the constituents of the Compositae mix, and furthermore it is the single extract that elicits positive patch test reactions most frequently in European Compositae mix-positive patients (2, 7). Apparently this is due to direct contact with the plant or cross-reactions with chrysanthemum (*Dendranthema*) rather than sensitization through herbal remedies (7).

***Taraxacum officinale* Weber (dandelion; INCI name *Taraxacum officinale*)**

Dandelion has been used as a folk remedy since the Middle Ages and is still used officinally in some European countries (4). Some of the many indications are chronic eczema, warts, liver diseases and gallstones (4). Furthermore, it is used in salads, as a spice in cooking and liqueurs, and in herbal cosmetics (4). The most important SL allergen is probably taraxinic acid-1'-*O*- β -D-glucopyranoside (4). The plant is weakly allergenic and prolonged and/or intensive contact seems necessary to sensitize (29). There are no reports on allergy from the use of herbal cosmetics containing this plant, but we have seen 2 cases of dandelion sensitization in younger males who had treated their warts with the milky plant juice. One of them had also handled dandelions for years because he used them as a pet food (e.g. for rabbits and tortoises), which is a common way to acquire this rare allergy (78). Furthermore, Mark et al. reported a case of a recurrent papular facial eruption due to dandelion tea prepared from loose leaves (79).

Table 2 Suspected sensitizing Compositae species in herbal remedies and cosmetics: their allergens and prevalence of sensitization

Plant	Allergen	Prevalence
Yarrow (<i>Achillea millefolium</i>)	SLs such as α -peroxyachifolid, flavonoids in the tea?	Rare (few cases)
Great burdock (<i>Arctium lappa</i>)	Actiopicrotin (SL)	Relatively rare, probably due to limited use
Arnica (<i>Arnica montana</i>)	SLs as, e.g., xanthalongin, helenalin, etc.	Frequent (> 100 cases)
Mugwort (<i>Artemisia vulgaris</i>)	Psilostachyin, psilostachyin-C (SLs)	Rare (1 case)
Marigold (<i>Calendula officinalis</i>)	Unknown	Frequent in 1 recent study, formerly rare
German chamomile (<i>Chamomilla recutita</i>)	Anthecotulide (SL), possibly bisabolol (sesquiterpene alcohol), pollen (CU from the tea), herniarin (coumarin), flavonoids?	Rare compared to frequent use (several cases)
Roman chamomile (<i>Chamaemelum nobile</i>)	SLs as, e.g. nobilin, possibly bisabolol (sesquiterpene alcohol), possibly terpenes	Probably rare compared to frequent use
Dog fennel (<i>Anthemis cotula</i>)	Anthecotulide (SL)	Rare (1 case) (recent reports)
Purple coneflower (<i>Echinacea purpurea</i>)	Unknown, but possibly pollen	Rare
Elecampane (<i>Inula helenium</i>)	SLs as, e.g., alantolactone and isoalantolactone	Relatively frequent (several cases)
Sticky elecampane (<i>Inula viscosa</i>)	Possibly 2-desacetoxy-xanthinin and inuviscolide (SLs)	Rare (1 case)
Costus (<i>Saussurea lappa</i>)	Dehydrocostus lactone and Costunolide (SLs)	Formerly frequent due to perfume
French marigold (<i>Tagetes patula</i>)	α -Terthienyl (thiophene)	Rare (1 case)
Feverfew (<i>Tanacetum parthenium</i>)	SLs as, e.g., parthenolide	Rare (0.4 of 270 patients surveyed)
Dandelion (<i>Taraxacum officinale</i>)	Taraxinic acid-1'-O- β -D-glucopyranoside (SL)	Rare (1 case from (tea))

SL = sesquiterpene lactones. CU = contact urticaria.

Conclusions

The key information is summarized in Table 2. The prevalence of sensitization from Compositae-containing therapeutic or cosmetic preparations is high for a few species such as arnica (the tincture) and elecampane, but low for the majority, especially the widely used German chamomile. Patch testing with constituents of the suspected products is not routinely performed, let alone testing with single allergens, but SLs are the most likely allergens in preparations based on alcoholic extracts or essential oils. The association between Compositae and cosmetic allergy reported by, e.g., Thune & Sandberg and Thomson & Wilkinson may be causal due to related substances such as monoterpenes, but it may also be due to concomitant sensitization to these 2 common groups of allergens (5, 80). At any rate, it is important to test with the relevant plant and the actual extract used in the suspected product to establish a causal association – and this is rarely done. Likewise, only a few case reports describe elicitation of dermatitis from the use of Compositae-containing remedies and cosmetics, and apart from the extensive studies on the allergenicity of the continental Ka-

millosan® preparation, the risk of using such products in Compositae-sensitive patients remains unknown (2, 11, 51).

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