Plant Contact Dermatitis

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Domenico Bonamonte, Caterina Foti, Giulia Gullo and Gianni Angelini

From the pathophysiological perspective, plants can induce various clinical skin conditions (Table 16.1). Plant contact dermatitis that, being among the most common forms, is of the greatest clinical concern, is caused by contact with flowers, trees, grass, fruits, weeds, vegetables, and pollens [1–15]. In general, in both occupational and non occupational contexts this contact is direct, while indirect contact through medicaments and cosmetics containing plant extracts, or various plant-based foods (teas, spices, etc.) is less frequent.

16.1 General Information and Incidence

Bearing in mind the huge number of plants in existence (more than 300,000), surprisingly enough the number of plant families implicated in phytocontact dermatitis is relatively limited. However, it is difficult to estimate the incidence of plant contact dermatitis; generally considered low, it is probably underestimated for a number of reasons, among which the remarkable number of plants involved, the difficulties in making a taxonomic classification of them, and the considerable number of substances implicated, often belonging to different parts of the same plant. Yet other reasons are the lack of a peculiar clinical picture, except in some exceptional cases, and the difficulty in tracing the etiopathogenic path, that may be a long and complex process.

The cases of plant contact dermatitis that come to our observation are likely only a small proportion of those that actually occur. Rural workers and florists normally know the offending agent but often do not report the incident and just avoid subsequent harmful contacts. On other occasions workers do not mention their dermatitis because they regard it as an occupational risk and so the resulting disability is considered insufficient to require the suspension of their working activities.

It is also important to remember the possibility that the allergen could be carried far from the plant of origin and so the resulting dermatitis might not be recognized as of vegetable origin. That is what occurs in the case of dermatitis forms induced by pollens (particularly anemophylous substances in suspension in the atmosphere) or of airborne phytocontact dermatitis,

D. Bonamonte (✉) · C. Foti · G. Gullo
Department of Biomedical Science and Human Oncology, University of Bari "Aldo Moro", Bari, Italy
e-mail: domenico.bonamonte@uniba.it

G. Angelini
Professor of Dermatology, University of Bari "Aldo Moro", Bari, Italy

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Table 16.1 Pathophysiological mechanisms of phytodermatoses

1.	*Traumatisms*
	Pricks from thorns
	Inclusions of vegetable material in the skin
	Microtraumatisms of hairs and beard
2.	*Infections (pseudophytodermatoses)*
	Plants as vectors of infections (bacteria, fungi and parassites) and of pesticides, insecticides, and fungicides
3.	*Toxicities in general*
	Allergy to foods (urticaria)
	Allergy of respiratory type (rhinitis, asthma)
	Allergy to medicaments of vegetable origin
4.	*Contact phytodermatitis*
	Irritant contact dermatitis
	Allergic contact dermatitis
	Contact phytophotodermatitis

or dermatitis linked to contact with an animal or object that has previously come in contact with the plant, for instance.

Clearly, the incidence of phytodermatitis depends on the environmental, geographic and climatic conditions. In the USA, for example, there is a high population incidence of sensitization to the *Toxicodendron* genus and other plants of the Anacardiaceae family, while in Denmark there is a common incidence of dermatitis induced by primin. In the United Kingdom the culprit is often geraniums while in the Netherlands it is most often tulips. The frequency also depends on the season. Instead, the climate factor has no importance when the plant is grown in greenhouses or if the allergenic activity persists even in the dry plant (as in the case of poison ivy).

In a study of 1752 patients with occupational dermatoses, Fregert reported an 8% incidence in women and 6% in men of reactions to plant-derived products [16]. Ducombs and Schmidt estimated that perhaps 5–10% of all cases of contact allergy seen in European dermatology clinics are due to plants or their products [6]. In Europe, most phytodermatoses are of occupational origin and floristry appears to be the occupation at highest risk [17, 18]. Clinical and allergologic evaluations performed in four floriculture centers, where chrysanthemums, poinsettias, geraniums, roses, and *Alstroemeria ligtu* were cultivated, revealed that about 25% of 200 workers were affected by mechanical and physical cutaneous manifestations, 12% by irritant dermatitis from chemical agents, 89% by pseudophytodermatitis due to the use of pesticides, and only 5% by allergic plant dermatitis [13].

Apart from the various occupational activities, other categories at risk of plant contact dermatitis include hobby gardeners, housewives, and those who come in contact with plant materials. Indeed, any person enjoying leisure pursuits in the gardens or countryside (campers, walkers, children playing) comes in contact with plant material.

16.2 The Nature of Vegetable Substances

Irritant or sensitizing substances responsible for phytodermatoses are a highly heterogeneous group of components that are not essential to the plant, nor do they generally contribute actively to the plant metabolism. In short, those in question are not lignin, cellulose, or chlorophyll but secondary components.

Depending on the case, the substance implicated may be present in all the parts of the plant, so contact with any part will provoke the dermatitis, or else only in one part of the plant. In

some cases the causal substance acts on the skin simply through skin contact, whereas in others the plants needs to be chopped or in some way damaged for the pathogenic substance to come in contact with the skin. For example, the entire surface (stalks, leaves and roots) of primula, some varieties of which are highly allergenic, is covered by very fine hairs containing the allergen primin, that causes sensitization even when the skin just brushes against it. By contrast, the artichoke is sensitizing only when it is cut and releases the juice, whereas contact with the leaves or stalk is not sufficient to provoke a skin reaction. Another case in point is tulip, in which the pathogenic fraction is present in sufficient concentrations only in the bulb and so it is only when handling the bulbs that the subject can be sensitized. Thus, the pathogenic substance is synthesized at a certain stage of the plant growth and so the plant is sensitizing only during some periods of the year.

It is the specific vegetable genetic factors that determine the presence or not of the harmful substance. That is the reason for the possible cross-reactions among different varieties of the same family or the same species, and also, vice versa, the frequently very confined specificity of the pathogenic substance, limited to a single plant variety in that species.

The incriminated substances in the irritant mechanism underlying plant contact dermatitis can be acids (formic, acetic, oxalic, malic and citric acid), glucosides, proteolytic enzymes or crystalline substances (e.g. calcium oxalate microcrystals that penetrate the epidermis, present in the bulbs of tulips and hyacinths).

Sensitizing substances are above all phenol and terpene fractions constituting the vegetable oleoresins. These oleoresins contain an antigenic mosaic, and it is sometimes possible to purify them and identify the chemical constitution of the allergen.

In short, the risk of contracting a plant contact dermatitis depends on various factors: the type of plant, its diffusion and the concentration of offending substances it contains, as well as the patient's working activity, number and duration of contacts, together with climatic factors, the individual skin integrity and characteristics, and degree of susceptibility [1–12, 19]. Among the climatic factors, the season plays an important role; one example of this is phytophotocontact dermatitis due to *Ficus carica* (fig tree) [20], a plant cultivated widely in the Southern Mediterranean area. We observe cases of contact dermatitis in the late spring, the summer and early autumn because it is only during these months that the fig tree contains the various irritant and sensitizing substances (furocoumarins), present in the leaves, branches and skin of the fruit (but not inside the fruit). For this reason the dermatitis is most evident (intense erythema and edema, vesico-bullous lesions) in the late spring and especially in the summer due to the greater concentration of furocoumarins (8-methoxypsoralen) in the plant and the greater intensity of UVA. Instead, in the autumn when these conditions are less marked, the clinical picture is much more modest (mild erythema and a minor or no exudative component). Naturally, contact with the plant during the winter poses no dangers [20].

16.3 Clinical Features

The clinical aspects of phytodermatoses cover a very wide spectrum, depending on many factors. The vegetable substances implicated can induce the entire range of clinical aspects of contact dermatitis. Hence the lack of peculiar clinical pictures except in some rare cases. Even irritant contact dermatitis is not easy to differentiate from contact allergy.

The severity of phytodermatoses, as stated above in reference to dermatitis due to *Ficus carica*, is highly variable, spanning from modest forms to severe and chronic forms that have repercussions on the occupational, psychic and therapeutic spheres. The clinical pictures range from simple pruritus through erythemato-vesicular lesions to severe bullous or chronic lichenoid pictures. There can also be keratotic lesions, fissuring and pigmentation, as well as urticarious areas.

The dermatitis generally affects exposed sites, and this complicates the differential diagnosis between phytodermatitis and phytophotocontact dermatitis. It is also possible that the substance implicated may be carried to various body parts by the hands. Above all in cases of contact irritation, the lesions may be linear or figured, that could reproduce the shape of contact.

16.3.1 Irritant Contact Dermatitis

Irritant forms can be of a mechanical or chemical nature.

16.3.1.1 Mechanical Irritation

Various plants can provoke macrotraumatic lesions by mechanical means owing to the presence of prickles, spines, and thorns (Figs. 16.1, and 16.2). Others, due to the knife-like morphology of their leaf edges, can cut the skin. Although these are generally trivial and self-limiting events, such mechanical trauma can lead to the development of infections, sores and

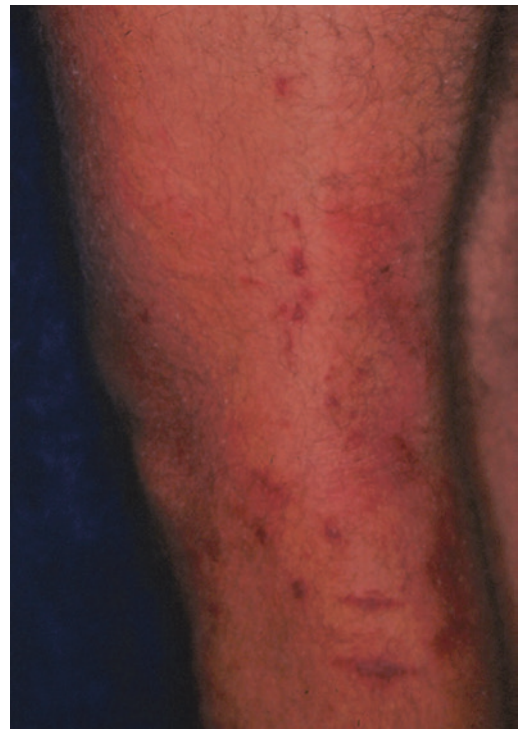

Fig. 16.2 Irritant (mechanical) contact dermatitis due to spines of plants

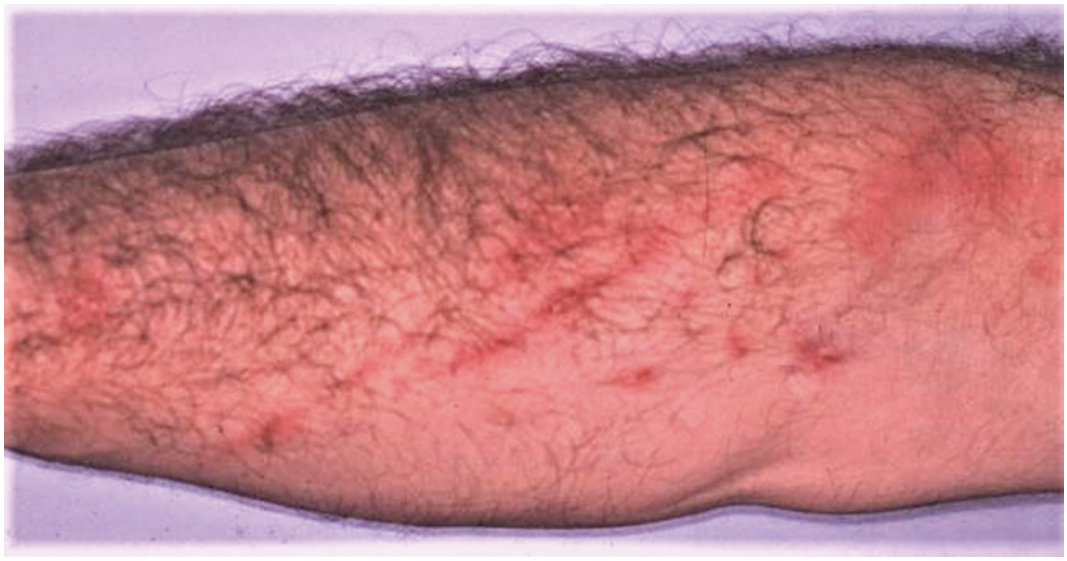

Fig. 16.1 Irritant (mechanical) contact dermatitis due to spines of plants

granulomatous lesions (foreign body granulomas), that have an insidious clinical course. For example, in arid regions, cacti (of the Cactaceae family) can cause granulomas [21].

Such traumas, that are very easy to diagnose, need to be differentiated from microtraumatisms due to bristles or barbs (trichomes or glochids) in particular on leaves. These structures penetrate the superficial layers of the skin and cause papular dermatitis, prurigo and even urticaria. In Israel, "sabra dermatitis" has been described, caused by contact with the prickly pear or Indian (or Barbary) fig (*Opuntia vulgaris* Miller, *O. ficus indica* Miller, Cactaceae family) [22]. This dermatitis, that is highly pruriginous, is observed from July to October in workers picking Indian figs; the rash affects the hands but can extend to the whole skin. Skin penetration by the glochids that cover the fruit can cause a clinical skin picture that mimics chronic eczema or scabies. Moreover, on very windy days the glochids can detach from the plant and be carried far away, thus making the etiological diagnosis very difficult.

Also microtrauma due to calcium oxalate needle crystals (raphides) causes a characteristic dermatitis similar to that caused by glass fiber [23]. The skin penetration by the raphides can be accompanied by intracutaneous injection of the plant sap, causing contact irritation or allergy to the sap constituents. In the same way, calcium oxalate raphides in dumbcanes (*Dieffenbachia* spp., Araceae family), a common decorative house plant, can induce an urticarial dermatitis or bullous and edematous stomatitis in people whose hands get damaged by plant material or who accidentally chew the leaves. The mouth reaction makes the victim speechless (hence the common name of the plant) and the airway may become obstructed. This severe reaction is due to a protease present in the plant sap named dumbcane [24, 25].

16.3.1.2 Chemical Irritation

Many plants can induce chemical contact irritation due to fluids or crystals in hairs or in other portions of the plant. Vegetable irritants range from weak (requiring repeated exposure and skin abrasion to exert their effects) to very strong (where microgram quantities elicit an inflammatory process), like the Euphorbiaceae, for example. Obviously, in such cases the mucosa may be affected, too, and an ocular irritation can arise, causing very severe damage.

The sites of contact are affected by acute (a few hours after contact) or chronic dermatitis. The clinical picture is polymorphous, ranging from simple skin dryness, through fissuring and hyperkeratosis to inflammatory reactions with erythema, edema, papules, vesicles and in cases of severe irritation, even blisters (in cases of contact with *Euphorbia* spp., Euphorbiaceae family), up to superficial necrosis and ulceration. From the subjective point of view, the symptom is pain rather than itching. The sap of *Agave americana* (Fig. 16.3) induces a characteristic papular irritant contact dermatitis (Fig. 16.4) [26], while contact with the leaves of *Zea mays* (maize) can give rise to a figured dermatitis with erythemato-purpuric lesions, as we have often observed (Fig. 16.5).

Mainly irritant plants belong to the families of plants such as Ranunculaceae (buttercups, anemones), Brassicaceae (Crucifers), like *Brassica nigra* (mustard) and *Sinapis alba* L., and Euphorbiaceae, such as croton (*Croton variegatum*). Croton oil, a well known blistering agent (mechanical acantholysis), induces bullous lesions with a clear content that rapidly become purulent. Other families inducing irritation are Rutaceae and *Dieffenbachia, Urtica* (Figs. 16.6, and 16.7)*, Philodendron,* and *Capparis spinosa* [27]. The culprit chemicals are diterpene esters (phenol esters) in Euphorbiaceae [1], and glucosides (ranunculin) in Ranunculaceae [28].

16.3.2 Allergic Contact Dermatitis

Allergic contact dermatitis can result from direct and/or indirect contact (contaminated objects including door knobs, shoes, clothing, work tools, pets, etc.) with plants; various plant extracts contained in cosmetics, foods, industrial products, and herbal remedies (Fig. 16.8) may also be the causes [29–31].

Fig. 16.3 *Agave americana*

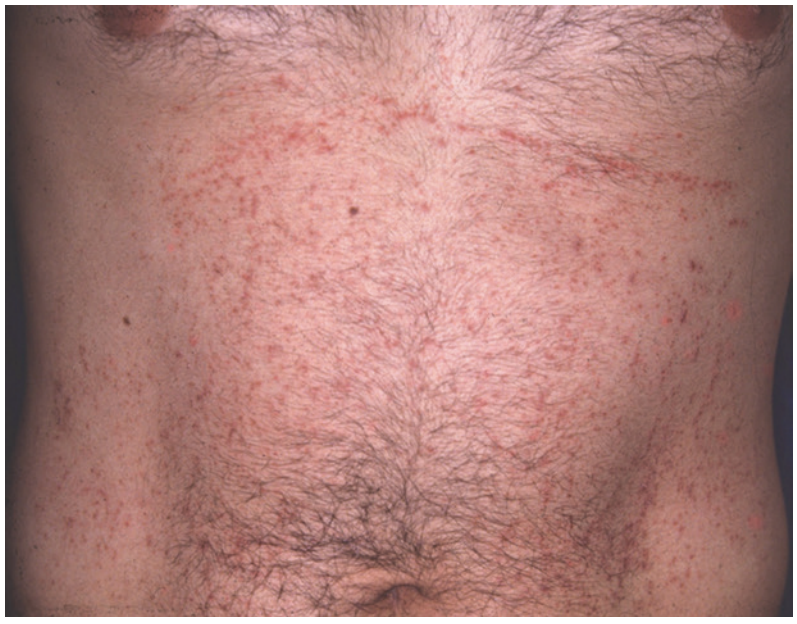

Fig. 16.4 Papular irritant contact dermatitis induced by rubbing a cut leaf of *Agave americana* on abdomen (self-artefact)

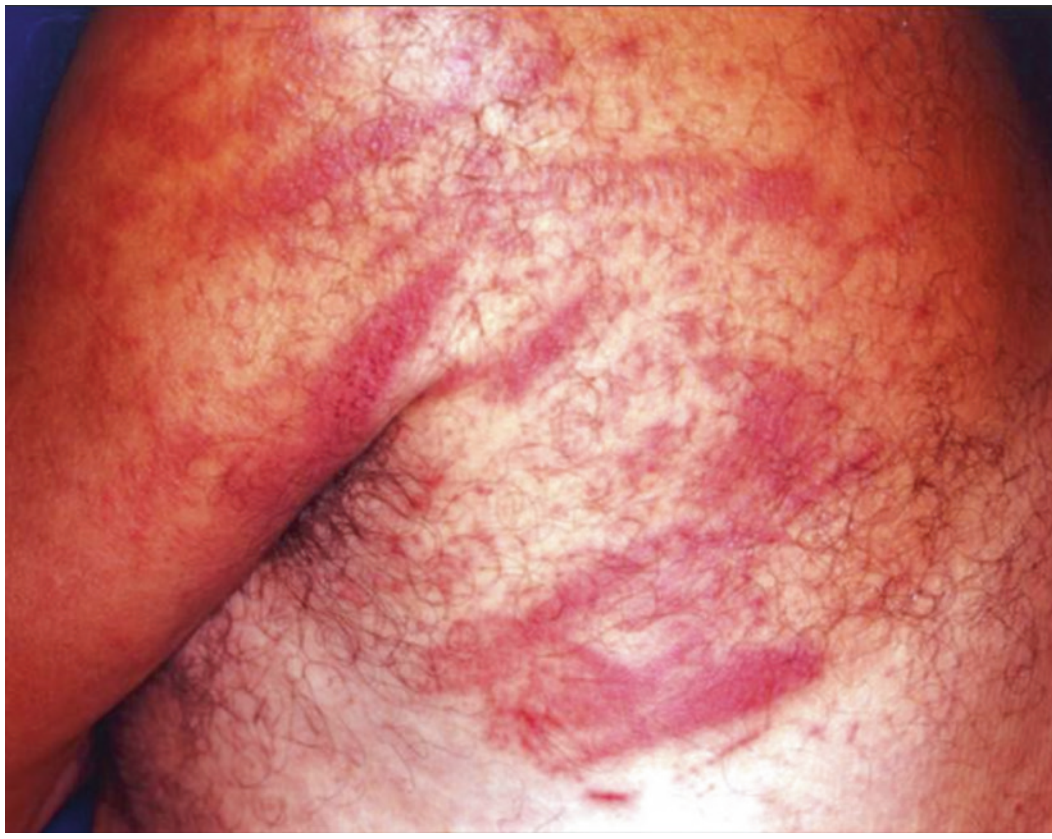

Fig. 16.5 Purpuric irritant contact dermatitis by leaves of *Zea mays*

Fig. 16.6 *Urtica dioica*

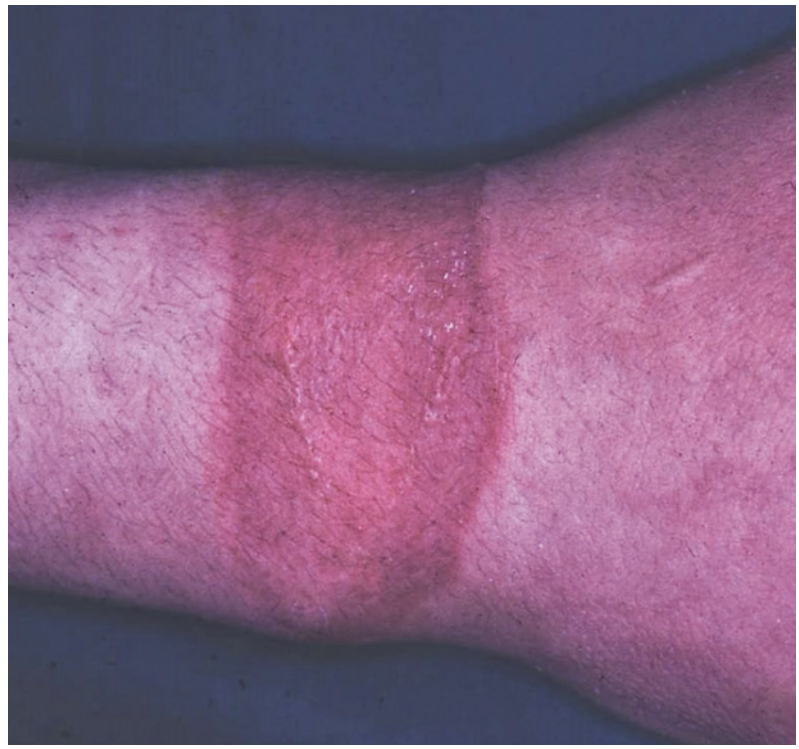

Fig. 16.7 Irritant contact dermatitis due to wet compresses of leaves of *Urtica dioica* (self-artefact)

A very wide range of vegetable species can induce contact allergy. Except in cases of peculiar clinical pictures and those due to occupational exposure, the identificaiton of the vegetable causal agent can often be very difficult, also because the vegetable allergens responsible are often not included in standard patch tests series.

The clinical pattern of the dermatitis depends on the source and means of contact. The onset of the lesions may also not feature frank eczema but rather pomphoid lesions that only later become exudative [32]. There are three main clinical types of allergic contact plant dermatitis: classic contact allergy, a characteristic hyperkeratosis form and the erythema multiforme-like eruption.

The normal presentation is that of a typical acute eczema with erythemato-edemato-vesicular lesions; sometimes blisters and infiltrative lesions are also present. The sites most often affected are exposed sites such as the hands and forearms; the eyelids, and sometimes the genitals can be affected when the allergen is carried on the hands or through clothes. This form can become chronic, featuring diffuse clinical pictures of lichenoid type.

A characteristic picture, usually of occupational origin, is periungual eczema of the fingertips, that presents as a fissured, hyperkeratotic and painful eruption, of which the classical example is the "tulip fingers" seen in tulip pickers (*Tulipa* spp., Liliaceae family). Similar eruptions may be observed in people handling daffodil and narcissus bulbs (*Narcissus* spp., Amaryllidaceae family), alstroemeria flowers (*Alstroemeria* spp., Alstroemeriaceae family), and garlic (*Allium sativum*, Alliaceae family) (Fig. 16.9). Generally, this picture is the result of a combination of skin sensitization and physical and chemical irritation [33–35].

Often, contact allergy to plants presents as erythemato-bullous figured lesions, like those

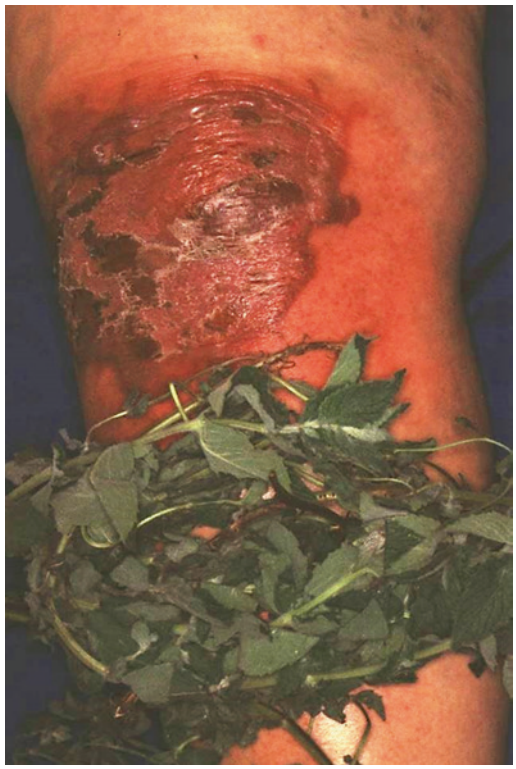

Fig. 16.8 Allergic contact dermatitis due to compresses with infusion of *Mentha spicata* for pain in gonarthrosis

of poison ivy or of a *Capparis spinosa* infusion used for painkilling purposes (Figs. 16.10 and 16.11) [36]. A compress of leaves and the fruit of capers resulted in a dermatitis detected by patch tests to the fruit and leaves as is, mustard oil 1 and 0.1% in petrolatum, allyl isothiocyanate 0.1 and 0.05% in petrolatum, and benzyl isothiocyanate 0.1% in petrolatum. Other isothiocyanate plants were negative [36].

An erythema multiforme-like picture is also a frequent observation, especially due to *Primula obconica* [37, 38] and to various woods.

16.3.3 Airborne Contact Dermatitis

This disease is often reported in the literature [39–43]. Conditions that favor the onset are high temperatures and a low environmental humidity index. It is these factors that facilitate the drying of plants, whose particles then spread in the environment. The various allergenic fractions can be contained in pollens, trichomes, fragments of leaves or in the dry branches. The complaint can also be brought on by smoke and vapors of burning plants and by sawdust from their woods.

Clinically, this form may resemble a photodermatitis. However, airborne contact dermatitis normally involves the upper eyelids, the triangle of skin behind the earlobe, and the region below the chin. The common culprit plants include *Ambrosia* spp., Compositae [44, 45], *Frullania* (Jubulaceae family) [46], and *Lichen* particles [47]. In North America, the smoke from burning poison ivy (*Toxicodendron* spp.), and related plants of the Anacardiaceae family, can be sensitizing if the allergenic oleoresin is vaporized rather than pyrolized [48].

16.3.4 Primary Contact Hyperpigmentation

Hyperchromia induced by plants can occur by means of two different mechanisms. The first and most frequent type is melaninic hyperpigmentation, that occurs as a post-inflammatory sequela of contact phytodermatitis or phyto-photodermatitis. The other type is primary skin non melaninic hyperpigmentation; this latter mechanism underlies the action of *Cynara scolymus* (artichoke), *Juglans regia* (walnut), and *Lawsonia inermis* (henna), just to name a few examples (see Chap. 17).

The brown hyperpigmentation resulting from contact with artichokes is due to cynarin, that undergoes oxidation: it stains the fruit itself and the hands (fingertips and palms) when cleaning or cutting artichokes.

In the autumn, the time of walnut hulling, we often observe a brown irritant pigmentation of the hands, that involves the skin and nail laminae. The staining is due to juglone, the active ingredient of *J. regia*, that is a naphthoquinone: the activated quinone C=O group has an active affinity for the $-NH_2$ group of keratin amino acids. The reaction elicits C=N chromophores groups, that are highly pigmenting and absorb in the visible range, in particular violet, while they

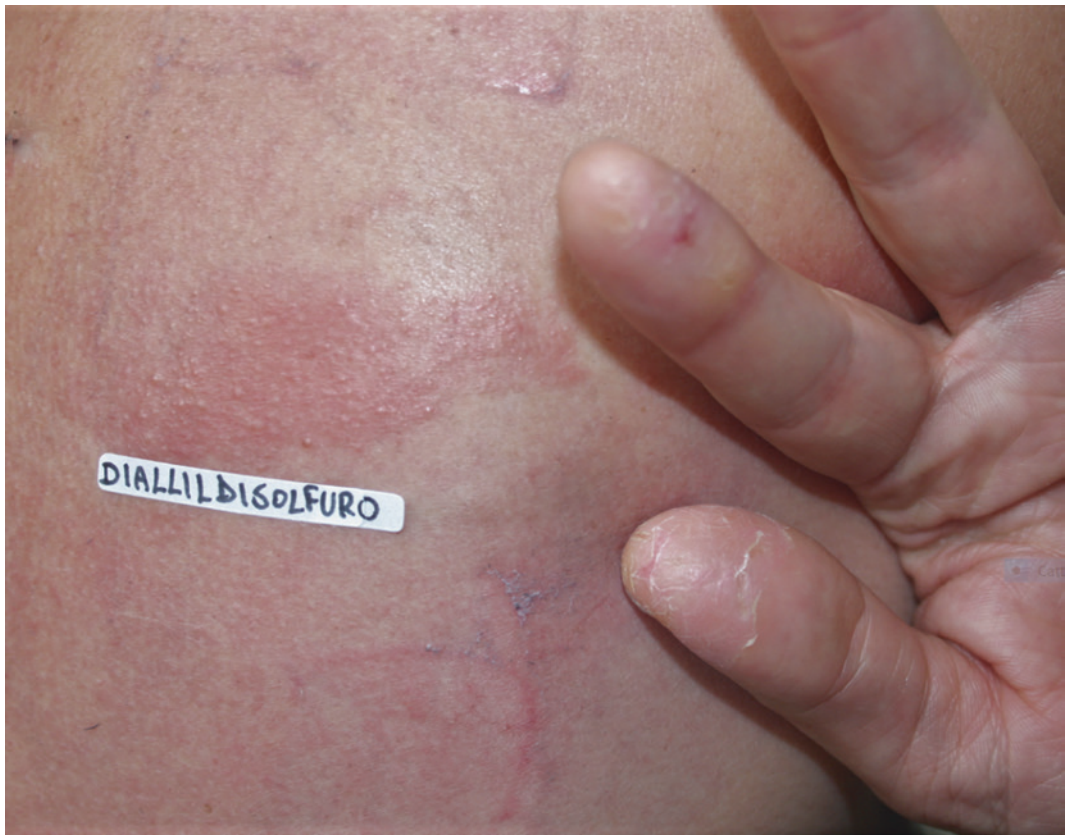

Fig. 16.9 Allergic contact dermatitis due to *Allium sativum* (positive patch test reaction to diallyldisulphide)

Fig. 16.10 *Capparis spinosa* (Reproduced with permission by Angelini and Coll [36])

reflect red and yellow, giving rise to the various tones of brown [48–50]. The same action mechanism drives lawsone, the active ingredient of *L. inermis*, and dihydroxyacetone ($OHCH_2–C=O–CH_2OH$) used for self-tanning [49–51].

16.3.5 Contact Urticaria

The pathogenic mechanism can be direct (non immunologic), mediated by phlogogenic substances injected into the skin by the prickly hairs disseminated on the surface of many vegetable species, or indirect (immunologic), mediated by antibodies in previously sensitized subjects.

Initially, the pomphoid lesions tend to be confined to the site of contact with the vegetable. However, above all in immunologic forms, over time the clinical picture will gradually extend to include manifestations at the level of the mucosa, and asthmatic, rhinoconjunctival or anaphylactic reactions [52–61].

Airborne contact urticaria, often associated with asthma, has been reported as an occupational complaint in hospital personnel, due to natural latex (generally derived from *Hevea brasiliensis*, Euphorbiaceae family) [59–61]. A case was reported in a warehouse worker, caused by dust derived from cinchona bark (*Cinchona* spp, Rubiaceae family) [58].

The species most commonly causing contact urticaria belong to various vegetable *phylum* families (Table 16.2).

16.3.6 Photocontact Dermatitis

The combined action of some plants on the skin and exposure to the sun has been known since ancient times, several centuries B.C. In India, *Psoralea corylifolia* (Leguminosae family) was used to treat vitiligo, and in Arab countries *Ammi majus* (Umbelliferae family). More recently, in 1834 the bergapten (5-methoxypsoralen) was isolated from *Citrus bergamia.* In 1916, Freund described skin pigmentation due to bergamot oil, contained in perfumes [62]. For the first time, in 1932

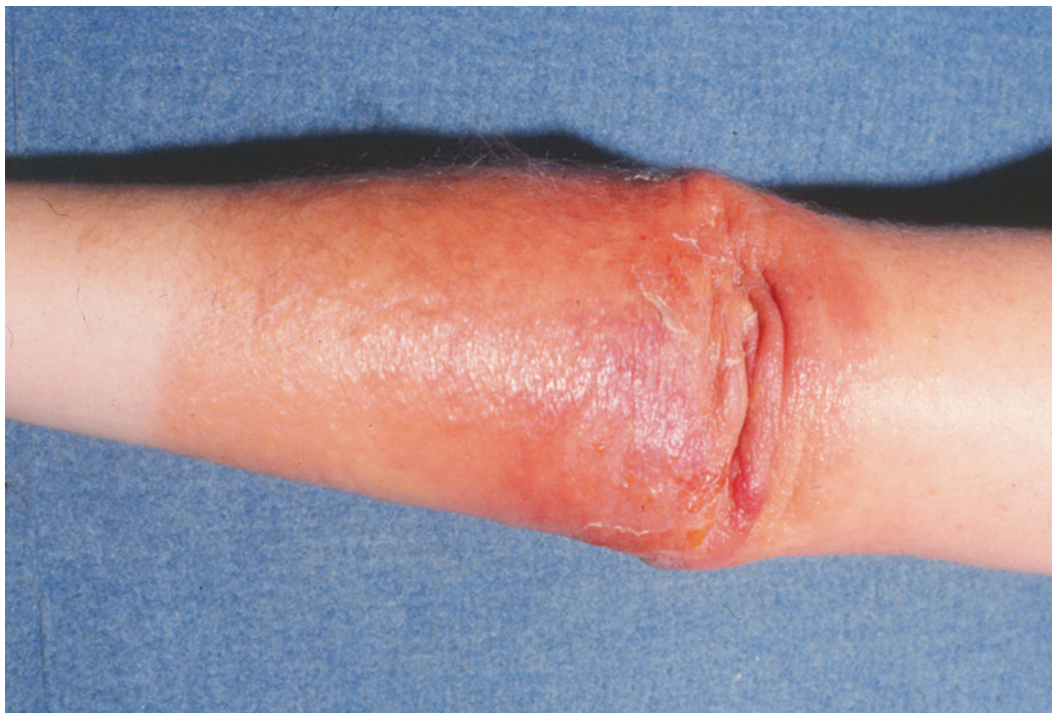

Fig. 16.11 Allergic contact dermatitis due to compresses with infusion of *Capparis spinosa* for articular pain (Reproduced with permission by Angelini and Coll [36])

Table 16.2 Plants known to elicit contact urticaria

Amaryllidaceae	Graminaceae
Agave americana	*Secale cereale*
Narcissus spp	*Zea mays*
Anacardiaceae	Iridaceae
Semecarpus anacardium	*Iris* spp
Araceae	Leguminosae
Monstera deliciosa	*Dalbergia latifolia*
	Trifolium pratense
Chenopodiaceae	Liliaceae
Salsola kali	*Asparagus officinale*
	Tulipa spp
Compositae	Lythraceae
Aster spp	*Lawsonia inermis*
Chrysanthemum spp	Myrtaceae
Gerbera spp	*Eucalyptus* spp
Helianthus annuus	Proteaceae
Lactuca sativa	*Grevillea juniperifolia*
Senecio cruentus	Rosaceae
Tanacetum cinerariaefolium	*Crataegus monogyna*
Coniferae	Pedaliaceae
Thuya plicata	*Sesamum indicum*
Equisetaceae	Rubiaceae
Equisetum arvense	*Cinchona* spp
Euphorbiaceae	Sterculiaceae
Hevea brasiliensis	*Triplochiton scleroxylon*
Ricinus communis	
Geraniaceae	Urticaceae
Linum usitatissimum	*Cannabis indica*
	Humulus lupulus
	Verbanaceae
	Tectona grandis

Oppenheim [63] reported "dermatitis bullosa striata pratensis", and then in 1942 Klaber [64] introduced the term phytophotodermatitis. In 1938 the cause of this manifestation had been shown to be furocoumarins, and the following year the UV range responsible was demonstrated to be in most cases between 320 and 380 nm (UVA) [65].

16.3.6.1 Phototoxic Plants

There are countless photosensitizing plants, that are ubiquitous in the environment (Table 16.3) [3]. Most of the species belong to the Umbelliferae, Rutaceae and Moraceae families; species contained in other families are less important. The phototoxic action of some Compositae is not due to furocoumarins but to thyophenes, that are phototoxic only in microbial systems [66].

Table 16.3 Some plants containing furocoumarins

Family	Species	Furocoumarins
Moraceae	*Ficus carica*	Pso, 5-MOP, 8-MOP
Rutaceae	*Ruta graveolens*	*Pso, 5-MOP, 8-MOP, Ang*
	Ruta montana	*8-MOP*
	Ruta chalepensis	*8-MOP*
	Citrus bergamia	*5-MOP*
	Citrus aurantium	*Berg*
	Citrus limonum	*5-MOP*
	Citrus aurantifolia	*5-MOP, Ber*
	Citrus acida	*5-MOP*
	Dictamnus albus	*5-MOP*
	Fagara zanthoxyloides	*5-MOP, 8-MOP*
	Fagara schinifolia	*5-MOP*
	Zanthoxylum flavum	*8-MOP*
Umbelliferae	*Angelica silvestris*	*Pso, 8-MOP*
	Angelica keiskei	*Pso, 5-MOP, Ang*
	Angelica archangelica	5-MOP, 8-MOP, Ang, Xan
	Angelica glabra	Ang
	Ammi majus	5-MOP, 8-MOP
	Ammi visnaga	5-MOP, 8-MOP
	Ligusticum acutifolium	5-MOP
	Ligusticum acutilobum	5-MOP
	Pastinaca sativa	5-MOP, 8-MOP
	Heracleum spp	Pso, 5-MOP, 8-MOP, Ang
	Pimpinella magna	5-MOP
	Pimpinella saxifraga	5-MOP
	Petroselinum sativum	5-MOP
	Apium graveolens	5-MOP
	Levisticum spp	5-MOP
Leguminosae	*Psoralea corylifolia*	Pso, Ang
	Coronilla glauca	Pso

Pso = psoralen (ficusin), 5-MOP = 5-methoxypsoralen (bergapten), 8-MOP = 8-methoxypsoralen, Ang = angelicin (isopsoralen), Xan = xanthotoxol, Ber = bergaptol

Umbelliferae. There are more than 200 species of *Heracleum* spp, that are ubiquitous worldwide, although there are major differences

in their phototoxic power, as demonstrated with the in vitro *Candida albicans* test [67]. Photodermatitis due to *Heracleum mantegazzianum* is a well known complaint [68] that has also been reported in Italy [69]. It has also been described in children who use the hollow stalks of *Heracleum* as telescopes, peashooters and flageolets: the onset of the manifestations occurs after about 36 hours in exposed sites (around the mouth or eyes or on the back of the hands) [1].

Angelica spp, native to central and northern Europe, is widely grown for its aromatic stems employed for industrial use in the production of sweets and liqueurs; the oil from the roots is used as a scented essence.

Ammi majus, a perennial that grows in fields and gardens, is native to the Mediterranean area and widespread in Europe, North America, Argentina and central Asia. It is particularly abundant in the Valley of the Nile, where it has been used to treat vitiligo since ancient times.

Phototoxic Umbelliferae also include some vegetables. *Apium graveolens* (celery) can be infected by the *Sclerotinia sclerotiorum* fungus. Infected plants can cause contact photodermatitis in workers gathering the crop, being an example of pseudophytophoto reactions. In fact, 8-methoxypsoralen and 5-methoxypsoralen have been isolated from infected celery but are absent in the healthy vegetable [70, 71]. *Daucus carota* (carrot) and *Pastinaca sativa* (parsnip) are phototoxic, too. *Petroselinum sativum* (parsley) contains 5-methoxypsoralen above all in the leaves, and in higher quantities during the summer. The quantitiy of parsley bergapten ingested during a meal has been estimated to be about 0.5–0.8 mg, not enough to cause skin phototoxicity [72]. Instead, it is possible for contact with the juice from chopped parsley to induce a modest dermatitis or photopigmentation of the hands.

Rutaceae. The *Citrus* genus is widely cultivated for the fruit and essential oils; the latter are used in perfumes, liqueurs, syrups and medicaments. The components present in this genus include psoralens (phototoxic), citral and lemonene (sensitizing substances). *Citrus bergamia*, the most famous bergamot strain, grows in the south of France and also flourishes in Apulia (Italy) and above all in Calabria (Italy). Although the phototoxic action of its oil has long been known, it was used until a few years ago in perfumes, some types of tea and in tanning cosmetics (nowadays, its use is banned by European norms unless the furocoumarin component has been removed). Clinical pictures induced by the *Citrus* genus include skin irritation, sensitization and contact photosensitization [73]. We have often observed a perioral pigmented dermatitis in subjects who suck bergamot fruits.

The *Dictamnus* species (from mount Dicte on Crete) grows wild in the Mediterranean area. The best known species is *Dictamnus alba*, also known as the "gas plant" or "burning brush", because it can self-combust on very hot days due to the inflammable oils content. Some varieties, with white or purple flowers, are also cultivated in northern Europe [74]. It has been demonstrated that *D. alba* contains not only furocoumarins but also dictamine, a phototoxic alkaloid [75]. This species induces linear vesicobullous photoreactions, followed by persistent pigmentation that lasts for months. The complaint is occupational in botanists but most often due to chance contact.

Common rue (*Ruta graveolens*) grows wild but is also cultivated in southern Europe and in America. Its medicinal properties have been known since early times and it is still used in homeopathic practice. Apart from being believed to chase off witches, in the Middle Ages it was attributed various diuretic and medicinal properties. It is used in cooking, and its oil in perfumes [76, 77]. A particular use is in grappa; moreover, dried rue flowers are very ornamental.

Moraceae. *Ficus carica* L., the fig tree, is believed to be native to the Middle East (Syria) but is widely cultivated in the Mediterranean area and other warm zones worldwide, in some of which it also grows wild (Fig. 16.12). The branches, leaves, and skin of the fruit, when cut, exude a rubbery sap that contains many different compounds, such as various proteolytic enzymes (ficin, triterpinoids, protease, lipodiastase, amylase), and furocoumarins (psoralen,

Fig. 16.12 *Ficus carica*

8-methoxypsoralen, 5-methoxypsoralen and 4′-5′-dihydropsoralen). The enzymes have an irritant potential and so can aggravate the phototoxic effect of the coumarins [78–84].

Various cases of photocontact dermatitis from the fig plant have been reported [62, 79, 81–89]. The condition is frequent in Southern Italy [20, 90–92] and in Turkey, where about 10% of fig pickers develop a contact dermatitis [93].

Other Phototoxic Plants. The Leguminosae, Rosaceae, and Compositae families contain some phototoxic species. Among the Leguminosae, *Psoralea corylifolia* is known for its therapeutic effect on vitiligo; the plant has a strong scent and grows in tropical and subtropical areas. A phototoxic effect of the polyacetylenes contained in the stems, leaves, and roots of some Compositae (ambrosia, chrysanthemum, dahlia, chamomile) has been demonstrated [94].

16.3.6.2 Photoactive Agents

Furocoumarins are tricyclic hydrocarbons with a furan ring condensed to a coumarin ring (benzopyrone) (Fig. 16.13) [62]. They increase the skin susceptibility to light, causing an exaggerated erythematous reaction (sunburn) and resulting pigmentation. Some of the furocoumarins isomers are called psoralens. Of the various isomers, only those with a linear structure resembling psoralen are photoactive; the angular structure, like that of pimpinella and angelicin, annul or reduce the photoactivity of the compound. Furocoumarins absorb photons and form photoadducts with the DNA pyrimidine bases cytosine, uracyl and thymine. This gives rise to short-lived high energy states, whose dissipation is what causes the cellular damage. Psoralen is much more phototoxic than 5-methoxypsoralen and 8-methoxypsoralen. The phototoxicity of furocoumarins is increased by the presence of the methyl groups CH3 in positions 5′, 4, 3 and above all 5 and 8. This phototoxicity is decreased in the presence, at the same sites and in 4′, of other chemical groups (OH, Br, etc.) [3]. The absorption spectrum of furocoumarins lies between 210 and 330 nm, and changes, as

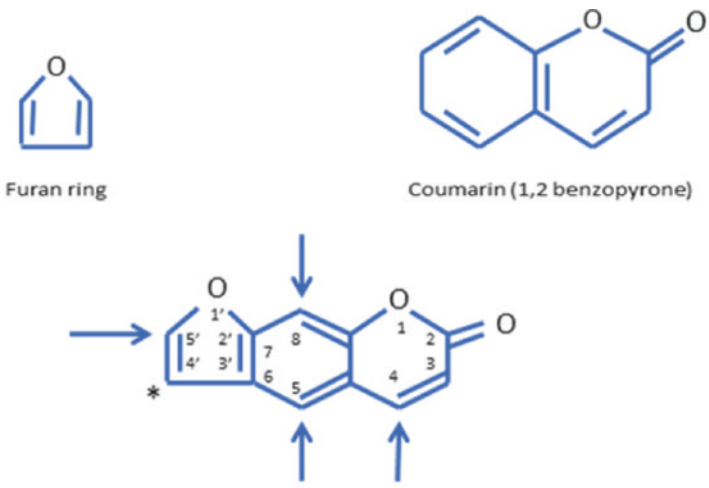

Fig. 16.13 Chemical structures of furocoumarins

does the action spectrum, at longer UVA wavelengths when the furocoumarins are complexed with the DNA. Among the linear psoralens, 5-methoxypsoralen is present in most phototoxic plants; 8-methoxypsoralen is also contained in various plants, while psoralen is only present in few species.

Plants with a phototoxic action contain about 0.5 g of linear psoralens per 100 g of dry material. In any case the content varies in the different portions of the plant, according to its age, and in the different seasons.

16.3.6.3 Clinical Features

Phytophotocontact reactions are observed during the warmer months, both because of the stronger sunlight and of the greater quantity of photoactive compounds in plants. An important factor in determining these reactions is also the environmental humidity, that increases the percutaneous absorption of furocoumarins. The pictures, of occupational or non occupational type, can be acute or delayed and are due to a direct toxic mechanism in most cases, an immunologic mechanism being more rarely observed. The onset of acute clinical manifestations occurs after about 24 hours from the contact, and includes intense erythema, edema, vesicles and blisters, with a figured, bizarre pattern. The lesions affect sites of contact and are accompanied by pruritus and above all burning. The inflammation process will reach a peak after about 72 hours and then resolve in 1–2 weeks, leaving hyperpigmentation that may even last for months.

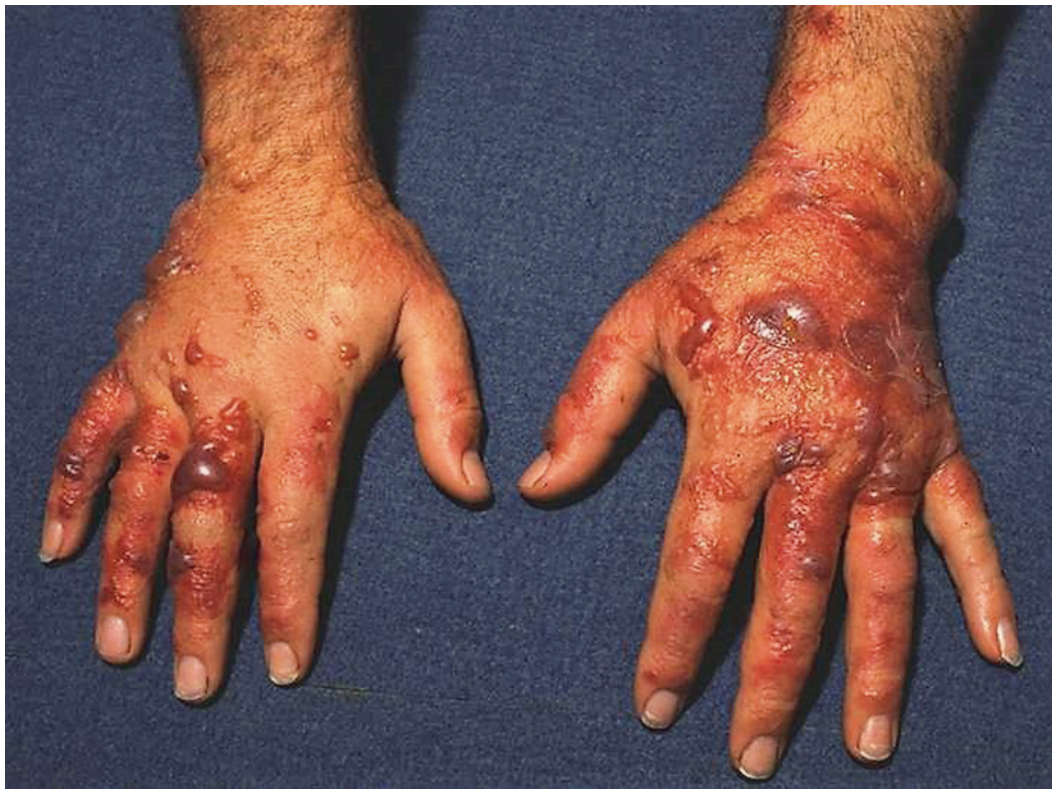

Fig. 16.14 Bullous phototoxic contact dermatitis from *Ficus carica* (in the summer) (Reproduced with permission by Bonamonte and Coll [49])

Phototoxic Contact Reactions

Phototoxic reactions manifest in three possible clinical forms.

Phototoxic contact dermatitis. The clinical picture varies according to the season. Every year, in the late spring, summer and early autumn, we observe many cases of photocontact dermatitis from *Ficus carica* (Fig. 16.14). In late spring and especially the summer, the lesions are intensly erythemato-edemato-vesico-bullous because of the greater content of furocoumarins in the plant and the stronger light, while in early autumn (Fig. 16.15) the lesions are more modest, featuring mild or no exudation, because of the different conditions. In children, we sometimes observe a modest erythemato-vesicular dermatitis around the mouth, resulting from contact with the sap that leaks from the peel when the fruit is detached from the plant and immediately eaten. It should be noted, however, that the fruit itself is not harmful as it does not contain furocoumarins [81].

The sites affected will vary according to the mode of contact with the plant. In general, the hands and forearms are most frequently affected but the trunk may also be involved due to the sap dripping down the body.

As well as being a spontaneous complaint, the dermatitis induced by *F. carica* can be induced by a decoction of the leaves, which may be used as a tanning agent (Fig. 16.16) [20, 92], or as a remedy for a pre-existing dermatosis [95]. Cases induced by a tanning decoction are obviously severe, both because of the vast surface involved and of the deliberate exposure to the sun.

Dermatitis Bullosa Striata Pratensis. This form, whose name was coined by Oppenheim [63], occurs only when two conditions are present: the skin must be wet, and must be exposed

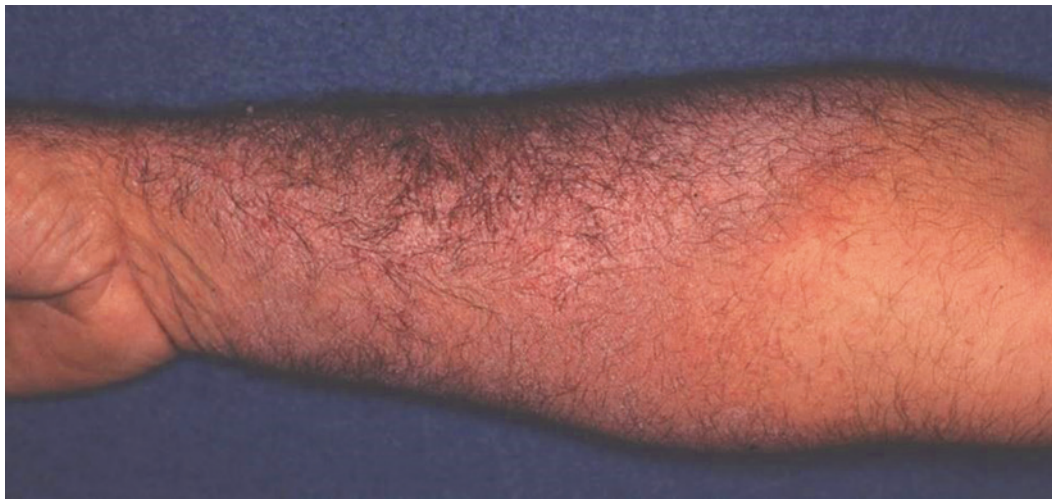

Fig. 16.15 Erythematous phototoxic contact dermatitis from *Ficus carica* (in the autumn)

to the sun. The complaint appears most frequently after sunbathing in meadows. The onset occurs after 24–48 hours from the contact, and features striped erythemato-edematous and vesico-bullous lesions in various sites, with a bizarre distribution (Figs. 16.17, 16.18, and 16.19). The dermatitis persists for 8–10 days and leaves a hyperchromic outcome that is very slow to resolve.

The culprit plants vary from country to country, of course. Characteristically, the complaint, that affects all exposed subjects, is not experimentally reproducible even if the plant responsible is used, due to the impossibility of reproducing the appropriate climatic conditions. Perhaps for these same reasons, the frequency of this dermatitis varies from year to year.

Berloque Dermatitis. This disease, the most discrete of all phototoxic eruptions, appears as a characteristic pigmentation; the patient does not generally remember what conditions elicited it. The eruption onset is due to contact with cosmetic products (lotions, eau de toilette, aftershave lotions) containing furocoumarins (see Chap. 17). This dermatitis should no longer be observed since the European norms ban the use of psoralens in cosmetics unless they have been defurocoumarinized. In rare cases it would present with an initial acute erythematous phase, of fairly modest proportions that, in fact, often went unnoticed.

There is certainly an individual susceptibility to this form, even if the mechanism is not entirely clear. The complaint is difficult to reproduce. The sites most often affected are the sides of the neck, but we have also observed it on the trunk and limbs. The hyperchromic manifestations, that reflect the track of the perfume sliding down the skin, persist for months. Diffuse forms are also possible, linked to the use of suncreams with a bergamot oil base. They mimic post-inflammatory streaked pigmentation. To elicit the complaint, the interval between the use of the perfume and exposure to the sun must not exceed 1–2 hours.

Photoallergic Contact Reactions

The pathogenic mechanism underlying contact dermatitis to psoralens is still debatable. Phototoxic dermatitis is certainly the most frequent type of reaction resulting from psoralens.

Many cases of contact allergy [96–99] and photocontact allergy [97, 100–104] after exposure to furocoumarins have been reported in the literature, acquired during topical or systemic therapeutic procedures for eczema, psoriasis, vitiligo, and alopecia areata. By contrast, photoallergic reactions to psoralens resulting from

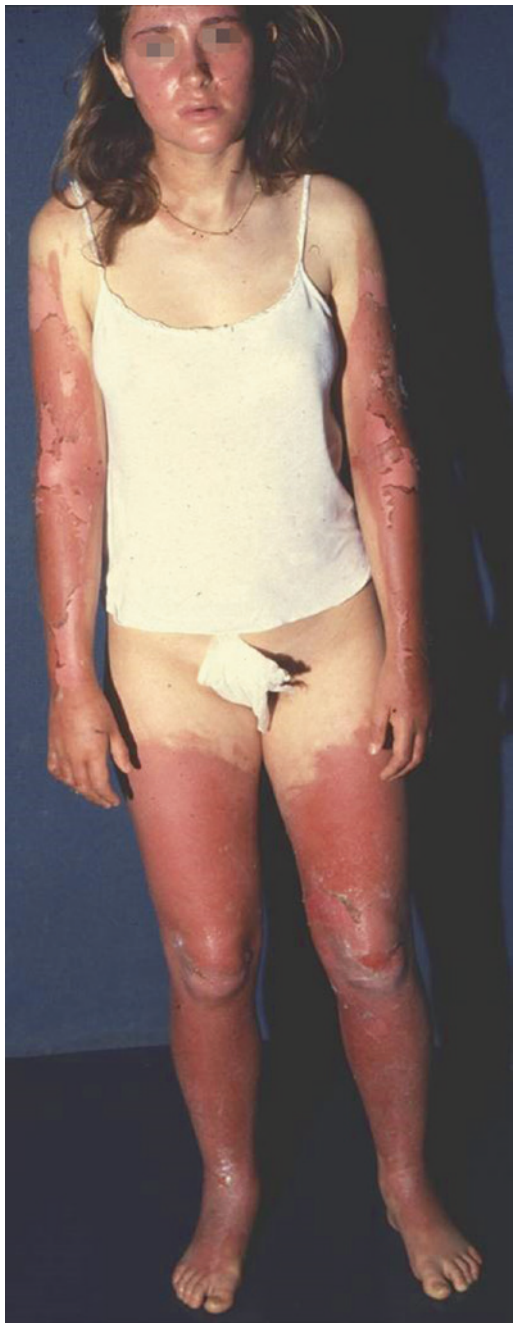

Fig. 16.16 Phototoxic contact dermatitis induced by decoction of leaves of *Ficus carica* used as tanning agent

contact with plants have rarely been reported. Ljunggren reported a patient with photocontact allergy to the psoralens xanthotoxin, bergapten, and imperatorin in parsley (*Petroselinum sativum*) [105]. Kavli and Volden exposed themselves repeatedly to psoralens and plant parts from *Heracleum laciniatum*, and photocontact allergy was induced to the psoralens sphondin and isobergapten after five and six exposure sessions, respectively [62]. Two cases of occupational photocontact allergy to the leaf, stem and latex of *Heracleum mantegazzianum* were also reported [68, 69].

In a study of ours, we reported the results of patch and photopatch tests in 47 cases of contact dermatitis to *Ficus carica* [20]. In 12 subjects, photopatch tests revealed positive reactions to ethanol extract of cut leaves and 8-methoxypsoralen, in some cases down to a concentration of 0.0001%. All non-irradiated control tests were negative in these patients, thereby ruling out ordinary contact allergy. The histological picture of the positive photoreaction sites to 8-methoxypsoralen at 0.0001% was strongly consistent with contact allergy, featuring spongiosis and exocytosis in the epidermis and a perivascular lymphohistiocytic infiltrate in the superficial dermis (Fig. 16.20) [20].

Psoralens have a variable sensitizing potential. It would seem from literature reports and our findings that of the various compounds, 8-methoxypsoralen is the strongest agent (both when used for therapeutic purpose and after accidental contact with the plant), followed by 5-methoxypsoralen. Both these psoralens are present in *Ficus carica* but our patients were positive only to 8-methoxypsoralen and not to 5-methoxypsoralen or 4,5',8-trimethylpsoralen (TMP), a synthetic compound [20]. This positivity to 8-methoxypsoralen could be linked to its higher photoreactivity as compared to the parent molecules. It is not possible to state for certain that negative photopatch tests to 5-methoxypsoralen and TMP exclude the possibility of a cross reaction with 8-methoxypsoralen [20].

The differential diagnosis betwen phytophototoxic and phytophotoallergic contact dermatitis is not easy. In our experience, the clinical picture is similar in the two conditions, featuring erythemato-vesico-bullous lesions with a bizarre distribution (Figs. 16.21, 16.22, 16.23, and

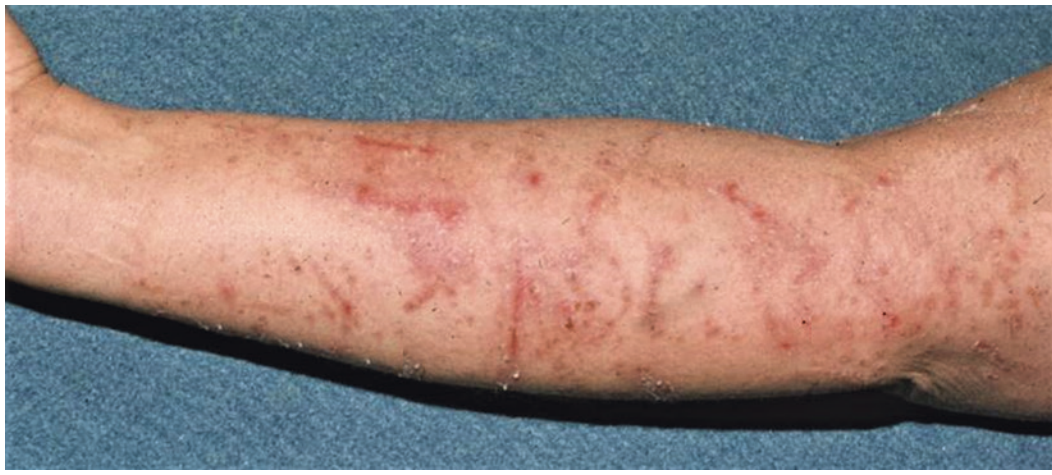

Fig. 16.17 Dermatitis striata pratensis

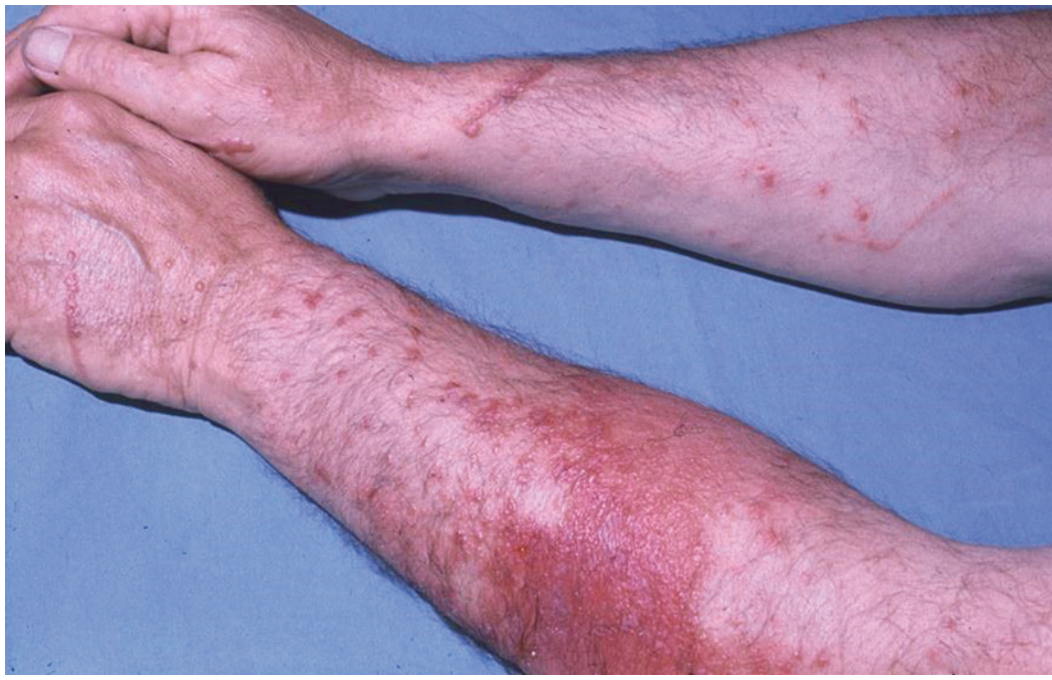

Fig. 16.18 Dermatitis striata pratensis

16.24) [107]. Some relative clinical differences are the involvement of unexposed sites and the more modest residual pigmentation in cases of allergy. Clearly, photopatch tests are necessary to ascertain whether the clinical picture is of a toxic or an allergic nature (Table 16.4).

16.4 Occupations Posing Individuals at Risk

Obviously, occupational plant dermatitis occurs more frequently in certain occupations, depending on the risk of exposure to the plant and its toxic

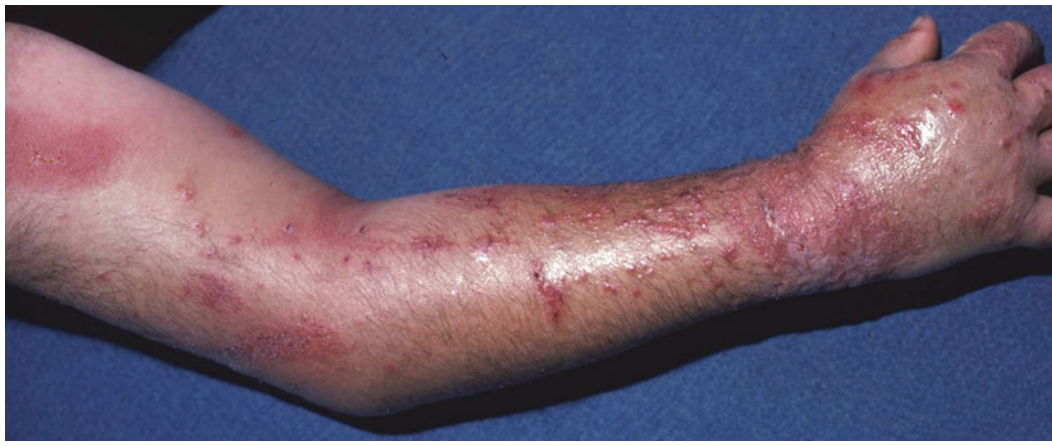

Fig. 16.19 Dermatitis striata pratensis

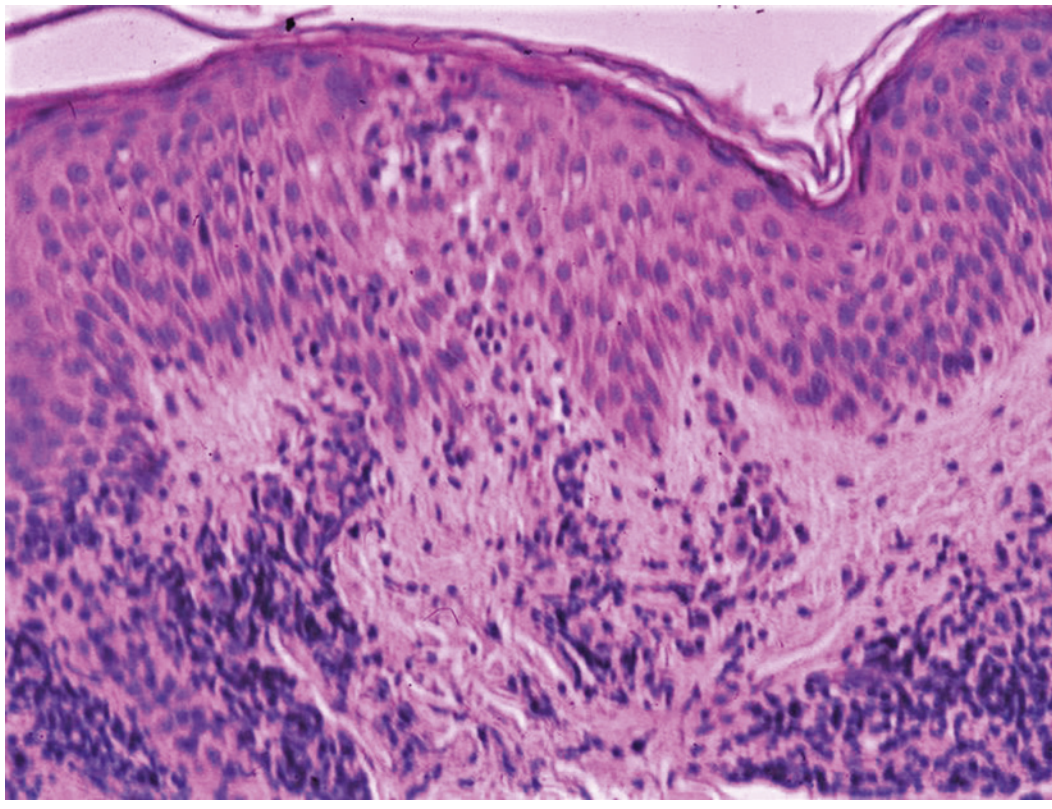

Fig. 16.20 Histological picture of positive patch test reaction to 8-methoxypsoralen: spongiosis, exocytosis and perivascular lymphohistiocytic infiltrate

capacity [5]. Table 16.5 shows the occupations most often affected. There are several possible clinical pictures, some of which are more frequent or less frequent within specific occupational groups.

Certainly, contact reactions to plants are very frequent in farm workers, and Compositae dermatitis is perhaps most often observed in this occupation. The risk of plant dermatitis is

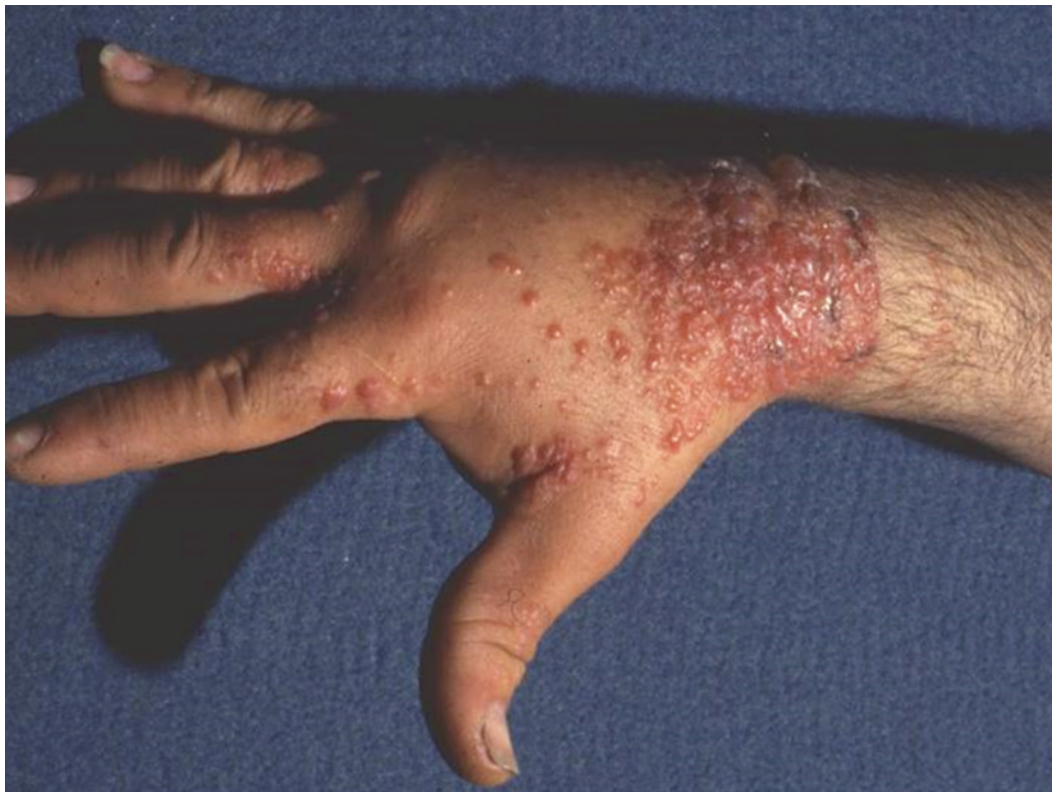

Fig. 16.21 Photoallergic contact dermatitis from 8-methoxypsoralen in *Ficus carica*

also high in bakers, and higher in women than men. Among the various clinical forms, the most frequent in this category is protein contact dermatitis.

Bar-tenders can be exposed in a more limited number of ways; contact is above all with citrus peel (lemons, limes, and oranges) and mint. Beekeepers may be exposed to allergens present in propolis, while healthcare workers can develop allergic contact urticaria from some plant derivatives, such as natural latex from *Hevea brasiliensis* and cornstarch from *Zea mays*. Masseurs may sensitized to various ointments containing fragrances. Foresters are exposed to a great variety of plants and lichens [106]. Floristry is considered to be a rather risky occupation; the most common contact reactions are those to Compositae [107, 108]. Pharmaceutical workers are sometimes exposed to plants materials, as also textile workers. Among tobacco workers, the leaves of *Nicotiana tabacum* tobacco may cause hand dermatitis more commonly in workers producing cigars than cigarettes because the latter process is more automated. In this work category, in any case, the most prevalent complaint is irritant plant dermatitis [109–111].

16.5 Dermatologically Important Plants

Only the plants most commonly causing phytodermatoses are considered below [1, 3, 5–7, 19].

Alliaceae. Members of this family are widely grown and used for culinary purposes. Occupational dermatoses (immediate and delayed reactions) are commonly reported due to garlic (*Allium sativum* L.) and onion (*Allium cepa* L.). A characteristic dermatitis is circumscribed hyperkeratotic eczema of the fingers, generally of the left hand, in particular the thumb, index and middle fingers used to grasp

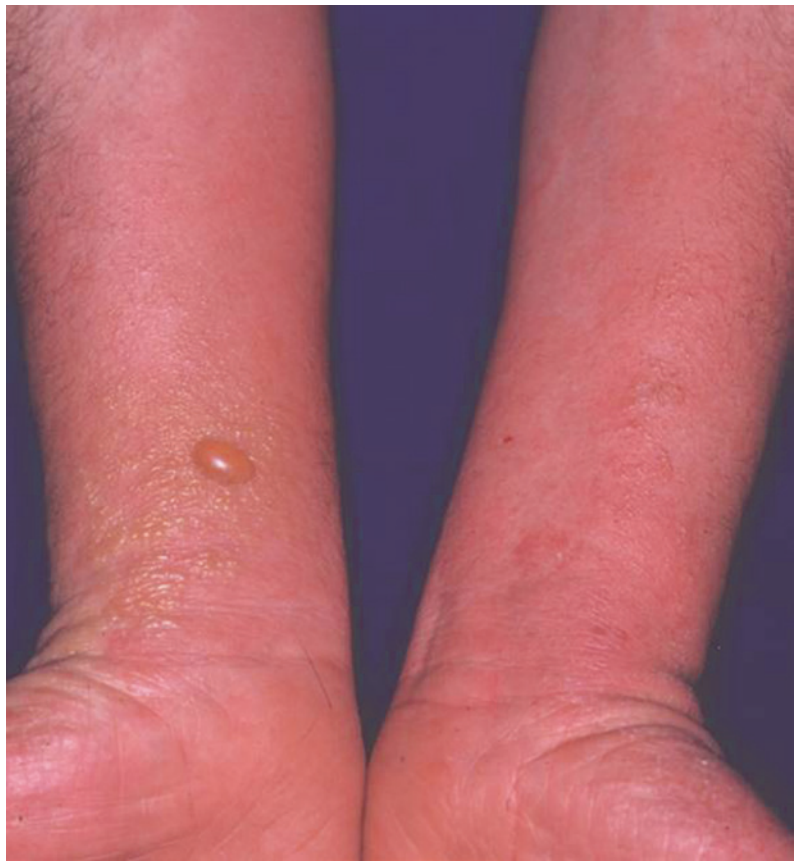

Fig. 16.22 Photoallergic contact dermatitis from 8-methoxypsoralen in *Ficus carica*

garlic bulbs. The incriminated substances are lachrymatory thiopropanal-S-oxide from onion and allicin, diallyl disulphide and allyl propyl disulphide from garlic. Diallyl disulphide 5% seems to be useful in patch tests in cases of garlic dermatitis, although 1% pet. may carry a lower risk of irritancy.

Alstroemeriaceae and *Liliaceae*. The *Alstroemeria* (Alstroemeriaceae family) and *Tulipa* (Liliaceae family) genera release the allergen tulipalin A (α-methylene-γ-butyrolactone) when the plant material is damaged. Contact dermatitis in bulb handlers and florists is an important and common occupational risk; both contact irritation and contact allergy can be observed. Collectors and packers of tulip bulbs present the characteristic dermatitis called "tulip fingers", a painful dry fissured hyperkeratotic dermatitis of the periungual regions, fingers and hands. This eczema is common in the Netherlands and other parts of Europe. The allergen is present in particular in the skin of the bulbs, but those handling the cut flowers can also be affected.

Amaryllidaceae. This family comprises many species, some of which are extensively cultivated for cut flowers and the perfume industry, including daffodils, narcissi, and jonquils. The *Narcissus* genus is an important occupational hazard owing to its irritant and allergizing properties. Raphides of calcium oxalate, contained in the bulbs, cause irritant dermatitis; the alkaloids masonin and homolycorin in the calyx and corolla induce allergic contact dermatitis.

Anacardiaceae. This family comprises over 600 species and is considered to be responsible for more dermatitis forms than all the other plant families taken together [1]. The *Toxicodendron*

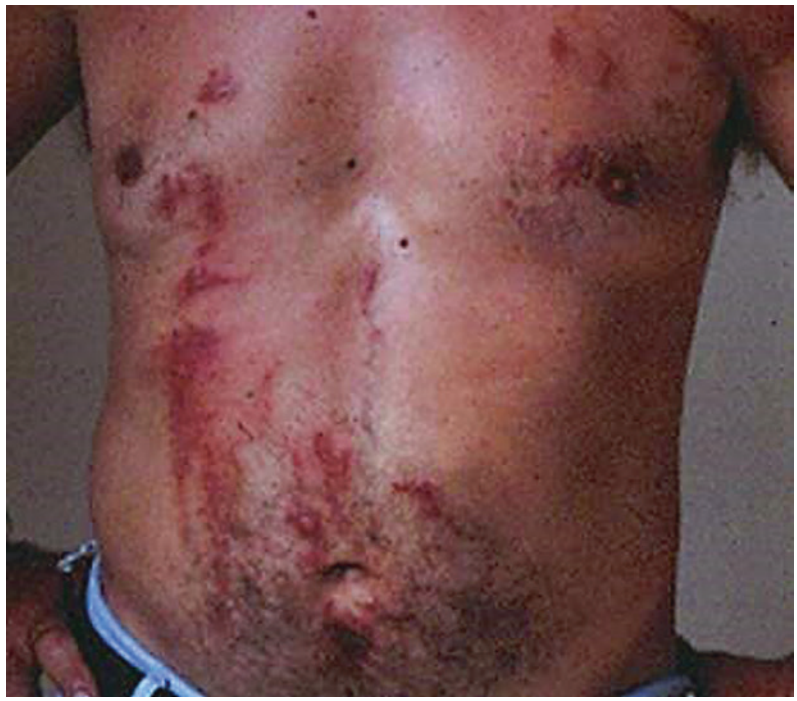

Fig. 16.23 Photoallergic contact dermatitis from 8-methoxypsoralen in *Ficus carica*

genus, that includes poison ivy (*Toxicodendron radicans*), poison oak (*T. toxicarium*), and poison sumac (*T. vernix*), is dermatologically the most hazardous. About 50 to 60% of North Americans develop contact allergy to poison ivy and related plants [112]; in contrast, poison ivy dermatitis is extremely rare in Europe because these plants are not a part of the natural flora. The allergens are alkyl catechols (pentadecylcatechols, urushiol) [113], present in all parts of the plant even when dry. In addition to allergic contact dermatitis, airborne contact dermatitis can be observed, due to the fumes from burning plants. There is also a risk of dermatitis induced by indirect contact with urushiol-contaminated clothing or pets. The Ginkgoaceae and Proteaceae families contain the same contact allergens, raising a risk of cross-reactions.

Compositae (or *Asteraceae*). Contact allergy to Compositae (over 20,000 species) is the most frequent cause of plant dermatitis worldwide. This family includes ornamental plants such as flowers (e.g., chrysanthemums, dahlias), vegetables (e.g., chicory, lettuce), herbs and common native and imported weeds (e.g., ragweed, feverfew, yarrow, *Ambrosia*, *Parthenium hysterophorus*). The dermatitis initially affects the hands and can then extend, also depicting a characteristic airborne pattern in skin folds and areas shielded from sunlight. Chronic actinic dermatitis can ensue after repeated episodes of airborne challenge. Horticulturists, florists, and nursery workers are frequently at risk although, in fact, nobody can really avoid being at risk. The onset of dermatitis can also follow contact with perfumed skin care products. Together with Anacardiaceae, Compositae are causes of systemic contact dermatitis resulting from the ingestion of homeopathic pills or teas, or of vegetables and spices [43, 114]. The sensitizing sesquiterpene lactones (of which there are more than 5,000), the terpenoids responsable for Compositae contact dermatitis, are contained in resin canals within the stem and on trichomes on the surface of the stem and leaves [115–117]. The various "sequiterpene lactone mix" formulae used in patch tests are unsatisfactory for various reasons: they only detect allergy in a low

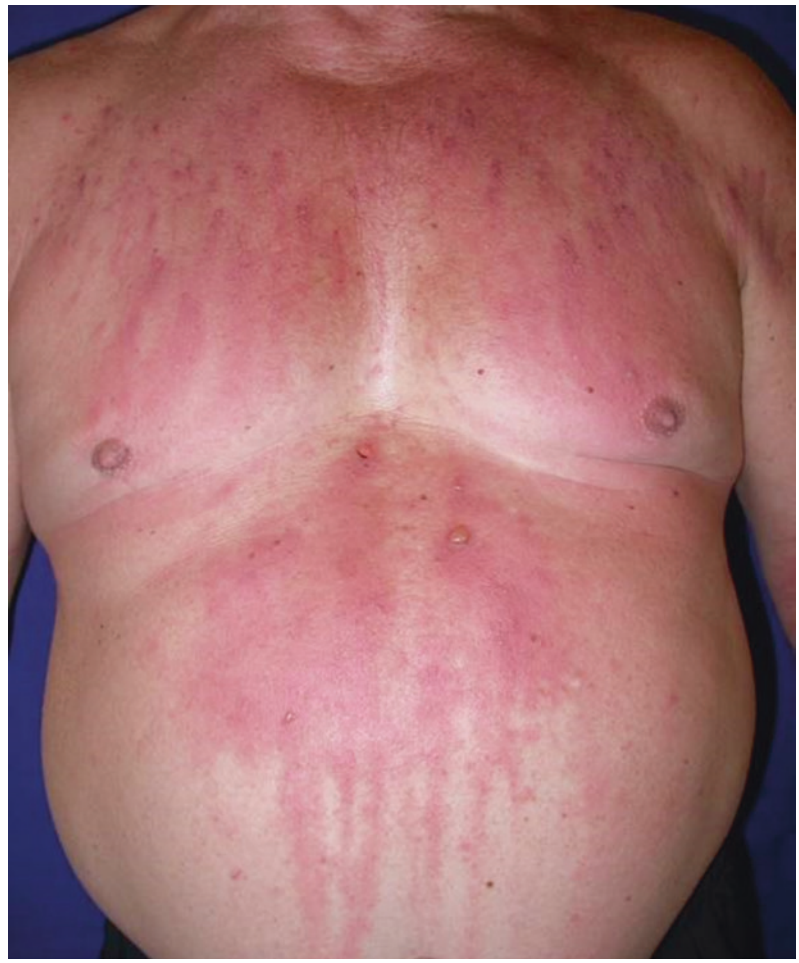

Fig. 16.24 Photoallergic contact dermatitis from 8-methoxypsoralen in *Ficus carica* (Reproduced with permission by Bonamonte and Coll [107])

Table 16.4 Clinical characteristics of phytophototoxic reactions and phytophotoallergic reactions

Phytophototoxicity	Phytophotoallergy
Collective effect	Individual effect
Erythema, edema, vesicles, bullae	Erythema, edema, vesicles, bullae
Lesions in photoexposed sites	Lesions extend beyond areas exposed to light
Figured and bizarre lesions	Figured and bizarre lesions
Intense residual pigmentation	Modest secondary pigmentation
Not experimentally reproducible	Difficult to reproduce
Negative photopatch tests	Positive photopatch tests

percentage of patients, carry a risk of active sensitization, and may yield a false positive irritant reaction. Recently, a modified sesquiterpene lactone mix has been proposed, that seems to be a more sensitive test material [118].

Cruciferae. Together with the Cleomaceae and Capparidaceae families (*Capparis spinosa*) [36], Cruciferae contain glucosinolates, many species of which release mustard oils (isothiocyanates) when the plant material is damaged. These mustard oils impart a pungency to the plants, which is the reason why they are often used as foods (cabbages, cauliflowers, Brussels sprouts, broccoli, radish, mustard, turnips, etc.). Due to their irritant potential, mustard oils are

Table 16.5 Occupations and workers exposed to plants and their products

Agricultural workers, farmers
Bakers, chefs, food-service workers, food handlers
Bartenders
Beekeepers
Botanists
Carpenters
Grocery workers
Healthcare workers
Gardeners, fruit pickers, horticulturists
Masseurs, homeopaths
Food processing workers
Foresters
Florists, flower sellers, flower pickers
Herbalists
Dentists (e.g., oil of cloves)
Musicians
Pharmaceutical workers
Cosmetologists, perfumiers, beauticians
Laboratory workers
Textile workers
Tobacco workers
Wood cutters
Wood workers
Sportsmen

also used in folklore medicine as counterirritants and in rubefacient ointments. These plants are responsible for contact allergy, prevalently in food handlers. The compounds that most often cause dermatitis are allyl, phenyl and benzyl isothiocyanates; in cases of dermatitis induced by Capparidaceae it is necessary to test methyl isothiocyanate, too [36, 119]. The concentration in patch tests must be in the range 0.1–0.05% pet. to avoid irritant reactions.

Lichens. They consist of a fungus and an alga growing together in symbiosis, and are found on walls, roofs, rocks and trees. The sensitizing species include *Parmelia*, *Evernia*, *Usnea*, and *Cladonia*. Affected subjects are above all forestry workers and lichen pickers. The dermatitis affects the hands, forearms, face and other exposed sites. Contact allergy is also possible due to perfumes containing oak moss (derived from *Evernia prunastri* Arch). An abnormal photoallergy and an airborne contact dermatitis are also possible [120–122]. The allergizing substances are atranorin, usnic acid, evernic acid and others; they need to be tested at 0.1 or 1% pet. [123, 124].

Primulaceae. Of this widespread family, only primula (*Primula obconica* Hance) is a common dermatological hazard. It grows everywhere in Europe as a house and greenhouse plant because of its long-lasting flowers (Figs. 16.25 and 16.26). Per many years, contact sensitivity to primula was the most common cause of plant dermatitis in Europe; nowadays the problem is much less serious, partly because contact with the plant is avoided owing to its reputation for inducing skin complaints and partly because of the development of the "hypoallergenic" cultivar, that contains less primin. There is ample literature on contact dermatitis to *Primula obconica*. Primin, a quinone, is the main allergen, but miconidin can be sensitizing, too [125, 126]. Primin can also induce erythema multiforme-like reactions (Fig. 16.26) [37, 127].

Ranunculaceae. Many members of this family can be irritant, and that is why they are used as counterirritants in medicine for the treatment of rheumatic joints. The family members most commonly implicated in contact irritation are *Anemone nemerosa* L., *Clematis vitalba* L., *Pulsatilla vulgaris* Miller, *Actaea spicata* L., *Ranunculus arvensis* L., *Ranunculus bulbosus* L., *Ranunculus repens* L., etc. The irritant substance is protoanemonin, released when the plant material is damaged.

Umbelliferae, Rutaceae, Moraceae. The members of these families are common causes of phototoxic and, more rarely, photoallergic contact dermatitis. The photosensitizing agents are psoralens. Since many members of these families are major sources of food (fig, citrus fruits, parsnip, and celery), phototoxic dermatitis can be linked both to occupational and non occupational contact. The word psoralen derives from the species *Psoralea corylifolia* L. (family Leguminosae), whose seeds have been used to treat vitiligo.

Woods. Contact dermatitis from woods is occupational and is observed in carpenters, joiners, and cabinet makers. This is generally an

Fig. 16.25 *Primula obconica*

airborne contact dematitis linked to the accumulation of wood dust adhering to sweaty skin areas (the axillae, groin) and the wrists and ankles, as well as the hands, face and neck. The dermatitis can be associated with systemic symptoms due to the inhalation of these dusts [2, 3, 128–130].

Although it is a rare occurrence, contact dermatitis can also arise in the end-users of wooden products, such as necklaces [131], bracelets (Figs. 16.27, and 16.28) [132], knife handles [133].

The most common sensitizer woods are those to be found in tropical and subtropical regions, while allergy to woods from temperate climes (ash, beech, birch, and poplar) are less frequent. The most common allergens are the quinones, such as 2,5-dimethoxy-1,4-benzoquinone. Given the ubiquitous nature of quinones, cases of cross-sensitivity are frequent [134]. Other well known allergens include turpentine oil and colophony, derived from pines (*Pinus* spp.), firs (*Abies* spp.), spruces (*Picea* spp.), of the Pinaceae family. Once the culprit wood has been identified, patch tests can be performed with freshly made sawdust, 10% pet., on the patients and on controls, in view of the possibility of an irritant reaction [128, 129].

16.6 Pseudophytodermatitis

These eruptions seem to be linked to contact with plants but are actually produced by parasites (mites) that infest plants or their products, by dyes and waxes applied to the skin of the fruit, or by various chemical substances used to treat plants [7].

Pseudophytodermatitis Due to Mites. Farmers and other workers in contact with cereals (wheat, barley, rye) can be infected by parasitic mites (*Pyemotes ventricosus)*

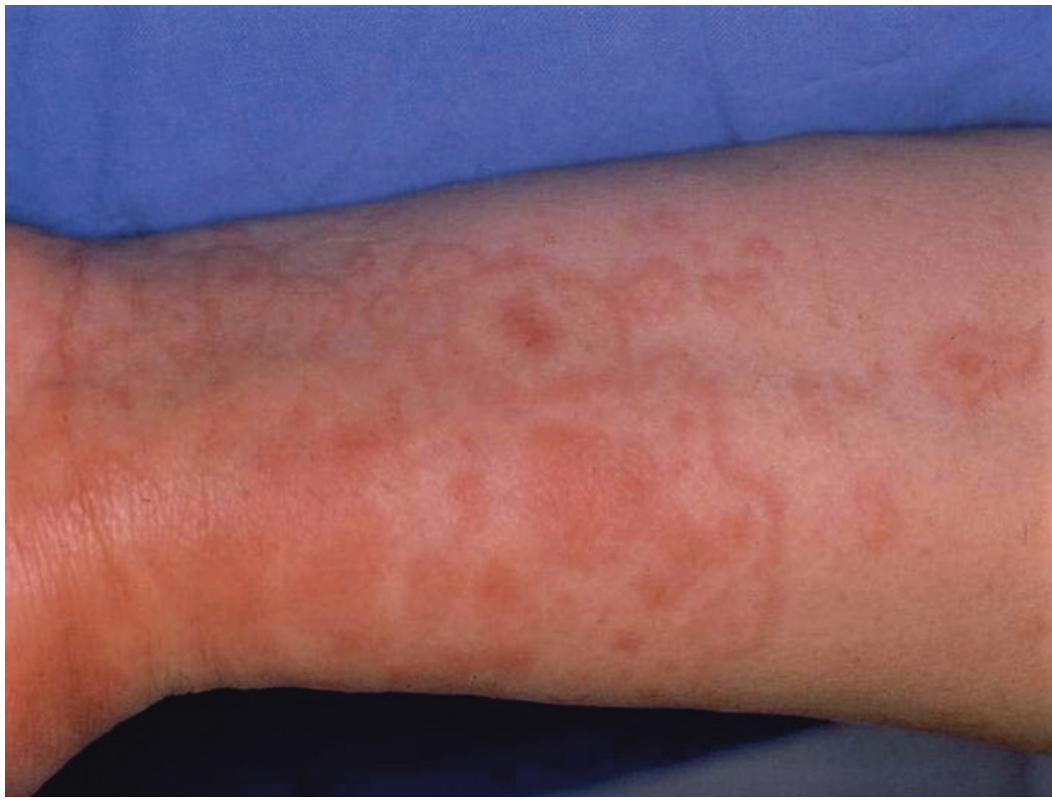

Fig. 16.26 Allergic erythema multiforme-like eruption from primin (Reproduced with permission by Bonamonte and Coll [37])

(Pediculoides). The skin eruption will be generalized, with pomphoid, vesicular, pustulous and petechial lesions. Frequent bathing and changes of clothes can prevent the infestation; impregnating clothes with benzyl benzoate can also be efficacious [7]. *Tyroglyphus farinae*, the flour mite, can parasitize food in homes, like *T. siro*, the cheese mite, that also parasitizes dried fruit, sugar and bulbs. Cheese mites do not suck blood but they migrate to the stratum corneum, inducing a pruriginous eruption that is difficult to differentiate from allergic contact dermatitis. Many other mites that infest cereals, cotton seed and dried fruit (*Carpoglyphus passularum*) can parasitize man.

Pseudophytodermatitis Due to Hairs of Caterpillars. Due to their microscopic hairs containing various histamine substances, pine caterpillars, can induce a peculiar urticarial and papular eruption [135]. The dermatitis is observed in occupational settings (lumberjacks, woodcutters, other forestry personnel, residential gardeners, nurserymen, resin collectors, stockbreeders, and entomologists) and even more in extraoccupational situations, such as among tourers and campers. Depending on the mode of contact, the lesions can be confined (direct contact with caterpillars) or multiple and extended (aeromediated contact with the irritant hairs that can pass through clothes). In the latter case the lesions will affect both sites open to airborne contact, and covered sites. The eruption onset occurs 1–12 hours from contact, or more rarely some days after. Itching is intense and continuous, with intermitting flares. Clinically, the eruption manifests with red macules and papules,

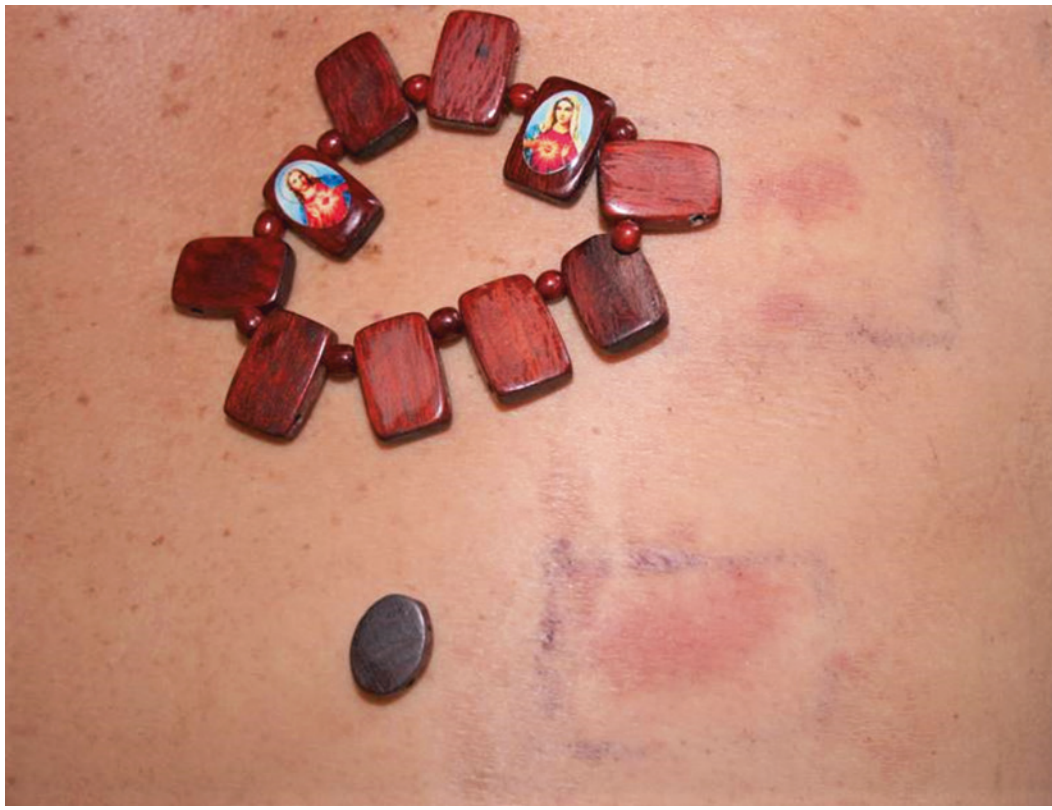

Fig. 16.27 Wooden religious bracelet with positive patch test reaction to furocoumarins

3–8 mm in diameter, overlapping an urticarial base; papules can be surmounted by vesicles. Purpuric and scratching lesions are common findings. Often, the clinical characteristics mimic those of strophulus, sometimes with bullous lesions. The eruption evolves in 3–4 days. In about 10% of cases there is ocular involvement, with an immediate inflammatory reaction that worsens over the following days, featuring photophobia, profuse tearing, and the formation of yellowish conjunctival nodules [135] (see Chap. 11).

Pseudophytodermatitis Due to Chemicals. In rare cases, certified azo dyes applied to the skin of oranges and grapefruits may cause dermatitis. Various plant insecticides may also produce contact dermatitis.

16.7 Clinical and Botanical Investigation

It is often difficult to identify the etiology of a plant contact dermatitis, since it is necessary to take into account the patient's occupation, hobbies and any recent outdoor excursions. The etiological study must proceed along the following steps [5–7, 13, 19, 136, 137].

Samples Collection. It is necessary to collect samples of all the plants the patient has come in contact with, including weeds. The whole plant should be gathered if possible, or the various portions (leaves, petals, branches, roots, fruits), since the allergens may be different from one portion to another. At least 3 samples of each species should be collected and stored in the

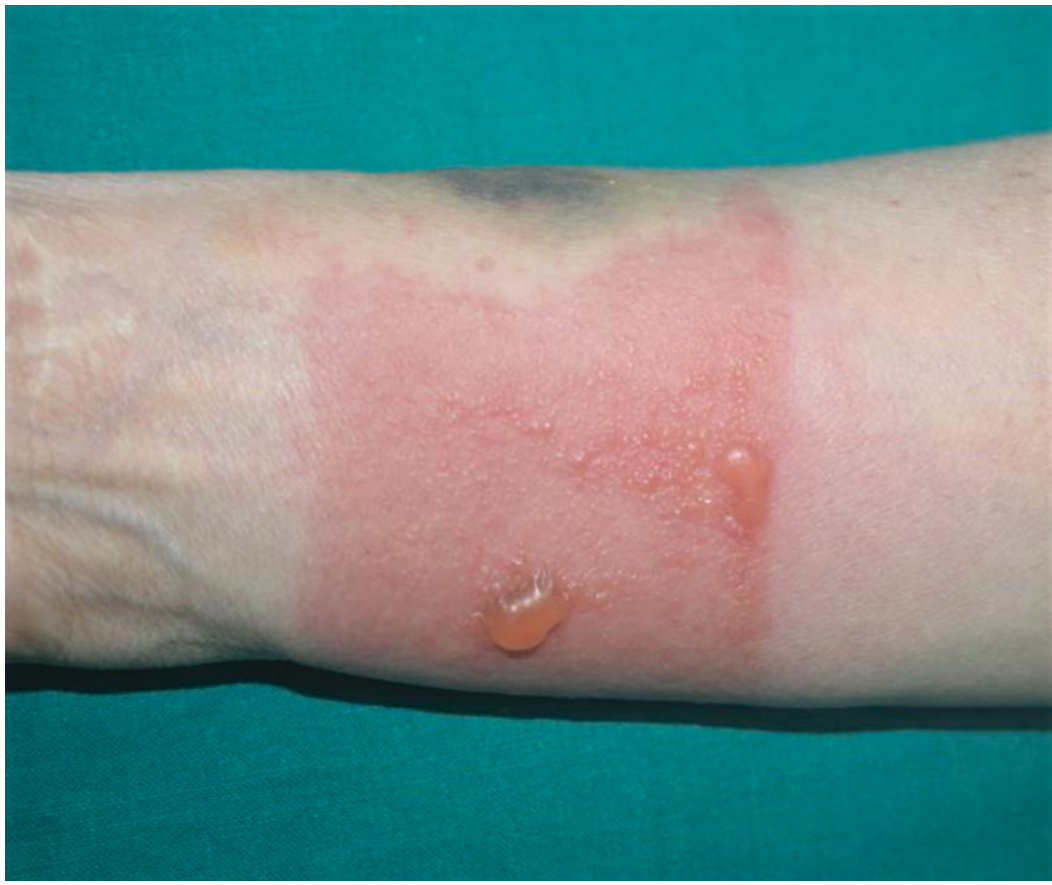

Fig. 16.28 Photoallergic contact dermatitis from furocoumarins in the bracelet in Fig. 16.27

Table 16.6 Some substances employed in plants series

Compositae mix 5% pet (adapt to local indigenous plants)
Propolis 10% pet
α-Methylene-γ-butyrolactone 0.01% pet
Primin 0.01% pet
Diallyl disulphide 1% pet
Tanacetum vulgare 1% pet
Chrysanthemum cinerariaefolium 1% pet
Achillea millefolium 1% pet
Arnica montana 0.5% pet.
Sequiterpene lactone mix 0.1% pet

freezer (one for identification purposes, one for skin tests and one to be used in chemical tests, if deemed necessary). Finally, the samples should be labeled by season and geographic area of collection.

Identification of the Species. Before proceeding to skin tests, it is necessary to identify the species. For this purpose, the colloquial or vernacular names of the plants are useless. To identify the plants it is best to rely on experts from botanic gardens, university botanic taxonomists, the Ministry of Agriculture, and herbalists.

Literature Data. After the identification, it is wise to consult the literature about the antigens (names, chemical formulae, irritant and/or sensitizing potential, concentrations and vectors for skin tests) contained in the various plant portions in this species.

Obtaining the Haptens. Consult the appropriate catalogs of haptens already available on the market. If the substances are not yet available for skin tests, the catalogs of pure raw materials must be consulted.

Preparation of the Plants to Be Tested. If no hapten is available on the market it is best to use the plant as is, preparing it in the following manner. First of all, there is no need to test plants that are notoriously irritant. Secondly, the different parts of the plant must be tested separately, using 'ripe' plants (that are potentially more allergenic than unripe plants), and that are also "fresh", because over time the sensitizing power declines. Next, it is essential to perform the same tests in at least 20 controls to exclude irritant type reactions.

When possible, it is best to use essential oils in the tests, appropriately diluted according to literature data. Otherwise the procedure is as follows: (a) petals and small leaves are delicately compressed; (b) leaves and branches are minced with scissors; (c) bulbs are cut in small pieces after removing the dry external layers; (d) wooden objects are tested through wood shavings; (e) for woods, the sawdust is used.

To extract the antigens from these samples the sample must be immersed (after treatment as above) for 60–90 s in ether and left to dry by evaporation. Then the dry extract is resuspended in ether/acetone/ethanol/vaseline at concentrations ranging from 1 to 10%. Each author has their own method also as regards the extraction vector and the subsequent dilution. The above indications are satisfactory for most antigens but literature data need to be consulted about particular haptens, whose concentration in patch tests may be less than 1%.

In the case of the more common Compositae plants, once treated as above, the respective portion can be tested directly because the antigen is usually present on the surface in the trichomes.

Patch Tests. In addition to the standard series, these must include the appropriate plant series. However, only a few plant-derived haptens are available on the market, even if these can detect allergy to the majority of plants or provide clues on the basis of cross-reactions (Table 16.6) [19]. When necessary, the hapten material can be added with materials obtained directly from the plant, as described above.

Allergodiagnostic Skin Tests with Foods. For these purposes, the rub test and the scratch chamber test can be performed. The former involves gently rubbing a piece of raw food on the flexory face of the forearm. In cases of contact urticaria the immediate reading is obtained after 20 min. IgE-mediated forms need to be confirmed by in vitro immunologic tests. If the rub test is negative, the scratch chamber test can be done: the food (if dry it should be dampened with blotting paper) is applied on scarified skin (a scratch 5 mm long), that is then covered. Reading is made after 20 min for immediate reactions, then the site is again covered and readings made at 1, 2 and 4 days for delayed reactions.

Results and Relevance. The validity and relevance of patch tests results may be difficult to establish. As regards positive reactions to plant material used "as is", it must be taken into account that the reaction could be due to contaminants of the plant material such as pesticides or other agricultural chemicals, or by fungi. Even the use of high concentrations of the extract can be a cause of false positivity, nor must the possibility of active sensitization be underestimated. There could also be possible false-negative reactions in cases of insufficient concentration of the allergen, especially when the plant material is not fresh.

The relevance of positive patch tests is particularly difficult to establish if the patient has handled various plants and for a certain length of time, and so could be sensitized to some or all of them. The cross-sensitization phenomenon further complicates the issue.

16.8 Prevention and Treatment

Wearing gloves can help to protect those handling plants, although some types of gloves are permeable to allergens or can easily be penetrated by thorns. Nitrile gloves, for example, are resistant to tuliposide A, present in *Alstroemeria* and tulips [138]. In general, barrier creams are of little aid, although in the USA some preparations can limit or prevent reactions to poison ivy urushiol [139, 140].

The treatment of plant contact dermatitis is symptomatic. Potent topical corticosteroids and tacrolimus are valid (systemic corticosteroids

are justified in severe reactions). In cases of chronic active dermatitis due to airborne allergens and persistent *Parthenium* dermatitis, azathioprine, cyclosporin or mycophenolate mofetil are helpful.

Hyposensitization measures, such as using poison ivy in certain outdoor occupations, have so far proven ineffective [141]. The induction of tolerance in naïve subjects appears to be a more successful practice than desensitization of those who are already sensitized [142].

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