Plant-Caused Skin Disorders

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Edited by

Vaskrsija Janjić

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Vaskrsija Janjic and Gorica Djelic

FOREWORD

It is estimated that 10,000–50,000 plant species of the world's total flora are able to be used in the diet. Today, only about 5000 species are used directly in the human diet, while three basic edible plants—maize, wheat, and rice—satisfy as much as 60% of human energy and protein needs (Anon., 1999). There are more than 1000 species known in the world today that can be used as vegetables in the diet in a fresh, dry, cooked, processed, or preserved state. About 150 species are grown in the world, and about 30–50 species of vegetables are widely used (Lopez, 1994).

Of the 5,000 plant species used in the diet, only 57 species are staple crops that feed all of humanity. There are eight species of plants belonging to cereals, seven legumes, seven oil-producing species, three tuber species, and two sugar-producing species. In addition to these plants, there are 15 vegetable and 15 fruit species of great importance for the population's nutrition. These cultivated plants provide the necessary proteins, carbohydrates, fats, vitamins, minerals, and bioactive substances for the normal development and functioning of the human body and all of the heterotrophic species in the animal kingdom.

According to Chinese traditional medicine, there are about 5000 medicinal plants, while today's folk medicine relies on about 400 medicinal plants (Petrovska, 2012). Even today, about 80% of the population in developed countries rely on medicines derived from plant extracts; thus, even in highly technologically advanced countries, such as the US, about 25% of prescriptions are for medicines with active ingredients obtained by plant extraction or processing.

Biochemical analyses show that plants produce very different compounds, including those that have toxic and dermatological effects on humans and domestic animals. Plants that are characterised by the synthesis and accumulation of large amounts of these substances are considered to be toxic and dermatologically active. At the same time, these plants are not necessarily harmful. Many of them are known to be excellent medicinal plants, and some of them are decorative and edible plants that are fairly regularly used in the diet. However, on this occasion, our attention in this monograph is focused on plants that cause dermatoses, which can have undesirable and sometimes fatal consequences for humans and domestic animals. Our goal was to point out some of their traits and their importance, outline the basic properties of the major groups of compounds that cause dermatoses and, especially, to focus on introducing certain species of plants, as well as their dermatosis-inducing constituents and specific effects on humans and animals.

In recent years, science has developed new methods and techniques that are of great importance for the isolation, identification, and characterization of the various organic compounds found in plants and other living organisms. Thus, in many plants, very complex organic compounds have recently been discovered and there is still little known about their function. Without a knowledge of the structure of their compounds, it is almost impossible discuss their physiological functions, including their toxicity or their pharmacological activity outside the organism in which they were formed.

When preparing this monograph, the authors had in mind a long-known and well-tried system of giving theoretical explanations for many phenomena and processes occurring in the process of biosynthesis and metabolism of toxic compounds in plants in addition to basic phenomena. However, due to the volume of the material and the basic purpose of this monograph, not all of the theoretical explanations have been given for the many biosynthesis or transformation processes of the numerous compounds included in the composition of a large number of plants which exhibit dermatological properties and which are very difficult to separate from their medicinal effects and use in traditional medicine. Very often it is the same plant or its constituent, but it will have different effects in living organisms at different doses. This is most likely to cause misunderstanding among a wide readership: how can one and the same plant or its constituent can have a dual effect? This is best explained by the famous words of Paracelsus: "Sola dosis sola facit venenum", meaning "the dose makes the poison".

This monograph has two parts. The first part covers the basic concepts of phytodermatoses and the groups of compounds in plants that have this type of physiological effect on humans and animals. The most common form of phytodermatosis is contact dermatitis, and the most common dermatological symptom is eczema. In order to better understand phytodermatoses, the skin reactions caused by contact with plants can be classified as follows:

- Allergic contact dermatitis
- Irritant contact dermatitis
- Contact urticaria
- Phytophotodermatitis

Dermatoses are caused by certain plant constituents that are often classified into groups, such as alkaloids, glycosides, glucosinolates, saponins, phenols, and other compounds.

The second part of the monograph describes 68 plants species that cause dermatoses in humans, especially in those who are engaged in their production, cultivation, planting, pruning, arranging, and selling. These plants are classified into 25 families. Each plant’s morphological description, habitat, ecological indices, distribution, variability, and main constituents with toxic and dermatological effects have been provided. Most of the plants covered in this monograph belong to the following families: Apiaceae (12), Ranunculaceae (7), Araceae (6), and Asteraceae (6 species), which make up 45,59% of all the plants covered in this monograph. A colour photograph is provided for each plant to help with their identification. These plants are most commonly found in our region and there are some constituents in their organs or other parts that exhibit dermatological activity at certain stages of their growth and development. It would be repetitive if the function, biosynthesis, and action of these constituents were explained again in this section. This is why this part of the monograph covers the constituents, their distribution, symptoms of dermatological activity, and similar properties, given that many properties are explained in more detail in the first part of the monograph.

Not only have chemists succeeded in gaining knowledge of some natural products and their materials, as well as synthesizing them in an artificial environment (first in the laboratory and then in the industry as a true "replacement" of natural materials), but they have also managed to produce more complex substances and synthetic products than nature has provided. In chemical laboratories, various substances are synthesized and technological processes for production are tested under very complex and diverse conditions; this includes the natural constituents of the plants that are the subject of this monograph. However, because of their complex structure, steroisomerism, and other properties, the question remains to what degree these two groups are identical.

And finally, of course, the civilizations, societies, and peoples that lived before us did not know as much as we do today. However, we cannot be flattered because we do not know much about their level of understanding. It is enough to mention the achievements of the ancient peoples of Tibet, India, and China, as well as their knowledge of self-hypnosis, telepathy, and telaesthesia, which are only now being studied in the West. Even with the help of modern technology, we probably do not know how much these ancient peoples knew about plants and their uses for various purposes, particularly in terms of medicine.

INTRODUCTION

The world of plants is extraordinarily rich and diverse; it includes over 270.000 known species on Earth today, and it is assumed that there are further undiscovered plant species, which are currently unknown to botanists. The flora of Europe is particularly diverse and distinctive. In Europe, due to its geographical position, climatic, edaphic, and geomorphological conditions, there are eleven vegetation zones with a large number of endemic plant species (Janjic, 2008). The flora is more or less widespread everywhere. Plains, hills, and highlands, as well as areas by the sea, rivers, and lakes, are characterised by typical vegetation. Plants are found in rivers, lakes, seas, and other bodies of water. It is diverse, rich, and extremely interesting. Of this number, only a few hundred are of particular practical importance. The enormous abundance of plants is not yet sufficiently known or exploited.

In recent years, there has been an increasing interest in sources of plant food found in nature. Since substantial amounts of food from nature decay or remain unused, one should not ignore the fact that considerable savings in the national economy could be achieved by both harvesting and industrially processing some of these plants. However, natural reserves of food will be useful to anyone at risk of getting lost or who finds themselves helpless in nature. The awareness that they will be able to survive in any situation, wherever they are, will give them the security and confidence they need. It is understandable that the reserves of food found in nature are essential in cases of severe natural disasters, war, famine, and scarcity of other foods.

There are many plants in nature with certain characteristics. The use of medicinal herbs is widespread in traditional medicine, since many of them have been used since ancient times. It will be sufficient to only mention some of these herbs, such as marsh-mallow (*Althaea officinalis*), yarrow (*Achillea millefolium*), hoary plantain (*Plantago media*), sage (*Salvia officinalis*), thyme (*Thumus serpyllum*), and valerian (*Valeriana officinalis*), to be reminded of their role in treating people during difficult times and wars. These and other herbs are also often used as treatments in peacetime, because it has been observed that the massive and frequent use of synthetic preparations has certain effects on the body.

However, many plants, even herbs, exhibit toxic and dermatological effects on humans and animals under certain conditions. Therefore, the name, “poisonous plant”, is conditional and relative, since most of these plants are used in traditional medicine, and the substances that cause their toxicity are included in the composition of galenic preparations in small, precisely defined quantities to form the active components of specific physiological and therapeutic effects. When ingested in large quantities, these substances are highly toxic (Janjic, 1987; Janjic *et al*. 2008). The importance of this is illustrated by the example of aconitine alkaloid, which belongs to the group of the most potent herbal poisons; its lethal dose for humans is 4 to 6 mg. Therefore, it is of particular importance to know which wild plants are poisonous.

For a plant to have practical use, it is necessary to know its chemical composition among other things. Knowing the chemical composition and quality of individual plants is an important field of research, as it creates conditions for their wider use, which is not only important for wartime conditions but also for general economic progress.

The body of plants is composed of 21 elements: 16 of which (H, O, C, N, P, S, Na, K, Mg, Ca, Cl, Mn, Fe, Co, Cu, and Zn) are part of the composition of all living organisms, and five (B, Al, V, Mo, and J) of some species. It has been found that 29 organic molecules (glucose, ribose, fats, phosphatides, 20 amino acids, and 5 nucleotides), which exist as either monomers or polymers, form a huge number of the different compounds found in plants.

In addition to proteins, carbohydrates, and fats, the composition of plants, includes many other compounds whose role within the plant itself, as well as its physiological effect on other living organisms, is not fully known. First of all, these include organic acids, numerous phenolic compounds, essential oils, glycosides, resins, and alkaloids, as well as a number of other natural compounds. They all participate in the transfer of matter and exert specific and very important different functions. For example, some organic acids do not accumulate in significant amounts and, as a rule, after being formed, they are immediately consumed for other synthetic reactions. Other compounds tend to accumulate, such as alkaloids, essential oils, and saponins, and then are used to exert some physiological effect on living organisms outside the body of the plant.

The formation of primary and secondary metabolites in plants is a dynamic process that changes during their ontogenetic development; this also depends on many environmental factors. During ontogenesis, the plant goes through a phase of vegetative development, involving flowering and fruiting. Each cell and organ reaches a certain size, exhibits certain functions, and then dies. Ontogenesis is characterised by certain transfer of substances: carbohydrates, fats, and proteins (as well as enzymes and coenzymes, such as vitamins). This process includes changes in the dynamics of the synthesis of alkaloids, glycosides, terpenes, phenolic and compounds, etc.

It should be noted that there are specificities in the formation of some secondary metabolites that depend on the systematic affiliation of some plants. It is generally known that there are groups of plants that accumulate essential oils and alkaloids, etc. Furthermore, an uneven distribution of toxic compounds in plants is common. As a rule, the highest percentages of, for example, cardiac glycosides are found in leaves and essential oils in fruits. Likewise, different stages (different phenophases) in the development of one and the same plant are characterised by considerable differences in the number of toxic compounds. Therefore, a plant can be poisonous and dermatologically active only at a certain stage or only some of its organs or parts can be poisonous. Not only the quantity but also the qualitative composition of toxic compounds depends on the stage of plant development. The qualitative composition of toxic compounds may also be different for different organs in the same plant.

Even in species in which the whole plant is poisonous, the number of toxic compounds in different organs usually varies. Thus, for example, in the white hellebore (*Veratrum album*), all parts of the plant are poisonous, but different amounts of these substances are found in different organs: 2.5% in the root, 1.3% in the rhizome, and about 0.5% in the stem. As a rule, the highest percentage of toxic compounds is found in the leaves of the plant during its flowering stage, in the fruiting stage in seeds and fruits, and at the end of the growing season in underground organs, roots, rhizomes, and bulbs. It is not unusual that some plants' young shoots and spring leaves are edible, even delicious, but which become inedible, bitter, and even poisonous in the later stages of development. This effect can be found in the following species: asparagus (*Asparagus acutifolius*), black bryony (*Tamus communis*), rough bindweed (*Smilax aspera*), butcher's-broom (*Ruscus aculeatus*), old man's beard (*Clematis vitalba*), pokeweed (*Phytolacca americiana*), and common milkweed (*Asclepias syriaca*). The content of toxic compounds usually increases during the growing season and most often reaches a maximum during flowering.

Poisonous and skin irritant plants grow together with other plants; therefore, one must be careful when picking wild plants for food. Children are especially attracted by shiny red berries (similar to currants), and there are some deadly poisonous berries among them. These include the fruits of the February daphne (*Daphne mezereum*) and fly honeysuckle (*Lonicera xylosteum*). There have been reports of alder buckthorn (*Rhamnus frangula*) collectively poisoning children on school trips. Children are also attracted to the red berries of wild arum

(*Arum maculatum*) and lily-of-the-valley (*Convallaria majalis*), which are highly toxic. Deadly nightshade (*Atropa belladonna*) berries are also deadly poisonous.

For this reason, it is essential to know what these poisonous plants look like, their phenology, the degree of toxicity, and their physiological effects with symptoms of poisoning, as well as their frequency in different areas.

Depending on the conditions, the soil composition, and the degree of sensitivity of their botanical composition, certain poisonous plants can be found in the following areas:

- On wet meadows: hedge hyssop (*Gratiola officinalis*), creeping buttercup (*Ranunculus repens*), and common soapwort (*Saponaria officinalis*).
- In hilly and humid conditions: autumn crocus (*Colchicum autumnale*) and white hellebore (*Veratrum album*).
- In dry and warm areas: cypress spurge (*Euphorbia cyparissias*), pheasant's eye (*Adonis vernalis*), and yellow foxglove (*Digitalis ambiqua*).
- On slopes: royal knight's-spur (*Delphinium consolida*), corn-cockle (*Agrostema githago*), and charlock mustard (*Sinapsis arvensis*).
- In forest vegetation: fragrant hellebore (*Helloborus odorus*) and deadly nightshade (*Atropa belladonna*).
- In rural habitats: jimson weed (*Datura stramonium*), birthwort (*Aristolochia clematitis*), black henbane (*Hyosciamus niger*), and others.

Accidental poisoning almost always occurs after the ingestion of a plant’s attractive parts. Many researchers around the world have found that accidental poisoning, especially when it comes to children, is caused by ingesting the fruits of plants with a beautiful appearance, colour, shine, and shape. Berries are the fruits of plants containing fleshy and more or less succulent tissue with multiple seeds inside their outer layer. The berry is a juicy fruit with two parts of the fruit layer: an exocarp (in the form of a thin outer layer) and a mesocarp with an endocarp (the largest, fleshy part of the fruit).

It often happens that children, who are looking for blueberries or other fruits in the forest, find similar and very poisonous fruits, such as deadly nightshade (*Atropa belladonna*), Eurasian baneberry (*Actaea spicata*), herb-paris (*Paris quadrifolia*), or fly honeysuckle (*Lonicera xylosteum*). Many berries of poisonous plants are shiny and succulent, and similar in shape and colour to edible berries; they also often grow in the same habitats. Therefore, the most common victims of berry poisoning are preschool children and, less often older boys eager to prove themselves to their peers. Children are especially attracted to shiny red berries similar to currants, and there are some deadly poisonous ones among them. These include the berries of February daphne (*Daphne mezerum*) and fly honeysuckle *(Lonicera xylosteum*). There have been several cases of poisoning on school trips from fly honeysuckle berries.

Children are also attracted by the red berries of wild arum (*Arum maculatum*) and lily-of-the-valley (*Convallaria majalis*), which are deadly poisonous. The berries of bittersweet nightshade (*Solanum dulcamara*) are very poisonous and they resemble the edible red berries of European barberry (*Berberis vulgaris*) in colour and shape. Black bryony (*Tamus communis*) and white bryony (*Bryonica dioica*) climb up shrubs and trees that have edible fruits (e.g. rowans: *Sorbus aucuparia*); their beautiful red berries cause confusion, which can explain the rare cases of poisoning from this plant. There are also dark berries (blueberries: *Juniperus communis*) among edible berries, so one should take special care that children do not confuse them with the deadly poisonous berries of deadly nightshade (*Atropa belladonna*), herb-paris (*Paris quadrifolia*), Eurasian baneberry (*Actea spicata*), and blackberry nightshade (*Solanum nigrum*). There was also a case of the mass poisoning of French soldiers on manoeuvres by nightshade berries. It is not only wild species that are dangerous for children, but also berries from ornamental shrubs, which they come into contact with in playgrounds, parks, gardens, and urban areas. Ornamental shrubs with poisonous berries include guelder rose (*Viburnum* *opulis*), common holly (*Ilex aquifolium*), common yew (*Taxus baccata*), common snowberry (*Symphoricarpos albus*), common ivy (*Hedera helix*), and common spindle (*Euonymus europaea*). Fortunately, most poisonous berries have a sharp, bitter, or repulsive taste, but those that do not have this can be particularly dangerous (e.g., deadly nightshade, wild arum, and black bryony).

In the 1980s in Europe, particularly in Germany, Switzerland, and Austria, it was believed that herbs could only have a therapeutic effect and could not cause unwanted side effects and poisoning, despite the problems resulting from the intentional and unintentional consumption of poisonous plants (Sperl et al. 1995; Rasenack et al. 2003). Due to the dangers that may arise, the Federal Ministry of Health (BGA in Berlin) in Germany has drastically restricted the production and sale of plant products containing unsaturated compounds of necines to reduce the risk to public health caused by pharmaceuticals.

The number of toxic compounds in plants of the same species also depends on external conditions. Trace elements, such as magnesium, iron, manganese, nitrogen, sulphur, and phosphorus, have a great influence on the content of toxic compounds in plants. The number of alkaloids is known to increase in many alkaloid plants if fertilized extensively with nitrogen fertilizers, because alkaloids are derivatives of nitrogen. In addition to fertilizers, soil properties affect the percentage of toxic compounds in plants (e.g., humus content and irrigation). On the basis of comparative studies of the quantitative presence of alkaloids in deadly nightshade (*Atropa belladona*) in two habitats that differed in microclimatic conditions (insolation, temperature, and humidity), it has been shown that the plants that grew under the conditions of intense light, less precipitation, and higher temperature had about twice as many alkaloids. As a rule, most other poisonous plants in southern, sunny, warm, and dry areas contain more toxic compounds than plants that are widespread in northern, cool, and less sunny areas.

There are basically three groups of plants that have adverse effects on humans, as well as animals. The first group includes plants whose pollen has effect on the human body, by causing allergies (pollinosis), especially in people sensitive to it. The second group are plants which, when ingested, have toxic effects due to their constituents. Finally, in nature, there are plants that cause dermatoses when they come into contact with the human body. This third group of plants is the subject of this monograph. We have written a book, *Ragweed*, on allergenic plants, which particularly focused on ragweed as it is the most allergenic plant; this text was published by the Weed Science Society of Serbia (*Herbološko društvo Srbije*) (Janjić and Vrbničanin, 2007). The monograph, *Poisonous Plants and their Poisonous Constituents* was published by the Academy of Sciences and Arts of Republika Srpska (Janjić and Lazić 2016), and we are now preparing this monograph, *Plant Caused Skin Disorders*, which will be published by Cambridge Scholars Publishing (Janjić, 2020).

PART ONE

DERMATOSES AND THE PLANT CONSTITUENTS THAT CAUSE THEM

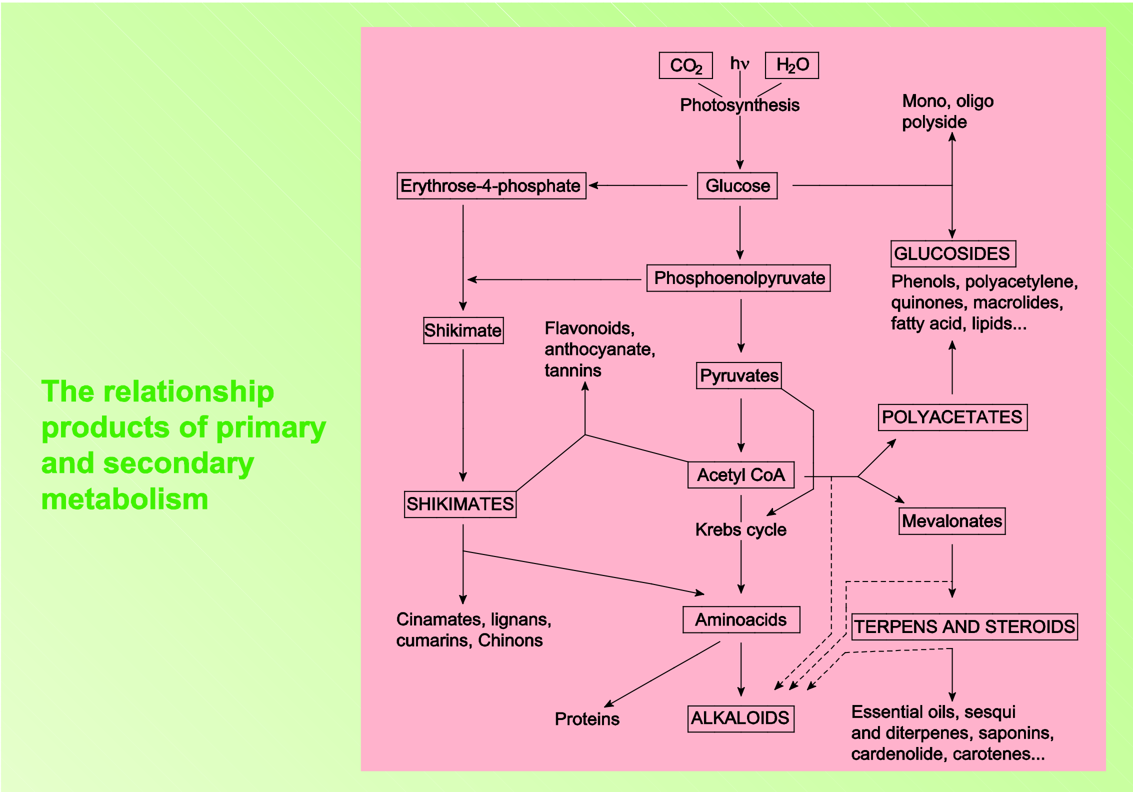
VASKRSIJA JANJIC AND VESNA GAJANIN

PRIMARY AND SECONDARY METABOLISM OF PLANTS: PRIMARY AND SECONDARY METABOLITES

Primary metabolism in plant cells includes the photosynthesis and the transformation of the resulting products. In these processes, the basic building compounds are formed, transformed, and broken down, which provides energy for the growth, development, and functioning of all of an organism's cells. The mechanism of all of the primary metabolism processes is the same in all plants. The main characteristic of the cells of plants and other living organisms is the very close interconnections between certain processes of matter and their energy transfer. In living organisms, there is a uniformity of metabolism that occurs as a result of the high integration between the metabolism of proteins, carbohydrates, lipids, minerals, and other substances (Plaxton *et.al*. 2006). Without the close connection between the catabolism and anabolism reactions, one could not imagine the maintenance, growth, development, and function of cells and the organism as a whole. Central to the metabolism are proteins, which are characterised by the exceptional richness and diversity of their chemical properties and functions, as well as a wide range of simple and complex compounds that are part of the cellular protoplasm. There are numerous examples which refer to the uniformity of metabolism in the major groups of organic compounds (Kruger *et al.* 1999). For example, amino acids may be subject to oxidative deamination, as they can be separated into keto acids and NH_3, which, by amination with other keto acids formed during the oxidation of sugar, breakdown products and produce new amino acids that are part of new proteins. However, the keto acids formed by deamination can be subject to oxidative decarboxylation, which forms CO_2.

The basic characteristics of plants' secondary metabolites are that they have low-molecular weight compounds which have no energy significance, they are very chemically diverse, and they perform certain biological and pharmacological activity. Secondary metabolism processes only partly occur using the same mechanism in different plants. There are certain specificities in the formation of secondary metabolites in different plant species, or in the same plant species, but in different tissues (Hussein and El-Anssary, 2018). These specificities are due to the presence of different enzymes in these plants or their organs and tissues, which contributes to changes in their basic biosynthetic pathway or its branches; this leads to the synthesis of different metabolites. The enzymes that cause the individual stages of certain secondary metabolic processes have only been partially identified and are still not fully understood.

Secondary metabolic pathways in plants are extremely complex and usually incorporate a number of different interconnected mechanisms. The enzymes involved in these mechanisms are mainly influenced by external factors. The pathways that regulate these enzymes represent a fascinating area of scientific research since many products from the secondary plant metabolism are of great importance, especially for the pharmaceutical and food industries. According to the chemical classification, secondary plant metabolites include organic acids (aliphatic, aromatic, and heteroaromatic), phenolic compounds (phenolic glycosides, phenolic acids, lignans, coumarins, hormones, xanthones, quinones, and tannins), terpenes (monoterpenes, sesquiterpenes, diterpenes, triterpenes, gibberellins, carotenoids, and polyterpenes), iridoids, volatile oils, steroid compounds, saponins, alkaloids, compounds containing sulphur, and other groups of secondary biomolecules (Pagare *et al*. 2015).



Scheme 1-1: Relationship between primary and secondary metabolism products

For a long time, the real function of secondary metabolites in the body of plants was unknown. It is now known that secondary metabolism compounds are inactive forms and that they are depots for harmful products. They are components of some enzyme systems (coenzymes); they have hormonal activity and a protective effect for the plants in which they are found; and they regulate relations to other plants (allelopathic effect). The role of secondary metabolites is the adaptation of a particular plant species to the function of various environmental factors. The function of secondary metabolites is not yet fully understood, and it is being extensively studied today.

THE MAIN CONSTITUENTS OF PLANTS THAT CAUSE DERMATOSES

Thousands of plant species and many of their constituents cause dermatoses in humans. Most reactions caused by plant chemical irritants come from seven basic irritant groups: calcium oxalate, protoanemonin, isothiocyanates, diterpene esters, bromelain, and alkaloids. They are dissolved or suspended in sap from a plant's stem, leaves, flowers, fruits, and roots.

Calcium salts of oxalate are insoluble in water and are in the form of crystals called raphides, which have a specific shape. Due to their sharp structure, they cause mechanical damage to the skin when they come into contact with it. Raphides longer than 180 µm are considered to have the strongest effects (Sakai *et al*. 1984). They are classified as chemical irritants because they enable the penetration of other chemical compounds, including proteases, saponins, alkaloids, and bromelain. *Dieffenbachia*, a very common and interesting decorative indoor plant, contains calcium oxalate in its leaves and flowers, which very often causes severe effects on the hands (Ippen *et al*. 1986). Then, saponins, glycosides, cyanogenic proteolytic enzymes, and alkaloids go through the damaged skin, which probably contributes to the formation of blisters on the skin. If the content is transferred from the hands to the eyes, then pain is felt, as calcium oxalate penetrates the cornea (Ippen *et al*. 1986). Other plants of the *Araceae* family, such as *Philodendron* spp., can cause similar symptoms due to the presence of calcium oxalate (Barabe *et al*. 2004).

The saps of tulips and other plants of the *Liliaceae* family contain the well-characterised Tulipalin A. The combined effects of irritants and allergens lead to the specific symptoms of a disease called "tulip fingers" (Bruynzeel, 1997). The hands become chapped and hyperkeratosis forms due to the effects of this irritant. This dermatosis is probably most common in florists (Lovell, 1993). Their stem contains plenty of calcium oxalate in the form of raphides. Following contact with their mucus and sap, which are found in its hollow stem, the so-called "daffodil itch" occurs, usually on the fingers and forearms (Bruynzeel, 1997; Julian and Bowers, 1997). Hyacinths and sentry plants also contain large amounts of calcium oxalate. Thus, for example, one drop of the sentry plant sap extracted from a leaf (0.03 mL) contains about 100 calcium oxalate raphides longer than 500 µm (Salinas *at al.* 2001). Raphides are also present in other plants. For example, the dry matter of some cacti, such as *Cephalocereus senilis*, contains about 85% calcium oxalate.

Protoanemonin is an irritant chemical compound that can be found in many plants of the *Ranunculaceae* family. It usually causes conjunctivitis and irritation to the nasal airways. Longer contact causes erythema, oedema, blisters, ulceration, and residual hyperpigmentation (Rudzki and Dajek, 1975). It is often confused with phytophotodermatitis (Lovell 1993, McGovern and Barkley, 1998). These phenomena are caused only by fresh macerated leaves, as protoanemonin is hydrolysed to anemonin, which does not cause skin irritation. *Ranunculus illyricus* has a particularly high content of protoanemonin; this plant grows as a weed and is used in medicine in South America and the Middle East (Polat *et al.* 2007; Oztas *et al.* 2006). In addition to the genus *Ranunculus*, this compound can be found in some genera of decorative plants, such as *Anemone*, *Clematis*, and *Helleborus*. The genus *Pulsatilla*, which includes the European species *Pulsatilla vulgaris* and the American prairie species *Pulsatilla patens* is particularly significant (Lovell, 1993). In this family, *Ceratocephalus falcatus*, an increasingly common weed species in the Middle East, is also known for this phenomenon; it also causes second-degree blisters (Karaca *et al.* 2005; Metin *et al*. 2005).

Isothiocyanates are major irritant compounds found in many species of plants of the *Brassicaceae* family. Glucosides (glucosinolates), which are precursors in the synthesis of isothiocyanates, are found in all parts of these plants, but particularly in their seeds. Irritants are formed under the influence of the myrosinase enzyme and released after damage to the plant. This reaction produces isothiocyanate, which reacts with the proteins in human skin and mucous membranes (Spoerke and Smolinske, 1990; Crosby, 2004). The spicy taste of these plants comes from isothiocyanate (Marks and De Leo, 2002). The symptoms appear in the form of erythema and urticaria. In addition to plants belonging to the *Brassicaceae* family, isothiocyanates and similar compounds can also be found in the following families: *Resedaceae*, *Caricaceae*, *Euphorbiaceae*, *Tropaeolaceae*, *Phytolaccaceae*, *Plantaginaceae*, and *Capparaceae* (Spoerke and Smolinske, 1990).

Phorbol, ingenol, and daphnane are also irritant chemical compounds, which are collectively referred to as diterpene esters. They are the most irritant compounds among all of the plant irritants (Crosby, 2004). They are most prevalent in the *Euphorbiaceae* family, which is a very large as it is comprised of more than 8,000 species in 300 genera (Webster, 1986). It is believed that diterpene ester is the primary substance found in the sap of these plants. In fact, almost 90% of species of the *Euphorbiaceae* family have irritant effects (Kinghorn, 1979; Kinghorn and Evans, 1975). In addition to their irritant effect, diterpene esters also play a role in tumourigenesis, through the activation of the cellular protein kinase C (Ono *et al.* 1989). Since the esters in their sap are irritants, the plants of this family are the most irritant plants. The skin and eyes are especially sensitive to these irritants. As a result of their toxic effects, pain, erythema, oedema, conjunctivitis, and even blindness might occur (Lowell, 1993; Asilian and Faghihi, 2004). If the leaves or fruits are ingested, bloody diarrhoea and vomiting will occur. *Euphorbia pulcherrima* is known as a decorative plant from this family, as well as for its low content of these irritant substances. Other plants of the *Euphorbia* genus, such as *Euphorbia maculata*, *Euphorbia peplus*, and *Euphorbia marginata*, are weeds known for causing irritation (Crosby, 2004; Marks and DeLeo, 2002). *Hippomane mancinella*, a woody species growing in Central America, and the southern region of Florida, is perhaps the most famous member of the *Euphorbia* family. This plant produces fragrant fruits which, when ingested, cause pain in the mouth and mucosal oedema, followed by vomiting and haemorrhagic diarrhoea (Morton and Miami, 1971). Every part of the stem can cause irritation to the skin on the hands, face, and genitals (Gunjan et al. 2009). Even when it is dried, it can still cause irritation. *Euphorbia tricualli*, a more widespread plant with a greater sap production, is known to cause dermatitis and even temporary blindness (Crosby, 2004). The majority of plants from the genus *Euphorbia* grow as shrubs in the USA. *Croton texensis*, which also belongs to this genus, causes blisters on the skin due to phorbol esters found in the leaves, stems, and fruits. There are about 45 species of the *Croton* genus in the USA, some of which are decorative (Crosby, 2004; Hausen and Schulz, 1977).

Bromelain is isolated from the fruit of *Ananas comosus* (the *Bromeliceae* family). This enzyme contains proteases, phosphatases, and peroxidases. Since it has distinct enzymatic activity, bromelain is used in the food and meat industry (Raison-Peyron *et al.* 2003). The proteolytic activity of bromelain causes skin irritation and also affects the dermal blood vessels (McGovern and Barkley, 1998). Due to bromelain's activity, workers who cut pineapple often lose their fingerprints. Many other plant constituents can cause dermatoses in humans, and they are described in more detail in this monograph.

Since ancient times, plants have been known to cause hyperpigmentation of the skin. As early as 2,000 BC, the ancient Egyptians used the plant *Ammi majus* (*Apiaceae*, *Umbeliferae*), which grows in the valley of the Nile, for sun exposure. Even today, Egyptian merchants and herbalists sell a yellowish-brown powder called "Aatrillal", which is prepared from the *Ammi majus* seeds to treat leukoderma. Indian medicine uses hot extracts from the *Psoralea corylifolia*'s leaves, seeds, and roots, which is known as "bevachee" in southern Africa. In India it is used for "white leprosy", which is also known as "vitiligo", while the Chinese recommend the leaves of *Angelica archangelicum* for the same purpose. The name for these extracted compounds is psoralenes; these are isolated from the plant *Psorela corylifolia (*Pathak, 1986; Pathak and Fitzpatrick, 1992).

Dermatitis caused by parsley (*Pastinaca sativa*) and/or garden angelica (*Angelica archangelicum*) was identified in the USA and England as early as 1897 (Mabberley, 1987; Stowers, 1897). Unfortunately, at the time, the authors were unaware that their reaction occurred in the presence of UVA. In 1916, Freund observed hyperpigmentation resulting from bergamot oil (Freund, 1916). This author also did not know that the presence of UVL was required to cause changes to the skin. Oppenheim (1932) found that the exposure to UVL was required to induce the reaction and that blisters appeared 24–48 hours later (Oppenheim, 1932). Kuske (1938) showed that plant furocoumarins cause photosensitisation. Jensen and Hansen found that UVL of a wavelength between 320 and 380 nm caused the maximum reactions (Jensen and Hansen, 1939). Klaber coined the term phytophotodermatitis in 1942, to emphasise that it takes a plant and light to cause the reaction (Klaber, 1942). Finally, an Egyptian professor at the Cairo Faculty of Medicine, Department of Dermatology, noticed that some plants were used in traditional medicine, which started the development of modern phytotherapy (PUVA) for vitiligo and psoriasis. In 1940, El Moftyhe used crystalline methoxsalen (8-MOP, xanthotoxin) and then treated vitiligo exposed to the sun.

Vitiligo or leukoderma is an acquired chronic skin disease that occurs in the form of smooth, white spots on different parts of the body. It is one of the most common diseases in the group of hypopigmentation disorders. The exact cause of the disease is complex and it has not yet been understood. In 30% of cases the disease is hereditary. It is assumed that melanocytes (cells that produce the skin pigment melanin) are destroyed for unknown reasons. Other contributing factors include repeated sunburn, trauma, and emotional stress; vitiligo is also increasingly regarded as an autoimmune disease. This disease is not contagious and occurs in all age groups and in both sexes. The incidence of the disease is about 1–2%.

Psoriasis has been successfully treated with PUVA since 1974 at Harvard Medical School's Department of Dermatology. PUVA is an acronym: P stands for psoralen, U for ultra, V for violet, and A for the part of the solar spectrum between 320 and 400 nanometres wavelength. Today, PUVA is used in the treatment of many diseases, including palmoplantar pustulosis, fungal mycoses, and atopic dermatitis (Pathak and Fitzpatrick 1992). Psoralens are chemicals found in certain plants. They have the ability to absorb ultraviolet light in the UVL part of the solar spectrum. When the light energy is absorbed, psoralen interacts with DNA causing the inhibition of cell division, which is its default mode of action.

There are a great many plants in the world that have toxic and irritant effects on humans and animals. Of course, it would be almost impossible to cover them in one book. Table 1-1 lists plants that commonly cause various dermatoses in humans, which are present throughout the world.

Table 1-1: Plants that cause dermatosis in the world (cited and adapted from Muenscher, 1960; Tampion, 1977; Janjić and Lazić, 2016).

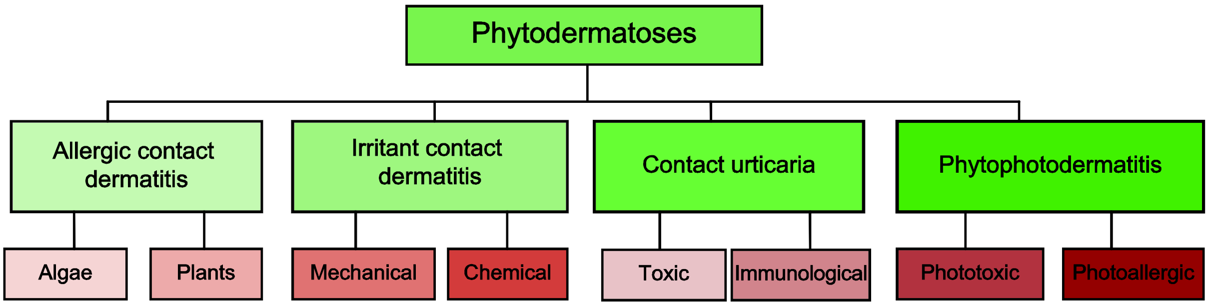
Species name	**Part of the plant**	**Species name**	**Part of the plant**
Ailanthus altissima (Mill.) Swingle	Flower, leaf	*Hedera helix* L.	Leaf
Anacardium occidentale L.	Sap	*Heleborus niger* L.	Leaf
Anagallis arvensis L.	Leaf	*Heracleum lanatum* Michx	Leaf
Anthemis arvenssis L.	Leaf, flower	*Hippomane mancinella* L.	Milky sap
Anthemis cotula L.	Leaf, flower	*Humulus lupulus* L.	Leaf
Aralia spinose L.	Seed	*Hypericum perforatum* L.	Leaf
Arctium lappa L.	Leaf	*Iris versicolor* L.	Rhizomes
Arisaema triphyllum L.	Leaf, root	*Iris spp.*	Rhizomes
Asarum canadense L.	Leaf	*Iva xanthifolia* L.	Leaf
Asimina triloba (L.) Dunal	Fruit	*Jatroha stimulosa* Michx.	Leaf, stem
Asparagus officinalis L.	Young stem	*Juniperus virginiana* L.	Fruit
Borago officinalis L.	Leaf	*Juniperus spp.*	Fruit

Buxus sempervirens L.	Leaf	*Laportea Canadensis* (L.) Wedd	Leaf, stem
Cannabis sativa L.	Leaf, flower	*Leonnurus cardiac* L.	Leaf
Catalpa speciosa (Warder) Warder ex Engelm	Flower	*Lycopersicon esculentum* (L.) H. Karst	Leaf, stem, fruit
Caulophyllum thalictroides (L.) Michx.	Root	*Maclura pomifera* (Raf.) Schneid	Milky sap, thorns
Chelidonium majus L.	Sap	*Mentzelia spp.*	Leaf
Chimaphila umbellata (L.) Barton	Leaf, stem	*Metopium toxiferum* (L.) Krug & Urb.	Leaf, bark
Clematis virginiana L.	Leaf, stem	*Nerium oleander* L.	Leaf
Colchicum autumnale L.	Leaf	*Pastinaca sativa* L.	Leaf, hairs, stem
Conium maculatum (L.,1753)	Leaf	*Phaecelia spp.*	Leaf
Convallaria majalis L.	Leaf	*Podophyllum peltatum* L.	Root
Cypripedium reginae Walter	Hairs, leaf, stem	*Polygonum spp.*	Leaf
Cypripedium parviflorum Salisb.	Hairs, leaf, stem	*Primula spp.*	Leaf
Daphne mezerum L.	Bark	*Ptelea trifoliate* L.	Leaf
Datura stramonium L.	Leaf, flower, fruit	*Ranunculus spp.*	Leaf
Daucus carota L.	Leaf	*Rheum rhaponticum* L.	Leaf
Delphinium ajacis L.	Leaf, seed	*Rus verniciflua* Stokers (RVS)	Leaf, bark, fruit, lacquer
Dictamnus albus L.	Seeds, leaf	*Rumex spp.*	Leaf
Dirca palustris L.	Bark	*Ruta graveolens* L.	Leaf
Echium vulgare L.	Leaf, stem	*Sanguinaria canadensis* L.	Stem, root sap
Encelia californica Nutt	Leaf	*Sedum acre* L.	Sap
Erigeron Canadensis (L.) Cronquist	Leaf	*Taxus spp.*	Tree
Euphorbia marginata Pursh	Milky sap	*Toxidendron radicans* (L.) Kuntze	Leaf, bark, fruit
Euphorbia spp.	Milky sap	*Toxidendron vernis* (L.) Kuntze	Leaf, bark, fruit
Fagopyrum esculentum Moench	Leaf	*Trifolium hybridum* L.	Leaf
Gelsemium sempervirens (L.) J. St-Hil.	Leaf, stem	*Urtica spp.*	Leaf, stem
Ginkgo biloba L.	Fruit	*Veratrum viride* Aiton	Leaf

TYPES OF PLANT-INDUCED DERMATOSES

Many plants cause dermatoses in humans and pose a problem for dermatologists and allergists (McGovern and Barkley, 1998). Even today, the frequency of plant-induced dermatoses is still not known. It is estimated that around 334 million people, that is, 3.5% of the world's population, are diagnosed with dermatoses every year (Anon., 2015). Dermatitis most commonly occurs in early childhood. About 20% of children in the UK and 10% in the USA suffer from different types of dermatoses (McAleer *et al*. 2012). Out of more than 500,000 species of plants in the world, it is estimated that around 10,000 can cause dermatoses in humans (McGovern, 2007). Phytodermatoses are plant-induced dermatoses. They are mainly caused by direct contact with a plant, but they can also occur due to sun exposure (Reis, 2010). Dermatoses that occur without direct contact with a plant can be caused by certain perfumes, creams, and other cosmetic products. Some cosmetic products contain substances, such as eugenol, isoeugenol, cinnamaldehyde, rosin, and turpentine, which originate from plants and are found in many cosmetic products (Figures 1-1 and 1-2). Lichens, which are not considered to be plants but are, instead, organisms formed by a symbiosis between fungi and algae, produce usnic acids, which are commonly used in cosmetics for sun protection (Quirino and Barros, 1995; Rademaker, 2000). In order to better understand phytodermatoses, skin reactions caused by contact with plants can be classified as follows:

- Allergic contact dermatitis
- Irritant contact dermatitis
- Contact urticaria
- Phytophotodermatitis



Scheme 1-2: Types of phytodermatosis in humans

Plants from the *Asteraceae* (Compositae) family most commonly cause dermatoses in humans, especially those who work with them frequently (farmers, gardeners, florists, etc.) (Stoner and Rasmussen, 1983; Mitchell and Rook, 1979; Hausen, 1973). There are about 150 plant species in this family that cause dermatoses in humans. Dermatoses caused by these plants occur throughout the world, but they are more frequent in areas with warmer climates (Stoner and Rasmussen, 1983; Mitchell and Rook, 1979; Lonkar *et al.* 1974; Pasricha and Fox, 1987; Burry *et al*. 1973; Menz and Winkelman, 1987; Tiwari *et al.* 1979). Due to the vast expanse and geographical variability, different genera from this family are present in various parts of the world. For example, the *Ambrosia* genus (e.g. *Ambrosia psilostachya*) is present in the USA, the *Chrisanteme* genus in Europe, and the *Arctotheca calendula* genus in Australia (Stoner and Rasmussen, 1983; Mitchell and Rook, 1979). In India, *Parthenium hysterophorus* from the *Asteraceae* (*Compositae*) family commonly causes contact dermatitis (Lonkar *et al.* 1974; Pasricha and Fox, 1987; Tiwari *et al*. 1979), while only 4 species, according to some studies, cause dermatoses in humans in northern India (Sharma and Kaur, 1990).

Figure 1-1: Allergic reaction and clearly restricted erythema: the patient applied sunscreen lotion (Vesna Gajanin, 2019)

Figure 1-2: Clearly restricted erythematous plaque: allergic reaction to deodorant with essential oils (Vesna Gajanin, 2019)

There are about 500 varieties of chrysanthemums in the *Asteraceae* (*Compositae*) family. They are the most common cause of dermatoses in florists. This family is one of the largest families and it includes about 20,000 species of plants. These are mainly herbaceous plants. Many of these species are weeds, and only some are vegetables or ornamental plants. Allergens, which are found in plants of this family, belong to sesquiterpene lactones. Over 100 identified sesquiterpene lactones are potentially allergenic (Salopoic *et al.* 2013). A problem may arise when it comes to determining which lactone is allergenic. Unfortunately, general tests cannot be used here, but instead they must be done with the actual plant to which the patient has been exposed. Diffuse redness and thickening of the skin occur, which resembles photodermatitis.

Table 1-2: Overview of families and genera that cause dermatoses in humans

Family	**Genus**	**Type of allergy**	**Substance that causes dermatosis**
Amaryllidaceae	*Alsmeria*	Allergic contact dermatitis	Tulipanin (methylene lactone)
	Narcissus	Irritant and contact dermal dermatitis	Alkaloids
Anacardiaceae	*Anacardium*, *Mangifera*, *Rhus*, *Semecarpus*, *Toxicodendron*	Allergic contact dermatitis	Phenol derivatives, urushiol
Apiaceae	*Anthurium*, *Arum*, *Caladium*, *Dieffenbacchia*, *Epipremnum*, *Philodendron*	Irritant dermatitis (Epipremnum = allergic contact dermatitis)	Calcium oxalate crystals
Araliaceae	*Hedera*	Allergic contact dermatitis	Falcarinol
Aspleniaceae	*Rahmora*	Allergic contact dermatitis	
Asteraceae	*Achillea*, *Ambrosia*, *Cichorium*, *Chrysanthemum*, *Cynara*, *Helenium*, *Lactuca*, *Leuchanthemum*, *Matricaria*, *Parthenium*, *Rudbeckia*, *Solidago*, *Tageted*, *Taraxacum*, *Xanthium*	Allergic contact dermatitis	Sesquiterpene lactones
Boraginaceae		Mechanical dermatitis, irritant dermatitis	Irritant hairs
Bromeliaceae		Irritant dermatitis	Acid derivatives, proteolytic enzymes
Cactaceae	*Opuntia*	Mechanical dermatitis, irritant dermatitis	Hairs
Capparidaceae	*Boscia*, *Bucholzia*, *Capparis*, *Cleoma*, *Crateva*, *Gynandropsis*, *Maerva*, *Polinasia*	Irritant dermatitis	Sulphur glycosides
Cladoniaceae	*Cladonia*	Allergic contact dermatitis	Usnic acid

Crassulaceae	*Sedum, Sempervivum*	Irritant dermatitis	Acid derivatives
Brassicaceae	*375 Rodova Brassica*	Irritant dermatitis	Glucosinolates
Cucurbitaceae	*Echballium*	Irritant dermatitis	
Davalliaceae	*Nephrolepsis*	Allergic contact dermatitis	
Euphorbiaceae (Podfam. Crotonoideae, Euphorbiodeae	*Aleurite*, *Codiaeum*, *Euphorbia*, *Hippomane*, *Hura*, *Synadenium*	Allergic contact dermatitis	Tetracyclic diterpene derivatives
Fabaceae	*Myroxolon*	Allergic contact dermatitis	Aldehyde, alcohol derivatives
Frullaniaceae	*Frunalia*	Allergic contact dermatitis	Sesquiterpene lactones (frullanolide)
Ginkgoceae	*Ginkgo*	Allergic contact dermatitis	Phenolic acids
Hydrophyllaceae	*Phacelia*, *Wigendia*	Allergic contact dermatitis	Quinone derivatives
Lauraceae	*Cinnamomum*, *Lauris*	Allergic contact dermatitis	Proteolytic enzymes
Lilliaceae	*Allium*, *Erythronium*, *Tulipa*, *Aloeas*	Allergic contact and irritant dermatitis	Sulphur derivatives, alkaloids
Magnoliaceae	*Liriodendron*, *Magnolia*, *Michelia*	Allergic contact dermatitis	Sesquiterpene lactones
Moraceae	*Ficus*	Phytophotodermatitis	Furocoumarins (psoralen, bergapten)
Orchidaceae	*Coleus*, *Cymbdium*, *Cypripedium*	Allergic contact dermatitis	Quinone derivatives
Papaveraceae		Irritant dermatitis	Alkaloids
Paremliaceae	*Parmelia*	Allergic contact dermatitis	Usnic acid
Polygonaceae	*40 genera*, *Rumex genus*	Irritant dermatitis	Calcium oxalate crystals
Primulaceae	*Anagalis*	Irritant dermatitis	Proteolytic enzymes
	Primula	Erythema multiforme, Allergic contact dermatitis	Quinone derivatives, primin allergen in trichomes
Protaceae	*Grevillea*	Allergic contact dermatitis	Phenols
Ranunculaceae	*Anemona*, *Caltha*, *Clematis*, *Ranunculus*	Irritant dermatitis	Lactone derivatives
Resedacea	*Reseda*	Irritant dermatitis	Thioglycoside derivatives

Rosaceae	*Reseda*	Mechanical irritation	Thorn
Rutaceae	*Citrus*	Irritant dermatitis, Allergic contact dermatitis, Phytophotodermatitis	Aldehydes, alcohols
	Dictamus, *Ruta*	Phytophotodermatitis	Acid derivatives
Solanaceae	*Capsicum*	Irritant dermatitis	Capsaicin
Thymelaeaceae	*Daphne, Thymelaea*	Irritant dermatitis	Terpene derivatives
Urticaceae	*Parietaria*, *Urtica*	Urticaria	
Usneaceae	*Evernia*, *Usnea*	Allergic contact dermatitis	Usnic acid

ALLERGIC CONTACT DERMATITIS (ACD)
(*Dermatitis allergica e contaactu*)

Allergic contact dermatitis is an inflammatory dermatosis that results from the skin's inadequate response to environmental allergens. According to the current classification, this dermatosis develops due to the delayed allergic reaction of type IV (according to the classification by Gell and Coombs, Descotes and Choquet-Kastylevsky, 2001), during which antigen and antigen-presenting cells (Langerhans cells) react in the small blood vessels of the dermis. Clinical symptoms occur between 24 and 72 hours after contact. According to their course, allergic reactions can be acute, subacute, subchronic, and chronic. The severity of an allergic reaction depends on the potential and the concentration of the contact allergen substance, damage to the skin's protective barrier (acidic pH of the skin and the protective lipid layer on the surface of the skin), and the length of exposure to the allergen.

There are three types of allergic contact dermatitis:

- Basic contact dermatitis
- Allergic dermatitis of the *Tulipa* type
- Contact dermatitis to allergens in the air

Basic contact dermatitis (an acute form of contact allergic dermatitis) is accompanied by severe itching of the skin. The clinical signs describe four stages:

- Erythematous: clearly limited redness and swelling of the skin (erythema and oedema) (Figures 1-3 and 1-4)
- Vesicular: emergence of blisters (vesicles or bullae) (Figures 1-5 A and B, 1-6)
- Wetting stage: emergence of bare, wet areas on the skin (erosion) due to a blister bursting
- Drying, changing, and healing

Figure 1-3 (left): Clearly restricted erythematous plaques at the area of contact with the allergen (Vesna Gajanin, 2020)

Figure 1-4 (right): Volar side of forearm: oedema and clearly limited erythematous plaques (Vesna Gajanin, 2020)

Figure 1-5: A) single erythematous papules, plaques, and bullae; B) erythematous plaques with vesicles and bullae on the surface (Vesna Gajanin, 2019)

Figure 1-6: Bullous: an acute form of allergic contact dermatitis (Vesna Gajanin, 2019)

Chronic allergic contact dermatitis occurs after prolonged exposure to allergens. It is characterised by skin writing, dry thickened skin with lichenoid papules, rhagades (cracks on the skin), and scabs. These changes result from scratching due to the intense itching (Figures 1-3 and 1-4).

A diagnosis of ACD is made on the basis of medical history and clinical presentation, and it is confirmed by laboratory patch tests. Patch tests are performed on clean back skin using allergens in petroleum jelly. Readings are performed after 24, 48, and 96 hours. Positive reactions are read in stages, from the occurrence of mild erythema and skin oedema at the site of application, through the occurrence of a moderate number of erythematous papules and vesicles, to the occurrence of a large number of papules and vesicles, and intense erosion and wetting (Lipozenčić, 2008; Karadaglić 2016).

Differential diagnosis. *impetigo*, *lichen simplex chronicus*, atopic dermatitis, nummular eczema, scabies, psoriasis, seborrheic dermatitis, and insect bites.

Treatment. The most important part of treatment is to avoid allergens. For changes on the skin, depending on the form (dry forms, i.e., non-wetting forms), a topical corticosteroid and antibiotic ointments and creams may be applied, or saline and silver nitrate pledgets if there are bare and wet areas on the skin. For severe allergic reactions, systemic corticosteroid and antibiotic therapy is administered, with the application of antihistamines (Lipozenčić, 2008). Phototherapy, azathioprine, and cyclosporine are also applicable in the third line of treatment (Ferri, 2011).

In addition to the above forms of allergic contact dermatitis, *Tulipa* allergic dermatitis can also occur, as well as contact dermatitis caused by allergens from the air. Allergic dermatitis of the *Tulipa* type occurs frequently in people who grow plants from the *Liliaceae* and *Alstroemeriaceae* families, and it is manifested by painful changes on fingers (Saint-Mezard, 2004). The following stages are described for allergic dermatitis of the *Tulipa* type:

- Hyperkeratosis
- Inflammatory granuloma
- Same symptoms as those following contact with the *Tulipa* bulb

Contact dermatitis of the *Tulipa* type occurs in about 30% of workers who cultivate these plants. Also, there is a difference in the allergic reactions caused by tulips grown in India compared to those grown in Europe. Since a manual process is used to grow these plants, it is necessary to use protective gloves because allergic changes can appear on both hands, the thumb, forefinger, and the thenar. The intensity of allergic changes on the skin depends on the stage of plant growth. The most severe lesions on the skin appear during the processing of the bulb (Hassan *et al.* 2017).

People who work in the field are usually exposed to contact dermatitis due to the presence of allergens in the air (Avalos and Maibach, 2000). Without treatment, this dermatitis lasts two to three weeks and sometimes longer depending on the degree of exposure. Out of the plants that are widespread in our country, chrysanthemums, tulips, lilies, and primroses are probably the most common causes of allergic contact dermatitis. The *Anacardiaceae* family includes *Toxicodendron vernicifluum* that cause specific allergic skin reactions called urushiol. This name derives from urushiol sap, which contains a mixture of catechol (1,2-dihydroxybenzene) and resorcinol (1,3-dihydroxybenzene). Catechols and their side chains are immunologically inactive, but the presence of long chains increases their allergenicity and irritancy (Schempp *et al*. 2002). Poison ivy and poison oak commonly cause allergic dermatitis in North America (Fisher, 1996). Severe reactions, such as multiform erythema, occur after contact dermatitis from *Toxidendron* sp., *Melaleuica alternifolia*, or *Parthenium histerophorus.* In plants from the *Asteraceae* family, the major allergen is sesquiterpene lactone (LSK), which is found in leaves, stems, and flowers. Alpha methylene groups linked to the lactone ring increase its allergenicity. Today, there are over 1,350 LSKs, some of which are described in more detail in this monograph. The major allergen in plants of the *Primulaceae* family *(Primula obconica*) is primin, which is found in glandular hairs. Today, there are Primula obconica varieties without primin in the European market.

Allergic contact dermatitis occurs, especially in the tropics, when working with technical wood. According to the clinical presentation, it resembles photodermatitis (Saint-Mezard, 2004). Allergens are found in the middle of the trunk, but rarely in the sap. Sometimes allergies can occur when processing wood to make musical instruments, jewellery, carvings, and furniture, etc. The major allergens belong to benzo, naphtha, furano, and phenanthrene quinones.

Aeroallergens are one of the most common causes of allergic diseases; they include pollen, dust mites, house dust, animal hairs, and products of animal origin. Allergy-causing pollen mainly comes from grass, weeds, and trees. The analysis of the allergic diseases found patients treated at the Clinical Centre of Banja Luka from 2001 to 2010 revealed that the most commonly diagnosed allergy symptoms were rhinitis (40.8%), dermatitis (27.6%), various allergy diagnoses (16.1%), and asthma (15.5%) (Balaban and Gajanin, 2012). Many people, especially in rural areas, resort to the use of plants to treat some diseases (e.g. arthritis) in the form of compresses on painful areas. An example is allergic contact dermatitis due to *Ranunculus arvensis* (An *et al*. 2019). Contact dermatitis due to allergens in the air has the following stages:

- Photodermatosis lichenified, which is when the skin is thickened and leathery
- Symptoms similar to those resulting from plant pollen from the *Asteraceae (Compositae)* family

Table 1-3: Plants that cause contact dermatitis

Botanical name	**Botanical name**
Amaryllidaceae	
Narcis sp. L.	
Anacardiaceae	
Anacardium occidentale L. *Comocladia sp.* (e.g. *Comocladia dodonaea* (L.) Urban) *Cotinus coggygria* Scop. *Mangifera indica* L. *Metopium toxiferum* (L.) Krug & Urban *Schinus terebinthifolius* Raddi	Toxicodendron diversilobum (Torr. & A. Gray) Greene *Toxicodendron pubescens* P. Mill. *Rhus toxicodendron* L. *Rhus quercifolia* (Michx.) Steudel) *Toxicodendron radicans* (L.) Kuntze *Toxicodendron rydbergii* (Small) *Toxicodendron vernix* (L.) Kuntze
Annonaceae	
Asimina triloba (L.) Dunal	
Apocynaceae	
Allamanda cathartica L.	*Nerium oleander* L.
Apiaceae (Umbelliferae)	
Ammi majus L. *Anthriscus sylvestris* (L.) Hofmann *Daucus carota L. var. carota* *Daucus carota var. sativus* Hoffm.	*Heracleum lanatum* Michx. *Heracleum mantegazzianum* Sommier & Levier *Heracleum sphondylium* L. *Pastinaca sativa* L.
Araceae	
Alocasia sp. (e.g. *Alocasia macrorrhiza* (L.) G. Don) *Anthurium andreanum* Linden *Arum italicum* Mill. *Arum maculatum* L. *Caladium bicolor* (Ait.) Venten. *Calla palustris* L.	*Colocasia sp.* Schott (e.g. *Colocasia esculenta* (L.) *Dieffenbachia sp. Schott* *Epipremnum aureum* (Linden & André) Bunt. *Raphidophora aurea* (Linden & André) Birdsey; Krause) *Philodendron scandens* C. Koch & H. Sello *Philodendron selloum* C. Koch
Araliaceae	
Hedera canariensis Willd.	*Hedera helix* L.
Aristolochiaceae	
Aristolochia elegans M.T. Mast *Aristolochia gigantea* Mart. & Zucc. Hook.	*Aristolochia grandiflora* Swartz
Asclepiadaceae	
Calotropis gigantea (L.) Ait.	*Calotropis procera* (Ait.) Ait.
Bignoniaceae	
Campsis radicans (L.) Seem.	
Bromeliaceae	
Ananas comosus (L.) Merrill	
Chenopodiaceae	
Sarcobatus vermiculatus (Hook.) Torr.	

Commelinaceae	
Rhoeo spathacea (Swartz) Stearn	*Setcreasea pallida Rose cv.* "Purple Heart"
Asteraceae (Compositae)	
Ambrosia sp. L. *Artemisia sp.* L. *Aster sp.* L. *Chrysanthemum sp.* L. *Erigeron sp.* L. *Franseria acanthicarpa* (Hook.) Coville *Gaillardia sp.* Foug. *Helenium autumnale* L. *Helenium microcephalum* DC. *Iva sp.* L. *Lactuca sativa* L.	*Oxytenia acerosa* Nutt. *Achillea millefolium* L. *Anthemis cotula* L. *Parthenium argentatum* Gray *Parthenium hysterophorus* L. *Rudbeckia hirta* L. *Soliva pterosperma* (Juss.) Less. *Tanacetum vulgare* L. *Tagetes minuta* L. *Xanthium sp*. L.
Convolvulaceae	
Dichondra repens J. R. & G. Forst.	
Cornaceae	
Cornus sanguinea L.	
Euphorbiaceae	
Hura crepitans L. *Euphorbia cotinifolia* L. *Euphorbia gymnonota* Urb. *Euphorbia lactea* Haw. *Euphorbia lathyris* L. *Euphorbia marginata* Pursh *Euphorbia milii* Ch. des Moulins *Euphorbia myrsinites* L. *Euphorbia tirucalli* L.	*Excoecaria agallocha* L. *var. orthostichalus* Muell. Arg. *Grimmeodendron eglandulosum* (A. Rich.) Urb. *Hippomane mancinella* L. *Pedilanthus tithymaloides* (L.) Poit. *Sapium hippomane* G.F.W. Mey. *Sapium laurocerasus* Desf. *Stillingia sylvatica* Gard. *Synadenium grantii* Hook. f.
Fumariaceae	
Dicentra spectabilis (L.) Lem.	
Ginkgoaceae	
Ginkgo biloba L.	
Poaceae (Gramineae)	
Oryza sativa L. *Panicum glutinosum* Sw.	*Secale cereale* L.
Hydrophyllaceae	
Phacelia campanularia Gray *Phacelia crenulata* Torr. ex S. Wats. *Phacelia minor* (Harv.) Thell. ex F. Zimm. *Whitlavia grandiflora* Harv. *Phacelia parryi* Torr.	*Phacelia viscida* (Benth. ex Lindl.) Torr. *Phacelia imbricata* Greene *Phacelia malvifolia* Cham. *Wigandia caracasana* H.B.K. *Wigandia urens* (Ruiz & Pav.) H.B.K.
Juglandaceae	
Juglans nigra L.	
Fabaceae (Leguminosae)	
Prosopis glandulosa Torr. *Lupinus hirsutissimus* Benth. *Mucuna deeringiana* (Bort) Merrill	*Mucuna pruriens* DC. *Mucuna urens* (L.) DC.