

Hypersensitivity Reactions to Homemade Topical Preparations

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ABSTRACT Homemade topical preparations are becoming increasingly popular due to the widespread belief that herbal and natural products are a safer and better option in the treatment of various conditions. However, homemade topical preparations can precipitate allergic and irritant reactions, depending on the herbal composition of the preparation. Hypersensitivity reactions to such preparations range from contact allergic dermatitis, contact irritant dermatitis, contact urticaria, toxic reaction, photosensitivity, and phototoxic reaction. In Europe, and especially in the Mediterranean area, medicinal herbs from the Compositae family and aromatic Mediterranean herbs are most frequently used in the formulation of topical preparations. Although plants are regarded as strong sensitizers, the number of reported cases of hypersensitivity reactions is relatively small. The problems are limitations in diagnostics due to the lack of necessary patch test substances and the danger of active sensitization during testing. Caution is required in patients prone to allergies and those with existing dermatoses, who should be advised to use registered preparations. The first step in management is cessation of exposure, followed by implementation of topical corticosteroids. Systemic corticosteroid therapy is reserved for more severe cases.

KEY WORDS: homemade preparations, *Compositae* family, *Lamiaceae* family, hypersensitivity reaction

INTRODUCTION

Herbal medicine has its origins in ancient cultures. It is based on the use of herbs for the treatment of various disease and enhancement of general health and wellbeing. Any plant that can be used for medicinal purposes is considered a medicinal herb, and the term medicinal herb is therefore relative and based on utility, regardless of if it is medically proven or not. Clearly, this raises the question of how safe herbal treatments and products are. Today, there is a popular belief that medicinal herbs are harmless, but many

studies show otherwise. Some plants contain pharmacologically active substances, but a far greater number contain toxic substances and/or are capable of interacting with other drugs.

The results of a study from 2013 showed that approximately 95% of women and 75% of men use cosmetics daily (1). The use of medicinal herbs and homemade botanical products has increased in recent years, especially in Western societies. One of the most common motives for their use is

curiosity. It is commonly thought that botanical products, especially homemade ones, are safe. Many people tend to use natural ingredients, which they prepare by themselves to make sure to use products without chemicals and/or harmful ingredients. Other reasons people use homemade preparations are the search for alternative treatments because conventional therapies had failed them, the perceived safety of botanical products, and mistrust in traditional topical products (2). Every day, there are more and more people who tend to choose these preparations because this matches their values, beliefs, and philosophical orientation to life and health.

There are about 250 recognized families of contact-sensitive plants in Europe. Of these, more than 200 belong to the *Compositae* family (3). We systematically reviewed hypersensitivity reactions to plants belonging to *Compositae* family and other families of plants, which are common ingredients of homemade topical preparations. The PubMed/MEDLINE database was searched, employing the search terms "medicinal herbs" and "hypersensitivity reaction". A hypersensitivity reaction to a topical homemade preparation can produce a range of reactions from contact allergic dermatitis, contact irritant dermatitis, contact urticaria, toxic reaction, photosensitivity, and phototoxic reaction (Figures 1-6). Only articles written in the English language were evaluated. We also scrutinized citation lists from retrieved articles.

CLINICAL FEATURES

The clinical picture resulting from topically applied homemade preparations varies based on their composition as well as on individual risk factors for hypersensitivity reactions such as atopic background, previous documented skin sensitization, degree of damage of the skin barrier, and preexisting dermatoses (such as for example stasis dermatitis or leg ulcers). The clinical picture resulting from homemade preparations can manifest either as worsening of a previous dermatitis or as development of a new dermatitis. Different cutaneous symptoms and/or signs often present, such as itching and burning sensation and deepening of the allergen/toxin erythema, swelling, vesiculation, ulcerations, and even necrosis in severe cases. Although all types of dermatitis generally share common features, the classic eczematous stages in contact dermatitis (allergic and irritant) are most readily identifiable.

CONTACT DERMATITIS

Contact dermatitis is an inflammatory skin reaction to irritating agents or allergens that come in

contact with the skin. We distinguish between more prevalent, non-allergic, irritant contact dermatitis (ICD) and allergic contact dermatitis (ACD) (4). ICD is caused by use of topical preparations in about 80% cases (5). Homemade topical preparations contain various plants or plant extracts that may cause irritant contact dermatitis with their specific chemical properties. Acute ICD is caused by toxins from plants and is characterized by a rapid onset (within minutes to a few hours) after exposure, a rapid clinical course, and usually also a rapid resolution; it is monomorphic and often presents with very intense clinical symptoms such as erythema, papules, and blisters. Chronicity occurs when the skin continues to be exposed to the allergen/irritant, thereby preventing spontaneous healing of the dermatitis, or when the dermatitis persists even in the absence of the culprit agent. From a morphological perspective, it is characterized by eczematous plaques, hyperkeratosis, fissures, scaling, and lichenification.

Plants belonging to *Compositae* family are the most popular ingredients of homemade topical preparations. Despite their healing properties, they can induce hypersensitivity reactions through sensitization related to the sesquiterpene lactones in their composition (6). Calendula or marigold (*Calendula officinalis*) is a plant often found as an ingredient of homemade topical preparations. Its flowers contain triterpenoids, which give it anti-inflammatory properties. It is commonly used for treatment of minor inflammations of the skin as well as to promote healing of more superficial wounds (5). Despite its generally low sensitization potential, it can be a cause of ACD in susceptible individuals (7). Chamomile (*Chamomilla*) is another frequently used plant from the *Compositae* family, and cross-reactions with other members of the family such as mugwort (*Artemisia vulgaris*) (8), chrysanthemum (*Chrysanthemum*), common yarrow (*Achillea millefolium*), and marguerite (*Argyranthemum*) are common (7). There are several different species, of which German chamomile (*Chamomilla recutita* L.) and Roman chamomile (*Chamaemelum nobile* L.) have medicinal properties, while stinking or dog chamomile (*Anthemis cotula* L.) is no longer in use due to its strong sensitization potential and irritative properties (7). The distinguishing parameter between the two is their sensitization potential; Roman chamomile contains substances such as flavonoids and limonene and therefore has moderate (mild) potential (7). There were also several reports of contact allergic nipple eczema after using Roman chamomile in nursing mothers in the United Kingdom (9). German chamomile, also known as true chamomile, has a low sensitization potential, has anti-inflammatory and

sedative effects, and can be consumed in the form of tea, extract, or an essential oil in the treatment of skin disorders and for stress relief (10). It has a low sensitization potential; skin reactions may therefore occur if contamination with stinking chamomile occurs (7). A few cases were reported in which contact urticaria and more severe reactions occurred after topical use or ingestion (11). Arnica (*Achillea millefolium*) is often used for treatment of various sport injuries, venous circulatory disorders, neuralgia, etc. It has anti-inflammatory and wound healing properties (Figure 1) (7). The whole plant, from the root to the flower, can be used in production of topical preparations, usually in a form of ethanol-based tincture (3,7). Its strong sensitizing potential is due to sesquiterpene lactones, which is also related to the occurrence of cross-reactions with other *Compositae*s. Even though arnica is a part of the *Compositae* mix, patch tests fail to identify all positive patients (12). Yarrow (*Arnica montana L.*) is another plant from the *Compositae* family that has been in use for some time. Its healing properties are so well known that it is traditionally named "soldier's woundwort" (3). Allergic reactions to yarrow are rarely reported, but caution must be taken due to cross-reactions in patients sensitive to *Compositae* (7).

Lamiaceae is a family of flowering plants known for their medicinal and aromatic properties. Many species from this family are represented in the Mediterranean region, and they are therefore indispensable ingredients of topical preparations characteristic of this area (13). Despite their healing properties, irritant and allergic reactions to the plants of the *Lamiaceae* family have been reported, as well as cross-reactivity inside the family (14-16). Rosemary (*Rosmarinus officinalis L.*), a member of the *Lamiaceae* family, has spasmolytic properties and is used in the form of dried leaves or essential oil. Applied to the skin or used in aromatic baths, it has a positive effect on myalgia and arthralgia (17). Additionally, it was found that topical application of rosemary oil had positive effect on hair regrowth in androgenic alopecia (18). Thyme (*Thymus vulgaris*) has the same properties but is less frequently used. To date, there have been a few reported cases of allergic contact dermatitis due to rosemary or thyme, and these were individual forms or cross-reaction forms (14). Sage (*Salvia officinalis*) as well as rosemary and thyme, belongs to the *Lamiaceae* family. Its leaves have anti-inflammatory, antimicrobial, and antioxidant properties and are used in treatment of various skin injuries and inflammation, dyspepsia, laryngitis, etc. Additionally, it has a positive effect on memory and relieves pain (19,20). In the limited number of reported cases of contact allergy to topical sage preparations, only one case is credible

(16). In the remaining cases, it is impossible to ascertain whether true sage was used in diagnostics (21). Lavander (*Lavandula angustifolia*), another plant from the *Lamiaceae* family, is used in cosmetics, for food flavoring, and in traditional medicine. Essential lavender oil has sedative, antidepressive, antimicrobial, hypnotic, and analgesic properties. Skin conditions such as eczema, psoriasis, and skin injuries respond well to the use of lavender oil (22). Although lavender absolute and the different types of lavender oil vary in their specific compositions, they share a common major constituent in linalool. With the exception of spike lavender oil, they also contain a significant amount of linalyl acetate. Both linalool and linalyl acetate have been identified as potent contact allergens when oxidized to form compounds such as hydroperoxides (23,24).

Laurel/Bay (*Laurus nobilis L.*) is a Mediterranean plant from the *Lauraceae* family, and its leaves are an important ingredient of Mediterranean cuisine as well as homemade topical remedies. Laurel oil has anti-inflammatory and pain reducing properties, and it is therefore used in treating inflammatory skin conditions and joint pain (25). Contact allergy has been described mainly to the essential bay leaf oil in masseurs, aromatherapists, and in patients who applied the plant extract for arthralgia (25,26).

Propolis is a resin-like substance produced by bees from the buds of poplar and cone-bearing trees. It is famous for its antimicrobial properties and treatment of various skin conditions like burns, ulcers, warts, psoriasis, etc. (Figure 2). Propolis has a complex composition that varies based on the geographic location of where the bees collect the exudates. Among other things, it contains flavonoids, aromatic acids, and their esters (27). The most important allergens in propolis are esters of caffeic acid (28). Allergic contact dermatitis is often observed with a sensitization frequency greater than 2% for European countries (28). On the other hand, immediate irritant reactions after topical use are rarely seen. Cross reactivity with *M. pereirae resin* (balsam of Peru) has also been reported (28).

Tea tree oil is an essential oil from the tea tree plant (*Melaleuca alternifolia*) and is a very popular ingredient in today's cosmetic products and homemade topical preparations. It has found its use in the treatment of a huge number of skin conditions, from wounds and burns to acne and skin infections (3). Tea tree oil contains 1,8-cineole and terpinene-4-ol, to which antimicrobial and healing properties have been ascribed (7). Due to d-limonene, alpha-terpinene, aromadendrene, terpinene-4-ol, p-cymene,



and alpha-phellandrene, tea tree oil is a potent allergen which, when exposed to light, heat, or oxygen, can form compounds of even greater sensitizing potential (7).

Aloe vera (*Aloe barbadensis*) is a succulent plant from the *Liliaceae* family. Its gel is used in treatment of burns, skin irritations, and inflammation. It also helps in achieving a youthful appearance by moisturizing and reducing the expression of visible signs of aging (29). Allergic contact dermatitis due to other *Liliaceae* are well known, but reactions resulting from the application or intake of Aloe vera are extremely rare (29). It may cause redness, burning, a stinging sensation, and, rarely, generalized dermatitis in sensitive individuals (29). Allergic reactions are mostly due to anthraquinones such as aloin and barbaloin (29).

Garlic (*Allium sativum*), a vegetable that can be found in almost every kitchen, is very often an ingredient for homemade preparations, both external and internal, and has been used for thousands of years. Its "medicinal benefits" are numerous, so it is used to treat illnesses such as diabetes and its complications, hypertension, hyperlipidemia, inflammation and infections, asthma, various skin conditions, etc. Raw garlic is a potent irritant and can result in burn wounds, especially if applied under occlusion. Those wounds have been described as erythematous, vesicobullous lesions with defined borders (30). The severity of the condition depends on the concentration of applied garlic, duration of exposure, treated area, pre-existing skin conditions, and individual characteristics (31). Besides irritative reactions caused by garlic, it can also cause ACD, mostly affecting people who cut and handle fresh garlic. The skin lesions are present on the tips of the thumb, index, and middle

fingers of the non-dominant hand (which typically hold garlic bulbs during the cutting). Diallyldisulfide, alliin, allylmercaptan, and allylpropyldisulfide are responsible for causing these reactions (32). Similar skin lesions are also observed in the patients handling hot peppers (*Capsicum*) (33).

PHOTOALLERGIC AND PHYTOTOXIC REACTIONS

Photosensitivity reactions arise as a result of sun exposure of the skin that has been in contact with a photosensitive substance or photoallergen. Lesions usually heal when contact with the photoallergen is cut off, but they can progress to chronic actinic dermatitis (34). Phytophotodermatitis presents with exanthema, pruritus, erythema, vesiculation, and residual hyperpigmentation, and appears in light-exposed areas. Furocoumarins or psoralens, which are potent photosensitizing agents, are the main culprits of plant phototoxicity (33). Psoralens react to UVA radiation, inducing photochemical reactions that cause damage and injury to the epidermis (35). The fig (*Ficus carica L.*) is a Mediterranean plant with edible fruits that are frequently used to treat constipation (36). Its leaves are traditionally used for skin conditions such as eczema, vitiligo, psoriasis, warts, etc. (Figure 3). Like the sap of the plant, they contain psoralen and other furocoumarins that make the epithelium sensitive to sunlight, causing burns, erythema, pruritus, and edema (37). The fig plant contains keratolytic enzymes, which further facilitate the effect furocoumarins have on epithelial cells (38). Psoralen can also be found in essential oils that have anti-inflammatory, antimicrobial and analgesic properties (39). Essential oils are a common ingredient of cosmetic products.

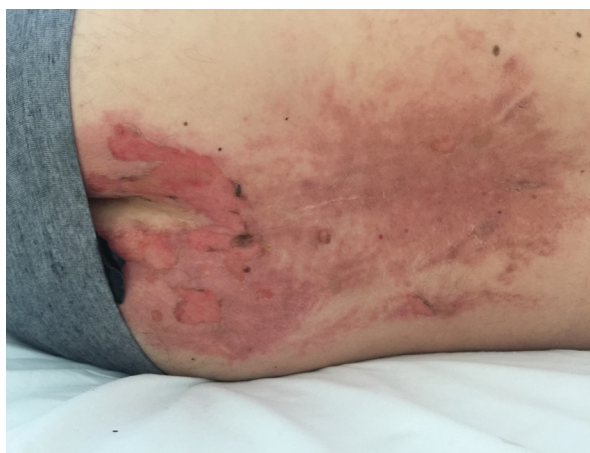


Figure 1. Acute contact allergic dermatitis to homemade cream used under occlusion for back pain made of jojoba oil, dried arnica, beeswax, shea butter, and filtered water.

*The offending allergen was arnica, proved by a patch test.



Figure 2. Contact allergic dermatitis to homemade cream made of melted beeswax, calendula oil, lavender oil, and propolis.

*The offending allergen was propolis, proved by a patch test.



Figure 3. Acute irritant reaction after occlusion of fig sap applied directly on a common wart.

Bergamot orange (*Citrus bergamia L.*) is a tree from the *Rutaceae* family that produces orange-sized lime-like citrus fruit. Its essential oil, when exposed to sunlight, causes berloque dermatitis (Figure 4) characterized by linear patterns of hyperpigmentation which lag on the skin (40). Cases of phytophotodermatitis were also reported after contact with citrus fruit (41).

CONTACT URTICARIA

Contact urticaria presents with erythematous, edematous papules or “weals” (42). There are many provoking factors, and urticaria is a common condition (42). However, contact urticaria, as a hypersensitivity reaction to topical preparations, is relatively rare. Common examples of a plant causing contact urticaria are stinging nettles (*Urtica dioica*), castor beans (*Ricinus communis*), citrus, garlic (*Allium sativum*), etc. (33).

DIAGNOSTIC APPROACH

The approach to a patient with a hypersensitivity reaction should always start with a detailed disease history and then with physical examination followed by various testing procedures that will likely confirm the diagnosis. Taking the patient’s history should allow us to more easily identify the potential triggers and to establish a connection with the disease, determine if herbal topical preparations and remedies were used and in which quantities, duration and for what purpose were they used for (Figure 5 and Figure 6). Upon suspicion of a hypersensitivity reaction to homemade topical preparations, a patch test, which is the golden standard for diagnosis of ACD, and the semi-open patch test for testing with the patient’s own products, should be performed. It is indicated in any patient with acute recurrent, chronic, pruritic, eczematous, or lichenified dermatitis (43). Testing

for plant allergy is challenging because of the limited number of commercially available standardized patch test allergens, and numerous cases of contact allergy may therefore go unrecognized. As previously described, plants contain strong sensitizers and irritants, and testing could lead to unwanted positive reactions. Testing with plants or individual extracts can result in active sensitization. When patch testing is performed, it is very important to evaluate the relevance of positive patch test reactions.

For detection of contact allergy, many centers perform patch testing with a “standard” baseline series (European Baseline Series, S-1000). Besides fragrances, preservatives, and lanoline, which are frequently used in cosmetic and pharmaceutical products, it also contains propolis and sesquiterpene lactone (SL), which is isolated from the family *Compositae* (44).

In diagnostics aimed at detecting dermatitis caused by herbal preparations, testing with a plant series (PL-1000) of allergens is recommended. Plant series contains 18 plant extracts and substances, including Roman and German chamomile, arnica, yarrow, propolis, and a SL mix (44). Positive patch test results are most frequently found for plants belonging to families such as *Alliaceae*, *Anacardiaceae*, *Cactaceae*, *Compositae*, *Cruciferae*, *Hennadiaceae*, *Lilliaceae*,



Figure 4. Phototoxic reaction to homemade hair lotion made of coconut oil, shea butter, bergamot essential oil, lime essential oil, tea tree essential oil, and baking soda.

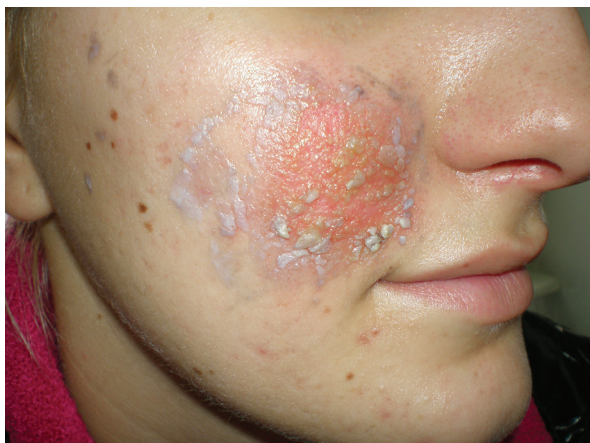


Figure 5. Acute irritant contact dermatitis to homemade cream made of pineapple and coconut.

Orchidaceae, *Primulaceae*, *Urticaceae*, etc., with the strongest sensitizers being catechols and lactones (45). In addition to these two series of allergens, it is also possible to patch test with a cosmetic series (C-1000) that, among other sensitizers, contains oxidized tea tree oil, peppermint oil, and turpentine oil (44).

The *Compositae* (*Asteraceae*) family is probably the most important skin-sensitizing plant family, resulting in the highest number of positive patch test results (45). However, a study by Green and Ferguson found that only 35% of patients with *Compositae* allergy were detected using a SL mix, which is included in the European Baseline Series and Plant Series (46). Werth *et al.* conducted a study using a *Compositae* mix and found it more sensitive in recognizing patients with *Compositae* allergy, with sensitivity reaching 90% in comparison with 42% for the SL mix (47). On the other hand, a study by the Swedish Contact Dermatitis Research Group estimated the difference in sensitivity between these two mixes at only 0.4% more recognized cases of *Compositae* allergy in favor of the *Compositae* mix (48). Differences in study results are probably due to phytogeographical sesquiterpene lactone variations.

TREATMENT

The treatment of reactions to homemade preparations consists of investigation and avoidance of trigger factors, skin care, and pharmacotherapy. The most important therapeutic approach is to stop exposure to the allergen/irritant. Acute dermatitis is generally moist and needs to be treated with a hydrophilic preparation (gel, lotion, cream), whereas chronic disease is more likely to require a water-in-oil-based preparation (ointment). Topical corticosteroids are the first line of treatment. They have both anti-inflam-



Figure 6. Toxic reaction to high-concentration to essential oils (peppermint, eucalyptus, coconut) used for a relaxing bath.

matory and immunosuppressant effects. The topical calcineurin inhibitors, tacrolimus, and pimecrolimus are suggested for contact dermatitis, particularly on the face, the genital area, and skin folds. Oral corticosteroids can be used for a short time (a maximum of 2 weeks) to treat acute severe reaction to homemade preparations or in case of systemic contact dermatitis (hematogenous contact dermatitis) (49). Perioral antihistamines are usually prescribed to relieve itching, but there is no evidence that they have an effect on pruritus in contact dermatitis. Peroral antihistamines are suggested for the patients with contact urticaria and/or widespread urticarial reaction to homemade preparations.

CONCLUSION

There is a misconception that everything that is natural must be safe. The number of reported cases of contact dermatitis seems small when compared with the widespread use of botanic remedies. Homemade preparation of herbal topical preparations most frequently implies the use of plants from the *Compositae* family, while typical aromatic Mediterranean herbs with medicinal properties are also used in the Mediterranean region. Care needs to be taken when using herbal homemade topical preparations and essential oils due to their common association to allergic, irritant, or toxic skin reactions. Patients should be warned of possible adverse reactions to the use of such preparations, and special care should be paid to patients with damaged skin and eczema, as they have a high risk of multiple sensitizations. Additionally, patients with *Compositae* allergy should avoid herbal remedies and natural cosmetics. The biggest problem is the diagnosis of hypersensitivity reactions to homemade topical preparations. The number of

commercially available allergens required for skin testing is limited. Testing is complicated by the occurrence of irritations due to the irritating properties of certain plants and the possibility of active sensitization. Considering the growing popularity of these preparations, there is a need to improve the series of allergens used in patch testing and take into account variations in SLs that often lead to negative test results. For now, possible changes are the addition of a *Compositae* mix to the baseline series in routine testing or replacement of the SL mix with the *Compositae* mix in the baseline series due to its slightly higher sensitivity.

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