15

Poisonous Plants

The separation of scientific fact from fiction is extremely difficult in the study of poisonous plants. Examination of the pertinent literature reveals considerable confusion that tends to mask an even greater amount of ignorance. Indeed, almost any plant may be judged toxic, questionable, or edible, depending on the reference consulted. For example, perhaps the most famous cookbook in the world, *Larousse Gastronomique*, once declared that rhubarb leaves could be "eaten like spinach," but well-documented fatalities resulting from their ingestion, both by human beings and by animals, have long been known to the medical profession.

J.M. Kingsbury, who has written extensively on the subject, points out that compilers dealing with poisonous plants often felt obligated to carry a plant into newer literature even though uncertain of the original authority. He concludes that only about one half of the names in current American compilations are based on domestic experimental or case evidence. The remainder have been copied from European sources which, in some cases, date back to Dioscorides (first century A.D.). S.B. O'Leary cites an incident in which "teenage soldiers in Hawaii" were fatally poisoned by oleander juice from sticks used as toasting forks. This passage may actually refer to the death of 8 French soldiers who cooked their meat ration on oleander sticks during the Napoleonic campaigns in Spain in 1808.

Unbelievable chaos reigns in the area of plant identification and nomenclature as applied by nonspecialists. In certain localities, poison dogwood refers not to a species of *Cornus* but to poison sumac (*Toxicodendron vernix*). Deadly nightshade is a common pharmaceutic synonym for *Atropa belladonna*, but in the Pacific Northwest it is often applied to *Solanum dulcamara*. Deadly nightshade is also known as European bittersweet, not to be confused with *Celastrus scandens* or *Euonymus* species, which are also called bittersweet. On the other hand, belladonna may designate not only the *Atropa* species of that name but also an *Amaryllis* species. One can only guess whether a reported case of poisoning by elephant's-ears refers to a species of *Caladium*, *Colocasia*, *Dieffenbachia*, or to mandrake, a name applied to some elephant's-ear and to *Podophyllum peltatum* and *Mandragora officinarum* as well. When it comes to the application of common names to mushrooms, which were probably not identified correctly in the first place, the situation becomes almost hopeless.

This field is where the practicing pharmacist, in his ever-expanding clinical role of adviser to both the physician and the layman, can make an outstanding contribution to public health and community welfare. No other professional in the health field has so extensive a background in both the botany and chemistry of plants as the pharmacist. By virtue of his scientific

training in these areas, the pharmacist is the only readily available authority on matters of identification and nature of the principles responsible for the toxic effects of accidentally ingested vegetable materials.

In smaller communities, where poison control centers do not exist, the pharmacist may be the only knowledgeable person in this field. The opportunity to function as a professional adviser to a poison control center offers even greater opportunities for the utilization of professional knowledge. Many of the most dangerous higher plants are cultivated species that exist in numerous varieties. Those found in any given community will vary according to climate, geography, and proximity to certain seed houses or nurseries. To serve to best advantage, the pharmacist should endeavor to become thoroughly familiar with both the indigenous and the cultivated flora of his community.

Poison antidote kits contain ipecac syrup as well as activated charcoal to be used as directed by the physician to counteract the effects of poisonous substances. Each kit contains a one-half-ounce bottle of ipecac syrup and a 5-gram container of activated charcoal packaged in a plastic box.

The following outline of the most important toxic plants found in the United States can serve as an important basic reference to this field. Because of the space limitations inherent in any textbook that must cover a broad area, the listing is neither complete nor excessively detailed. Many poisonous plants that are of primary interest as forage crops for animals are not mentioned. Students desiring to develop additional competence are urged to consult the specialized books and monographs on poisonous plants in the selected reading list.

HIGHER PLANTS

Abrus precatorius Linné **(jequirity)** is a climbing shrub common to tropical and subtropical countries of both hemispheres.

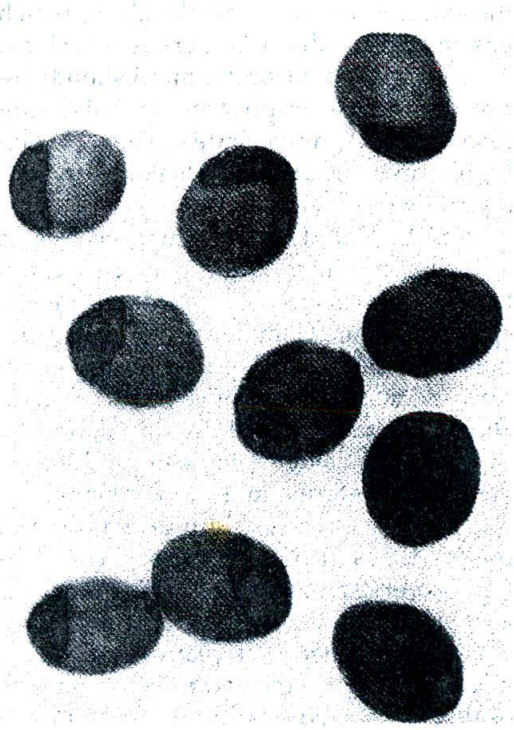


Fig. 15–1. Jequirity seed, magnified 3 times.

Abrus is Greek and means graceful, in allusion to the flowers; *precatorius* is from the Latin *precor*, meaning to pray, because the seeds are used as beads in rosaries. The seeds are ovoid, globular, from 5 to 9 mm in length, hard, smooth, and shining. They are 2 distinct colors. The lower or hilum portion is purplish black and has a large lenticular scar: the upper portion is scarlet red; and the testa is shell-like and encloses a light yellowish brown embryo that has 2 large cotyledons and an incurved radicle (Fig. 15–1). The seed contains **abrin** (jequiritin), a lectin or hemagglutin resembling ricin in its physiologic action. It is toxic, is soluble in a solution of sodium chloride, and has a melting point of 295° C.

Because jequirity seeds are colorful and attractive and because they are made into rosary beads, decorative table pads, necklaces, and other types of jewelry, they frequently are handled by small children. One must remember that these seeds contain

the extremely toxic principle, abrin, which has caused death on numerous occasions.

Aconitum spp. **(aconite, monkshood)** are not commonly implicated in poisoning cases in the United States. They contain highly toxic diterpenoid alkaloids, including the well-known aconitine.

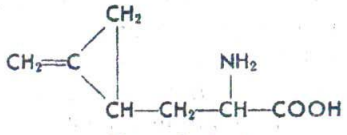
Aleurites fordii Hemsley **(tung-oil tree)** is a small tree cultivated along the Gulf Coast that produces brown, pendant, nearly spherical fruits. Commercial tung oil is obtained from the seeds which also contain toxic principles that have been defined chemically as esters of 16-hydroxyphorbol. Ingestion of a single seed can produce severe gastroenteritis in a human being.

Alocasia macrorhiza (Linné) Schott and other species of *Alocasia* are tropical herbs that generally have arrow-shaped leaves and are grown for their ornamental, often variegated foliage. The plant is an irritant poison owing to the raphides of calcium oxalate contained in the sap as well as to an additional unknown toxic ingredient, very likely a protein.

Atropa belladonna Linné **(deadly nightshade)** contains tropine alkaloids, especially hyoscyamine (see page 191).

Blighia sapida Koenig **(akee)** is a small tropical tree, widely cultivated in Florida, that produces clusters of straw-colored to reddish fruit. The fleshy arils of ripe fruits are commonly eaten after parboiling and frying, but the fruit wall and seeds are toxic. Ingestion of the fruit, especially by children, produces a condition known as "vomiting sickness," which is characterized by marked hypoglycemia. The mortality rate is high, ranging from 40 to 80%.

Two toxic principles, hypoglycin A and B, have been isolated from the fruit. Hypoglycin A has been characterized as β-methylene-cyclopropyl-L-α-aminopropionic acid, and hypoglycin B is a dipeptide formed of hypoglycin A and glutamic acid. No specific antidotes for these toxins have been found; therefore, treatment of akee poisoning is primarily symptomatic.



Hypoglycin A

Cicuta spp. **(water hemlock)** include a number of species of the genus *Cicuta*, especially *C. maculata* Linné. They constitute the most violently poisonous plants in the North Temperate Zone. The toxic principle, cicutoxin, an unsaturated higher alcohol (*trans*-heptadeca-8,10,12-triene-4,6-diyne-1,14-diol), has been isolated from *C. virosa* Linné. It is a violent convulsant that acts directly on the central nervous system.

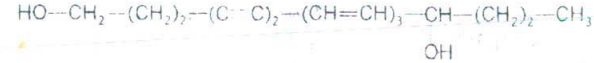
Water hemlock has tuberous roots that are often mistaken for edible wild parsnips or wild artichokes. Such confusion may lead to disaster and emphasizes the folly of uninformed persons who attempt to collect wild plants for food.

Colchicum autumnale Linné **(autumn crocus)** contains colchicine (see page 242).

Colocasia antiquorum, Schott and *C. esculenta* Schott **(elephant's-ear)** are tropical plants widely cultivated for their large showy leaves. They contain large amounts of calcium oxalate.

Conium maculatum Linné **(poison hemlock)** is a large herb indigenous to Europe and naturalized in North and South America and in various parts of Asia. The plant resembles wild carrot (*Daucus carota* Linné) but does not possess its hairy stem and leaves. Poison hemlock also has a characteristic "mousey" odor. Its fruits were formerly used in medicine.

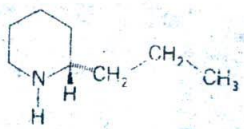
All parts of the plant are toxic because of the presence of several nicotinelike alkaloids, especially coniine, *N*-methyl-coni-



Cicutoxin

ine, γ-coniceine, conhydrine, and pseudoconhydrine. The juice of poison hemlock constituted the famous hemlock potion of the ancient Greeks and was used to put their criminals to death. It is commonly believed that Socrates was executed by means of a decoction of this plant.

Because of its occurrence as a weed in many parts of the United States and the relative attractiveness, especially to children, of its leaves, fruits, and root, this toxic plant should be recognized by every pharmacist. It is particularly important to be able to differentiate poison hemlock from other members of the family Umbelliferae, both edible and toxic, that bear a close resemblance.



(+)-Coniine

Convallaria majalis Linné **(lily-of-the-valley)** contains cardiac glycosides, especially convallatoxin (see page 171).

Daphne mezereum Linné **(mezereon)** is a small deciduous shrub with alternate leaves, purple flowers, and scarlet fruits. This plant and related species of *Daphne* are widely cultivated as ornamentals. Apparently, all parts of all species are toxic, but the drupes are particularly attractive to children. A few of these so-called "berries" can kill a child. The toxic principles of the plant have been identified as daphnetoxin, occurring in the bark, and mezerein, located in the fruits. Both are diterpene ester derivatives of daphnane.

Datura spp. **(stramonium, thornapple, Jamestown weed, jimson weed)** contain tropine alkaloids, especially hyoscyamine (see page 197 and Fig. 8–7).

Delphinium spp. **(larkspur)** include a large number of annual plants occurring as wild species throughout the United States, especially in the West but also widely cultivated in American gardens. They contain a number of toxic polycyclic diterpenoid alkaloids that account for their frequent involvement in the poisoning of livestock and human beings, especially children.

Dieffenbachia seguine Schott and *D. picta* Schott **(dumbcane)** are common ornamental house plants that grow up to 2 meters in height and have large entire leaves that are either uniformly green or, more commonly, mottled with white, yellow, or other shades of green. Ingestion of the leaves results in severe corrosive burns of the oral cavity, esophagus, and stomach caused by calcium oxalate and, possibly, by unverified proteinaceous toxins.

Digitalis purpurea Linné **(foxglove)** contains cardioactive glycosides, digitoxin, gitoxin, and others (see page 164).

Eupatorium rugosum Houttuyn **(white snakeroot or richweed)** is a showy, herbaceous, erect perennial, attaining a height of more than 1 meter. It has opposite, ovate to cordate leaves borne on long petioles and white flowers, small in composite heads, and grouped in open terminal corymbs. Positive identification of this plant is difficult. The disease known as "milk sickness," common among the early settlers in the United States, has been traced to the ingestion of dairy products derived from animals poisoned by this plant. An incompletely characterized, unstable alcohol that is designated tremetol and occurs in combination with a resin acid is apparently the toxic principle (Fig. 15–2).

Euphorbia spp. **(spurge)** number more than 1000 and range from herbs or shrubs to more or less succulent trees. All contain a latex that exudes when the plant is damaged. The latex is highly irritating and often produces vesication from contact and emesis and purgation from ingestion. These effects are caused by a large number of different esters of the tetracyclic diterpenoid phorbol, many of which have also been shown to act as tumor promoters (cocarcinogens). One of the best-known species is *Euphorbia pulcherrima* Willdenow, the common **poinsettia.** It is a favorite house plant during Christmas because of its

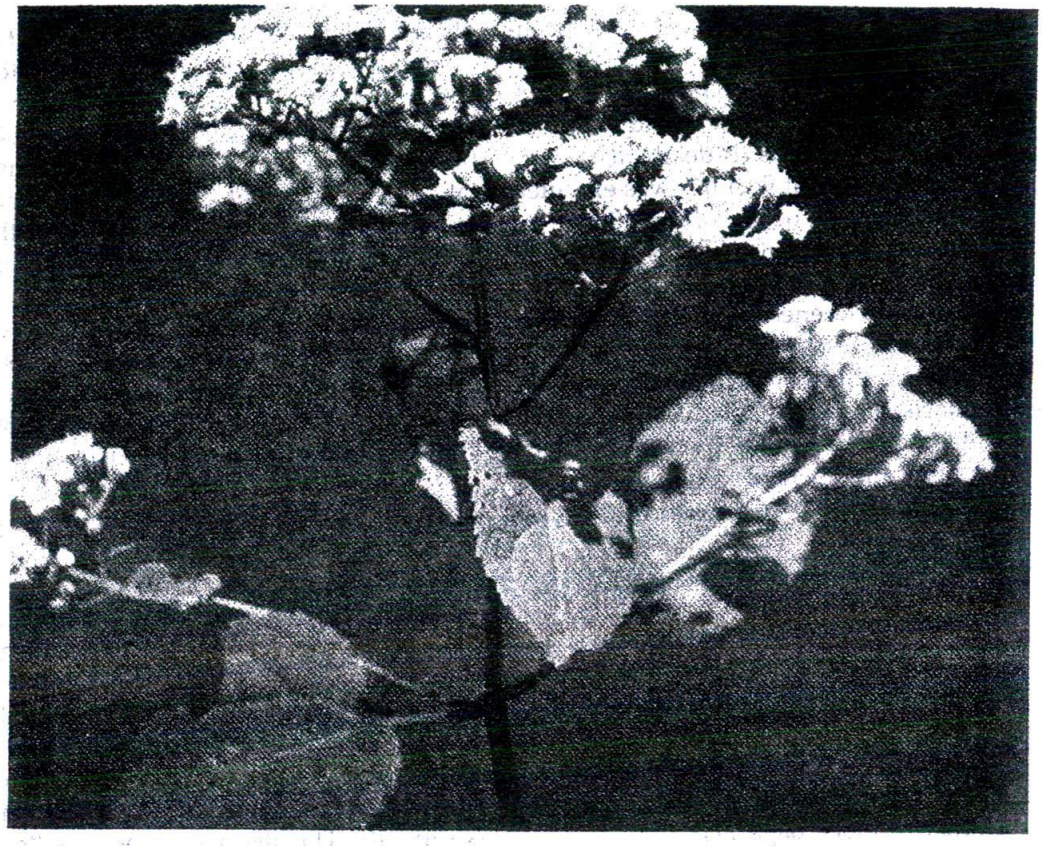


Fig. 15–2. *Eupatorim rugosum* (white snakeroot) illustrating the terminal corymbs of white composite flowers.

bright red bracts. The toxicity of poinsettia has apparently been greatly reduced as a result of long cultivation.

Gelsemium sempervirens (Linné) Aiton **(yellow jasmine)** is a perennial woody evergreen climber growing in the moist woodlands of the southeastern United States. Its dried rhizome and roots constitute the crude drug gelsemium, formerly employed as a central nervous system depressant. Ingestion of sufficient quantities of the plant may lead to respiratory failure. Children have been poisoned by tasting the nectar of the flowers, and honey prepared by bees feeding on the nectar has caused fatalities. The active principles are indole alkaloids, especially gelsemine and sempervirine (Fig. 15–3).

Hedera helix Linné **(English ivy)** is the well-known cultivated vine commonly employed as an external decoration on buildings. Ingestion of the berries by children has resulted in fatalities. Their toxicity is attributed to hederin, a saponin glycoside.

Hippomane mancinella Linné **(manchineel tree)** is a small tropical tree occurring in the southern part of Florida. All parts of the plant contain an extremely caustic, milky sap whose active principles are a complex mixture of esters of the tigliane and daphnane types. Similar compounds have been detected in many other members of the family Euphorbiaceae.

Hyoscyamus niger Linné **(henbane)** contains hyoscyamine and scopolamine (see page 197).

Ilex aquifolium Linné **(English holly)** and several related species of *Ilex* are small trees or shrubs with shiny green leaves and bright red berries. They are often used as

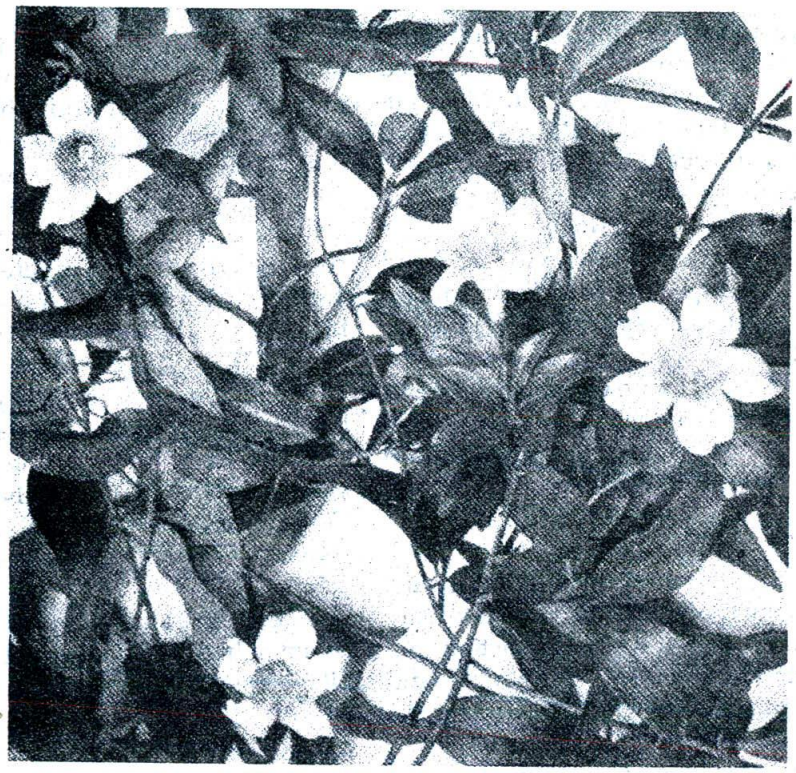


Fig. 15–3. Yellow jessamine or yellow jasmine *(Gelsemium sempervirens)* is a perennial woody climbing vine growing in the southeastern United States. (Photo courtesy of Dr. Julia F. Morton, Director, Morton Collectanea, University of Miami.)

Christmas decorations. Ingestion of the berries produces vomiting, diarrhea, and "mild narcosis." The active principle remains uncharacterized.

Ipomoea spp. **(morning glory)** are common, cultivated ornamental vines. The seeds of some species and varieties contain ergot alkaloids, especially ergine (see page 236).

Jatropha curcas Linné and *J. multifida* Linné **(physic nut)** are tropical shrubs or small trees occurring with several closely related species in Florida, Texas, Puerto Rico, and Hawaii. Closely related botanically to the castor plant, these plants produce seeds containing a purgative oil and a toxic lectin.

Kalmia angustifolia Linné **(dwarf laurel)**, *K. latifolia* Linné **(mountain laurel)**, and certain other members of the Ericaceae, such as species of *Ledum*, *Pieris*, and *Rhododendron (Azalea)*, are widely occurring shrubs or small trees. All contain the same poisonous principle, acetylandromedol, a diterpene derivative. That compound has been identified as the toxic agent in honey produced by bees that feed on these plants.

Laburnum anagyroides Medicus **(laburnum, golden-chain)** is a large ornamental shrub or small tree that is widely cultivated as a spectacular ornamental owing to its long, hanging, racemes of golden yellow flowers. The fruit, a legume pod containing up to 8 seeds, is commonly ingested by children. Laburnum seeds contain cytisine, a quinolizidine alkaloid resembling nicotine in its physiologic effects.

Lantana camara Linné **(lantana)** is an ornamental shrub, up to 1.5 meters in height, with aromatic leaves, orange or bright red flowers, and dark blue or black fruits (drupes). The plant is widely cultivated in

California and the southern United States, where cases of poisoning have occurred through ingestion of the fruit. Most authorities attribute lantana's toxicity to 2 pentacyclic triterpenes, lantadene A and B. Others deny this and state that the poisonous principle is unknown.

Lobelia inflata Linné **(Indian tobacco)** and several related species of *Lobelia* contain piperidine alkaloids, especially lobeline (see page 191).

Melia azedarach Linné **(chinaberry tree)** is a small, thickly branched tree with large compound leaves, purple flowers, and smooth ovoid fruits (drupes) that are yellow when mature. The plant is common in the southern United States, Puerto Rico, and Hawaii. Poisoning most often results from ingestion of the fruits whose toxicity is associated with a resinous fraction. Severe irritation, nervous symptoms, and fatty degeneration of the liver and kidneys characterize the toxic effects.

Menispermum canadense Linné **(Canada moonseed)** is a high-climbing vine, indigenous to the northern United States and Canada, that has broadly ovate, cordate, 3- to 10-lobed leaves. Its fruits resemble small purple grapes and have been the cause of poisoning in children. The toxic principles are isoquinoline alkaloids, including dauricine which has a curarelike action.

Metopium toxiferum Krug et Urban **(poisonwood tree)** is a large shrub or small tree with compound leaves and fleshy fruits. It is common in areas south of Miami, Florida, and frequently causes severe contact dermatitis. Presumably, the active principle is identical or at least similar to that of urushiol, the causative agent of poison ivy dermatitis.

Narcissus spp. **(narcissus, daffodil, jonquil)** are well-known cultivated plants. Ingestion of narcissus bulbs produces severe gastroenteritis and nervous symptoms, apparently owing to the phenanthridine alkaloids contained therein.

Nerium oleander Linné **(oleander)** is an ornamental bush or shrub with coriaceous, sharply pointed, oblong-lanceolate leaves and showy pink or white blossoms. It is widely cultivated in the southern United States and California and is grown elsewhere as an indoor pot plant. The plant contains a complex mixture of cardiac glycosides derived from 6 different genins that are closely related chemically and physiologically to the digitalis glycosides (see page 172).

Nicotiana spp. **(tobacco)** contain alkaloids, chiefly nicotine (see page 189).

Papaver spp. **(poppy),** the related *Argemone mexicana* Linné **(prickly poppy),** and *Chelidonium majus* Linné **(celandine poppy)** contain isoquinoline alkaloids (see page 208).

Philodendron spp. are perhaps the most common houseplants in the United States. Like certain other members of the family Araceae, they may contain irritant principles (calcium oxalate and others). Numerous cases of poisoning in cats, 50% fatal, have been reported.

Phoradendron villosum Nuttall and *P. flavescens* (Pursh) Nuttall **(mistletoe)** are woody perennial plants growing as parasites on oaks and other deciduous trees. The latter species is widely employed as a Christmas decoration. Leaves, stems, and berries of these plants are toxic, owing to their content of phoratoxin, a disulfide bond-containing protein found in the genus (see page 480).

Phytolacca americana Linné **(pokeweed, pokeberry)** is a tall, branched perennial herb that reaches a height of 3 meters. It has white or greenish flowers in racemes, and 10-celled, juicy, purple berries. When ingested, the various plant parts produce different degrees of gastrointestinal upset, accompanied by weakened respiration and pulse. The leaves and the roots are especially toxic, the berries much less so, because of their content of phytolaccatoxin and related triterpenes (see page 484).

Podophyllum peltatum Linné **(American mandrake, mayapple)** contains resinous

principles that produce dermatitis on contact and catharsis on ingestion (see page 141).

Poinciana gilliesii Hooker **(poinciana, bird of paradise)** is a shrub or small tree with showy terminal racemes of yellow flowers with red stamens. In the southern United States, it is cultivated as an outdoor perennial; elsewhere it is grown as a large indoor plant. The green seed pods are extremely irritating to the digestive tract. This plant should not be confused with *Strelitzia*, the florist's bird of paradise flower.

Primula obconica Hance **(primrose)** is a popular house plant that produces a severe contact dermatitis in sensitive individuals. This is attributed to the presence of the contact allergen primin, a benzoquinone derivative found in the glandular hairs that occur abundantly on the calyx and flower stalks of the plant.

Prunus serotina Ehrhart **(wild cherry)** and related species and varieties (*P. virginiana* Linné, *P. laurocerasus* Linné, etc.) contain cyanogenetic glycosides (see page 70).

Ranunculus spp. **(buttercup, crowfoot)** are perennial or annual herbs with yellow flowers. Some of these species are the most common weeds in fields and marshy areas in the United States. The juice of these plants has vesicant properties owing to the presence of a highly unstable γ-lactone, protoanemonin.

Rheum rhaponticum Linné **(rhapontic rhubarb, common rhubarb)** contains large quantities of oxalic acid and its salts in the lamina of the leaf (see page 64).

Rhododendron spp., see *Kalmia angustifolia*.

Rhus spp., see *Toxicodendron radicans*.

Ricinus communis Linné **(castor bean)** contains ricin, a lectin or hemagglutin, in the seeds (see page 88).

Robinia pseudoacacia Linné **(black locust)** contains a toxic principle in the seeds, leaves, and bark. The toxin, robin, is a lectin, related to abrin in jequirity.

Sanguinaria canadensis Linné **(bloodroot)** contains isoquinoline alkaloids, especially sanguinarine (see page 212).

Skimmia japonica Thunberg **(skimmia)** is an ornamental evergreen shrub with alternate simple leaves, small white flowers in terminal panicles, and bright red berries. All parts of the plant are toxic, but the attractive berries are most commonly ingested. The active principle is skimmianine, a furoquinoline alkaloid that acts as a muscle poison and may cause cardiac or pulmonary arrest.

Solandra spp. **(chalice-vine)** are woody, erect or climbing, tropical plants with large white to yellow, showy flowers. Species encountered in Florida and California include *S. grandiflora* Swartz, *S. hartwegii* N. E. Brown, and *S. longiflora* Tussac. The plants contain tropane alkaloids; atropine, hyoscyamine, and norhyoscyamine have been isolated from various species.

Solanum spp. **(nightshade)** are annual or perennial herbs and shrubs with alternate, simple or compound leaves and wheel-shaped or shallowly bell-shaped flowers, often showy in white, yellow, blue, and purple. The fruit is a berry that is often quite attractive. *Solanum dulcamara* Linné **(European bittersweet)**, *S. nigrum* Linné **(black nightshade)**, and related species, including *S. tuberosum* Linné **(potato)**, contain toxic steroidal glycoalkaloids (solanine, demissine, others) in the green shoots, leaves, and fruits. The toxicity of a single species varies widely according to the part used, the stage of development, and possibly the genetic factors. Following ingestion, the glycoalkaloids are not readily absorbed, but first undergo hydrolysis to release the free alkamines. These are then absorbed, producing nervous symptoms characterized by dulling of the senses and stupefaction.

Taxus spp. **(yew)** are evergreen trees and shrubs with linear leaves that are dark green on the upper surface and yellow-green on the lower, inconspicuous flowers, and berrylike red fruits composed of a stony seed nearly surrounded by a thick

Fig. 15–4. *Taxus* sp. (yew) showing the leaves, berrylike fruit, and the dark stony seed surrounded by the fleshy cup-shaped aril of the fruit.

fleshy cup. All species of *Taxus* that have been investigated contain a complex mixture of toxic alkaloids designated taxines in the leaves, bark, and seeds but apparently not in the pulp of the fruit. Ingestion of 50 to 100 needles can produce death in the human being through cardiac and respiratory depression (Fig. 15–4).

Thevetia peruviana Schumacher **(yellow oleander)** is a large, cultivated evergreen shrub or small tree with linear, sharply pointed leaves, fragrant, showy yellow flowers, and fruits that are fleshy drupes, broadly triangular, and black when ripe. The plant is cultivated as an ornamental in southern Florida and Hawaii. On the island of Oahu it is said to be the most frequent cause of serious poisoning in human beings. Yellow oleander contains cardiac glycosides (cerebrin, neriifolin, thevetin) that produce digitalislike effects.

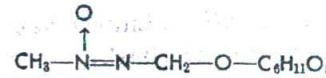
Toxicodendron radicans (Linné) Kuntze **(poison ivy)** as well as other species of the genus *Toxicodendron* (formerly *Rhus*), including *T. diversilobum* (Torrey et Gray) Greene **(western poison oak)**, *T. quercifolium* (Michaux) Greene **(eastern poison oak)**, and *T. vernix* (Linné) Kuntze **(poison sumac)**, all contain urushiol, a phenolic allergen that produces contact dermatitis (see page 432 and Figs. 15–5 and 15–6).

Veratrum viride Aiton **(green hellebore)** contains steroidal alkaloids (see page 238).

Wisteria spp. **(wisteria)** are ornamental woody vines with pinnate leaves and drooping terminal racemes of showy flowers, white, pink, blue, or purple in color, followed by fruits that are elongated pods, contracted at intervals. Ingestion of the plant produces mild to severe gastroenteritis, which has been attributed to the presence of wistarin, an uncharacterized glycoside, and a lectin.

Xanthosma sagittifolium (Linné) Schott **(malanga)** and related species of *Xanthosma* are large tropical aroids commonly grown as foliage plants. The leaves are extremely acrid owing to the presence of large amounts of calcium oxalate.

Zamia pumila Linné **(Florida arrowroot)** and other members of the order Cycadales, including species of *Cycas* and *Macrozamia*, are primitive cone-bearing palmlike plants indigenous to the tropics but cultivated elsewhere as ornamentals. These cycads contain a carcinogenic and hepatotoxic glycoside, cycasin, which has been characterized as methylazoxymethanol-β-D-glucoside. In some tropical areas, various parts of cycads are employed for the preparation of edible flour, and cases of poisoning sometimes result from the ingestion of an improperly prepared product. Acute intoxications resulting from a single ingestion of cycad roots or seeds are much less common.



Cycasin

Zigadenus spp. **(death camas)** are perennial herbs with grasslike leaves; underground bulbs or rhizomes; greenish white, yellow, or pink flowers; and capsular fruits. The plants contain steroidal glycoalkaloids, chemically and physiologically similar to those of *Veratrum viride*.

MUSHROOMS

Because the chemistry of the active principles in many poisonous mushrooms is

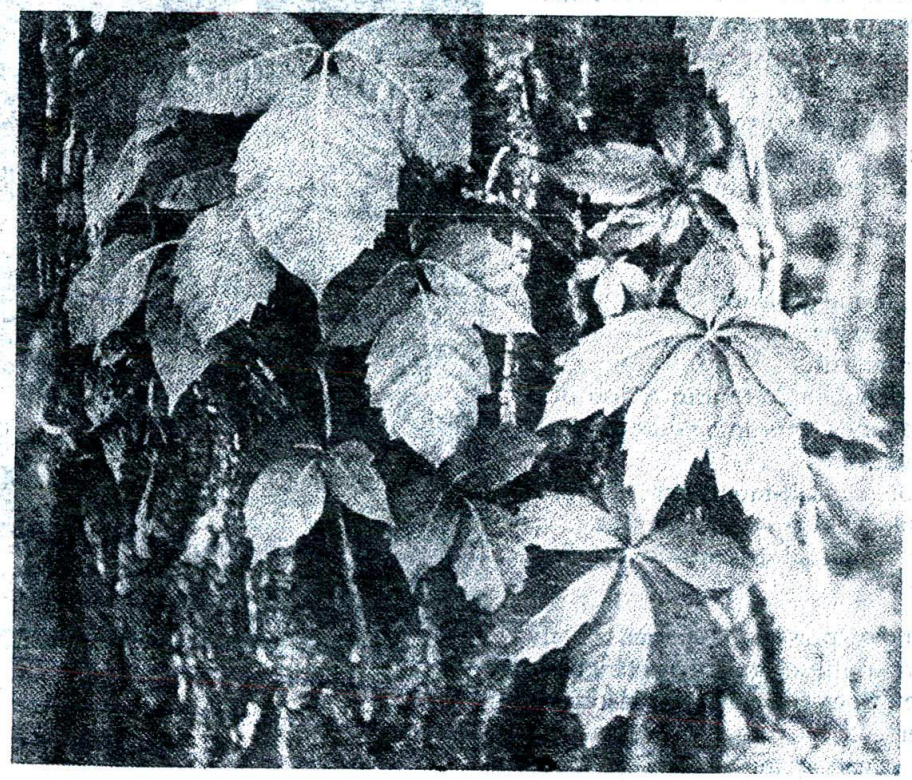


Fig. 15–5. Poison ivy *(Toxicodendron radicans)* is sometimes confused with Virginia creeper *(Psedera quinquefolia);* the former *(left)* is 3-foliate and the latter *(right)* is usually 5-foliate or more.

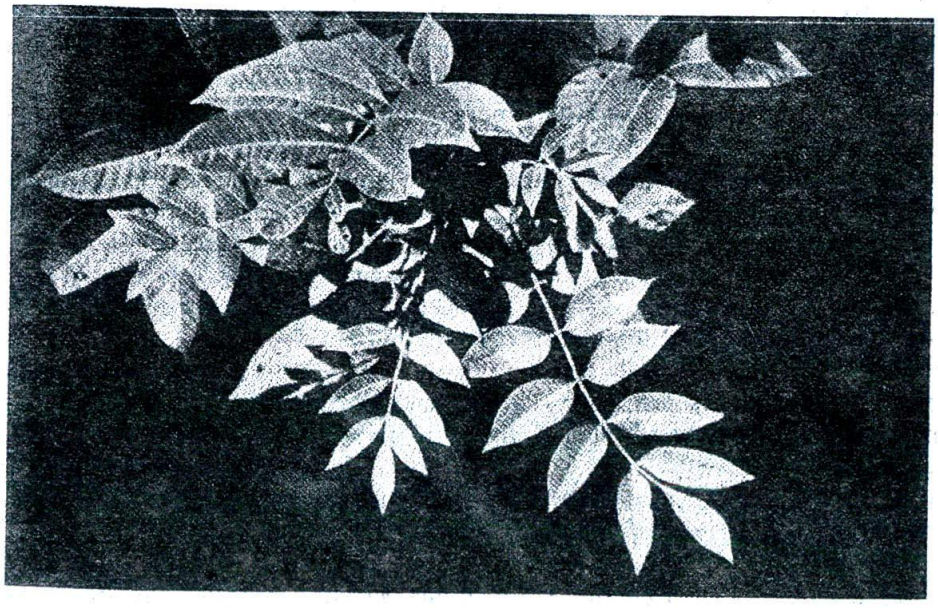


Fig. 15–6. *Toxicodendron vernix* (poison sumac) differs from the other toxic *Toxicodendron* species by its 7- to 13-compound leaves.

still imperfectly known and positive botanical identification is often extremely difficult, these species must be classified on a physiologic basis, that is, according to the type of symptoms observed in human beings following ingestion. Four basic types of mushroom toxins, with several minor subdivisions, are generally recognized:

1. Protoplasmic poisons
   a. amatoxins
   b. gyromitrins
   c. orellanine (Cortinarin A and B)
2. Compounds exerting neurologic ef-
   a. muscarine
   b. ibotenic acid-muscimol
   c. psilocybin-psilocin
3. Gastrointestinal irritants
4. Coprine

All the known poisonous species contain one or more of these principles. The basic classification does not include poisonings from hypersensitivity to mushroom protein or from eating mushrooms partially decomposed by microbial action. Also omitted are those mushrooms that may be poisonous if eaten in quantity because of their ability to accumulate toxic heavy metals from the soil.

Fig. 15–7. *Amanita verna* (destroying angel) is one of the most deadly mushrooms known.

Protoplasmic Poisons

Amatoxins. As the name implies, this mixture of peptide toxins was first detected in certain species of *Amanita*, a genus of mushrooms characterized by white spores, the presence of both an annulus and a volva, and typically free gills. Certain of these toxins have been found in some species of *Galerina*, a genus typified by small nondescript carpophores with yellowish brown spores, whose species are distinguished principally on the basis of microscopic characteristics.

About a dozen related cyclopeptides, the most important of which are α-, β-, and γ-amanitin, have been isolated from *Amanita phalloides* (Fries) Secretan **(deadly amanita)** of European origin. This particular mushroom is rare in the United States, apparently existing only as an introduced species. Related species, including *Amanita bisporigera* Atkinson, *Amanita verna* (Fries) Vittadini, and *Amanita virosa* Secretan, are more common and also contain these toxins (Fig. 15–7). *Amanita brunnescens* Atkinson, long confused with *Amanita phalloides* in this country and still designated by some as a brown form of the latter, does not contain amatoxins. Although its toxicity has not been scientifically verified, it does contain an unidentified alkaloid and is presumably poisonous.

Both α- and β-amanitin have been detected in *Galerina autumnalis* (Peck) Smith & Singer, *Galerina marginata* (Fries) Kühner, and *Galerina venenata* A.H. Smith. These species probably constitute a more serious health hazard than do the deadly amanitas because of the extreme difficulty in identifying them unequivocally and be-

cause they often occur in lawns and other grassy areas.

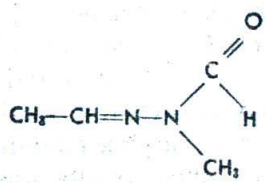
Regardless of the species involved, poisoning by amatoxins is characterized by a long latent period between ingestion of the mushrooms and onset of symptoms. An asymptomatic latent period lasting up to 24 hours precedes violent vomiting and diarrhea, which may continue until death results. If the patient survives this initial phase through appropriate therapy, he may appear to recover for a short time but generally will relapse owing to progressive injury to the liver, kidneys, heart, and central nervous system. Death results in about 30% of the cases within 4 to 8 days.

Modern treatment of amatoxin poisoning involves removal of the toxic material from the gastrointestinal tract, if necessary, followed by administration of analgesics to control pain, intravenous infusions of liquid to prevent dehydration and shock, hemodialysis or hemoperfusion to eliminate the toxins, and appropriate measures to maintain a brisk urine flow. Additional treatment is largely symptomatic and supportive.

Some success has apparently been obtained by using intravenous corticosteroids to inhibit toxin fixation in the liver and intravenous penicillin G or thioctic acid (α-lipoic acid) to protect that organ. Administration of cytochrome C, vitamins C, K, and B complex, and dextrose and sodium chloride injection have all been recommended. The compounds that have produced the greatest survival rate are penicillin G, chloramphenicol, phenylbutazone, and a combination of sulfamethoxazole and trimethoprim; however, at present, no antidote for amanitin intoxication is sufficiently established clinically for unequivocal recommendation.

Gyromitrins. A second type of protoplasmic poison, less dangerous than the amatoxins but still capable of producing fatal results, occurs in certain **false morels**, especially *Gyromitra esculenta* Fries, but also in *G. gigas* Cooke and other closely related species of *Gyromitra* and *Helvella*. These nongilled fungi are characterized by a pileus surface that varies from nearly smooth to strongly convoluted. However, it is never pitted (distinction from *Morchella* species—**morels**). Their pilei are nearly always lobed, usually more or less saddle-shaped.

Chemically, the gyromitrins are *N*-methyl-*N*-formylhydrazine derivatives of several low-molecular-weight aliphatic aldehydes. The first isolated was the hydrazone of acetaldehyde, but at least 3 others are now known. In the body, they release *N*-methyl-*N*-formylhydrazine (MFH) which is oxidized to produce the extremely poisonous *N*-nitroso-*N*-methylformamide (NMFA). NMFA is essentially hepatotoxic but does exert additional effects on the hematopoietic system and the central nervous system. Gyromitrins are, therefore, classed as protoplasmic poisons, but differ markedly in their chemistry and toxicity from the amatoxins.



Gyromitrin

Acetaldehyde *N*-(formyl-*N*-methylhydrazone)

Gyromitrins and their breakdown products are volatile, which explains why species containing them may be rendered edible by extended drying or by parboiling. Both of these procedures destroy more than 99% of the mushroom's hydrazine content. European specimens of *Gyromitra esculenta* contain nearly 10 times as much gyromitrins as similar specimens collected in the Pacific Northwest region of the United States. Obviously, different chemical races of the species exist, with marked differences in their content of the poisonous constituents.

A latent period of approximately 6 to 10 hours usually occurs between ingestion of the mushroom and the onset of symptoms that resemble those produced by amatoxins but are generally less severe. Although cases of poisoning are common in Europe and often involve large numbers of people, fatal poisonings are rare in the United States. The mortality rate ranges between 15 and 35%. Treatment is similar to that recommended for amatoxin poisoning.

Orellanine (Cortinarin A and B). The third type of protoplasmic poisoning is that produced by the mixture of compounds originally named orellanine contained in certain *Cortinarius* species. It has now been shown that 2 toxic cyclopeptides designated cortinarin A and B, closely related to the amanitins, are the responsible constituents accounting for the mushrooms' poisonous nature. Both are active nephrotoxins, but cortinarin B is the more toxic of the 2.

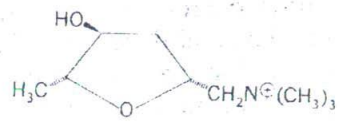
Of the species of *Cortinarius* examined, only *C. orellanus* Fries (from which orellanine was originally obtained), *C. orellanoides* Henry, and *C. speciosissmus* Kühner et Romagnesci have been found to contain cortinarin B. However, more than 60 species contained varying amounts of cortinarin A, and their toxicity was shown to be proportional to the sum of the concentrations of cortinarin A and B. Fortunately, none of the 3 deadly species containing cortinarin B has ever been found in the United States. There is, nevertheless, a possibility that they may occur on the West Coast.

Poisoning by cortinarius toxins is characterized by an extremely long latent period, varying from 3 to 14 days, between ingestion of the fungus and appearance of the symptoms. An intense burning thirst is first noted, followed by gastrointestinal disturbances, headache, pain in the limbs, spasms, and loss of consciousness. Liver and, particularly, kidney damage occurs and may result in death after several weeks or longer. Recovery in less severe cases may be prolonged for months. About 15% of the recorded cases have proved fatal.

Because of the long latent period, treatment can only be symptomatic and supportive, with particular attention to the maintenance of kidney function.

Compounds Exerting Neurologic Effects

Muscarine. Muscarine is a quaternary compound originally isolated from *Amanita muscaria* (Fries) Hooker, which occurs in that species and in the closely related *Amanita pantherina* (Fries) Secretan in small amounts. It is not, however, the principal toxic agent in either of these mushrooms. The compound has been reported to occur in a number of species of *Boletus, Lepiota, Hebeloma,* and *Russula,* but in many cases scientific verification is lacking. Certain species of *Clitocybe,* and especially *Inocybe,* contain muscarine in high concentrations, ranging in the latter species to more than 3% of dry weight when assayed physiologically. Both of these latter genera are readily recognized; *Clitocybe* by its typically white spores, fleshy central stipes, and broadly adnate to decurrent gills; *Inocybe* by its characteristic subconic to campanulate pileus, somewhat evanescent cortina, adnate or adnexed gills, and brownish spores (Fig. 15–8).



L-(+)-Muscarine

Symptoms of muscarine poisoning appear quite rapidly, usually 15 to 30 minutes after ingestion. Increased salivation, perspiration, and lacrimation are followed by abdominal pain, severe nausea and diarrhea. The pulse is slowed, the pupil is constricted, and breathing is asthmatic. The patient's mental processes remain clear. Death may result in severe cases from cardiac or respiratory failure, but it is infrequent. Treatment involves gastric lavage

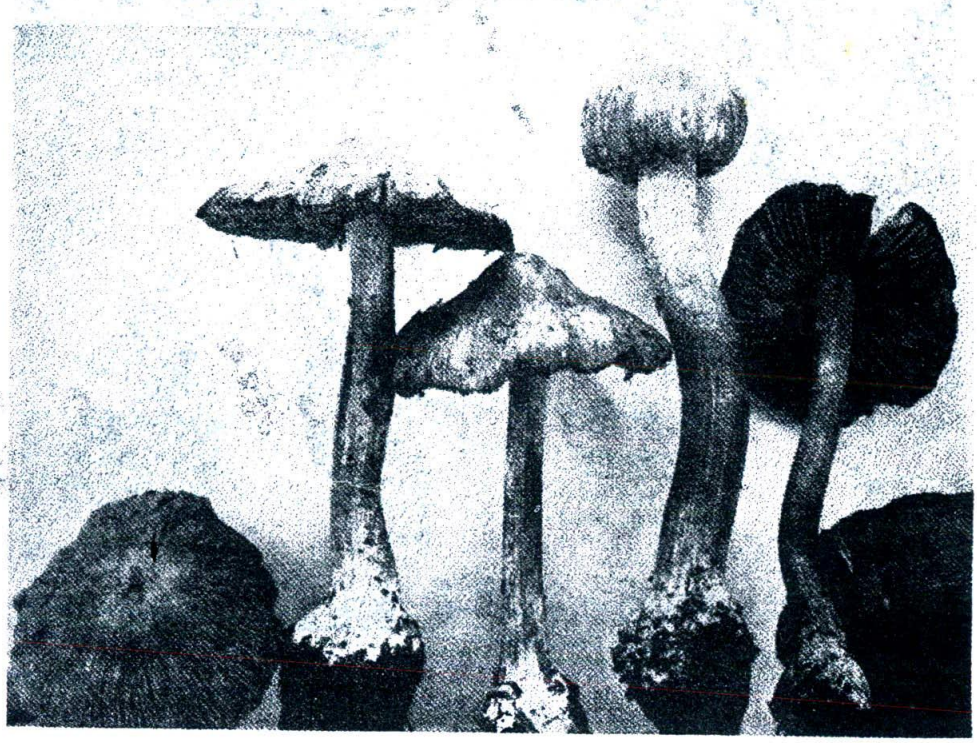
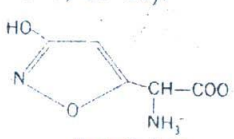


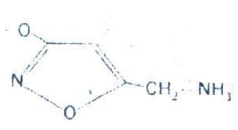
Fig. 15–8. *Inocybe napipes* J. Lange carpophores contain large quantities of muscarine. (Photo courtesy of D.E. Stuntz.)

and administration of atropine, a specific antidote.

Ibotenic Acid-Muscimol. Ingestion of certain species of *Amanita (A. muscaria, A. pantherina)* produces symptoms that are not typical of muscarine, which is present in the species in small amounts, but resemble the central nervous system stimulation induced by atropine. Travelers in Siberia during the early part of the 18th century reported the use of the **fly agaric,** *Amanita muscaria,* as an intoxicant by tribes of the Kamchatkan Peninsula. Vivid reports of orgies resulting from the use of this mushroom are found in the older literature (Figs. 15–9, 15–10).



Ibotenic Acid



Muscimol

The active principle was ultimately identified as a mixture of 2 isoxazole derivatives, ibotenic acid and its decarboxylation product, muscimol. The compounds differ little in their qualitative effects, but quantitatively, muscimol is at least 5 times as active as ibotenic acid. These 2 psychotropic compounds are accompanied, at least in some specimens of *A. muscaria,* by a third active constituent, muscazone, which is an oxazole derivative.

Symptoms appear within 30 minutes to 2 hours following ingestion. These are characterized by an initial state of excitement resembling alcoholic intoxication, followed by muscular twitching, depression, and ultimately, loss of consciousness. Death is infrequent and recovery is ordinarily rapid. Treatment is largely symptomatic, employing mild depressants at first, followed by stimulants.

Psilocybin-Psilocin. Ingestion of certain small mushrooms not commonly em-

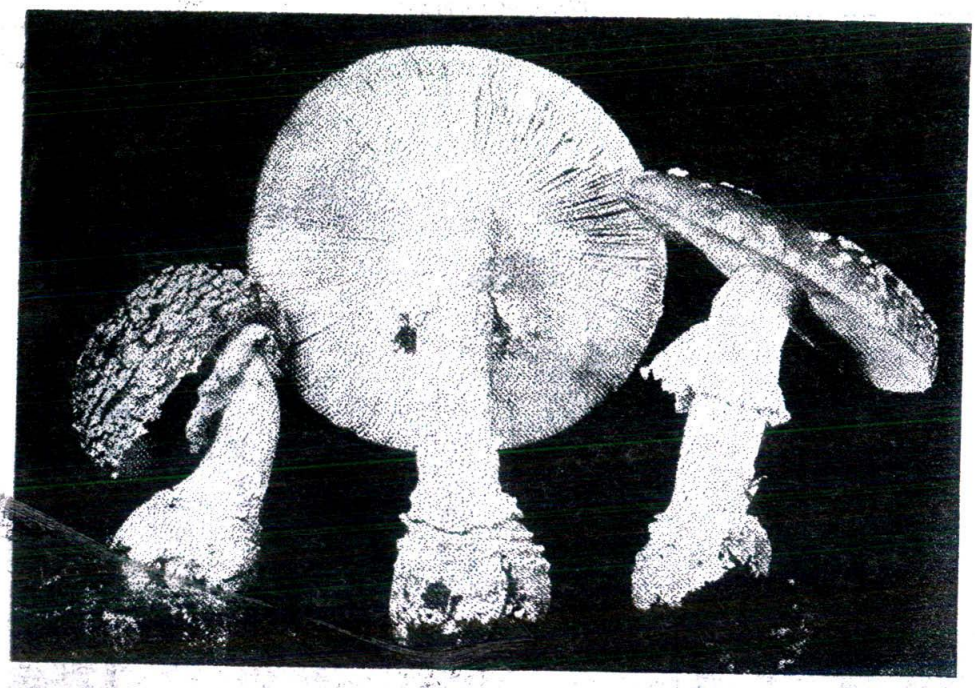
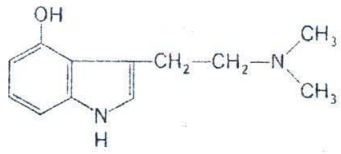


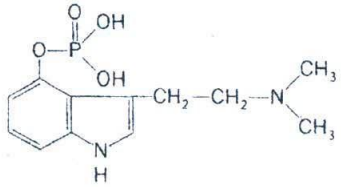
Fig. 15–9. Carpophores of *Amanita muscaria* (Fries) Hooker, commonly known as the fly agaric. This mushroom has been employed in Siberia as a hallucinogenic agent. (Photo courtesy of D.E. Stuntz.)

Fig. 15–10. Carpophores of *Amanita pantherina* (Fries) Secretan, the panther agaric. The brown pileus of this species readily distinguishes it from *Amanita muscaria* (red or orange pileus). (Photo courtesy of D.E. Stuntz.)

ployed as food can result in psychotropic manifestations in the human being. Most of them are species of *Psilocybe* and *Conocybe* [*P. cubensis* (Earle) Singer, *P. mexicana* Heim, *C. cyanopus* (Atkinson) Kühner] that have been used for many years by Indians in southern Mexico in magicoreligious ceremonies. Active members of both genera are brownish and somewhat nondescript in appearance (Fig. 15–11) but are readily characterized by the bluish stains that form, especially near the base of the stipe, when the tissue is damaged or becomes aged. Chemical studies have revealed that 2 tryptamine derivatives, psilocybin and psilocin, are the active principles in these mushrooms. Psilocybin has been investigated clinically to determine its value in the treatment of psychiatric disorders.



Psilocin



Psilocybin

Symptoms of psilocybin poisoning develop rapidly and continue for several hours. Anxiety and difficulty in concentration and in comprehension are common. Both elementary and true hallucinations may be experienced. Recovery is ordinarily spontaneous and complete after 5 to 10 hours.

Gastrointestinal Irritants

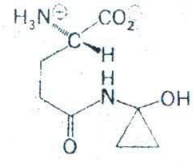
Mushrooms containing compounds that have an irritating effect on the gastrointestinal tract include such species as *Boletus satanus* Lenz, *Lactarius torminosus* (Fries) Gray, *Paxillus involutus* (Fries) Fries, *Rhodophyllus lividus* (Mérat) Quélet (Fig. 15–12), *Russula emetica* (Fries) S.F. Gray, and *Tricholoma pardinum* Quélet. The chemical nature of the active principles of these species is not known, but they are generally presumed to be resinlike substances.

Symptoms are prompt in onset and include nausea, vomiting, and diarrhea, ranging from mild to extremely severe. Fatalities have resulted, especially among children. *Rhodophyllus lividus* also displays some hepatotoxic activity. In most cases, recovery is spontaneous and complete, but symptomatic care, bed rest, and a light diet are indicated.

Coprine

Ingestion of *Coprinus atramentarius* (Fries) Fries and the concomitant or subsequent ingestion of alcohol give rise to symptoms resembling those of the alcohol-disulfiram syndrome. This species is recognized by its black spores, smooth or minutely scaly grayish pileus, and free gills that deliquesce into a dark-colored fluid as the spores are discharged.

Because of the similarity in its physiologic action to disulfiram or cyanamide, the activity of the mushroom has been attributed to one or the other of these compounds. In 1975, two groups of scientists, one in the United States and the other in Sweden, independently isolated the toxic constituent, *N*-(1-hydroxycyclopropyl)-L-glutamine. This compound has been named coprine.



Coprine

The compound itself is inactive, but it breaks down partially in the body to form cyclopropanone hydrate. This interferes with the function of acetaldehyde dehydrogenase in the liver. Normal alcohol me-

Fig. 15–11. Carpophores of *Psilocybe pelliculosa* A.H. Smith. This North American hallucinogenic mushroom contains psilocybin. (Photo courtesy of D.E. Stuntz.)

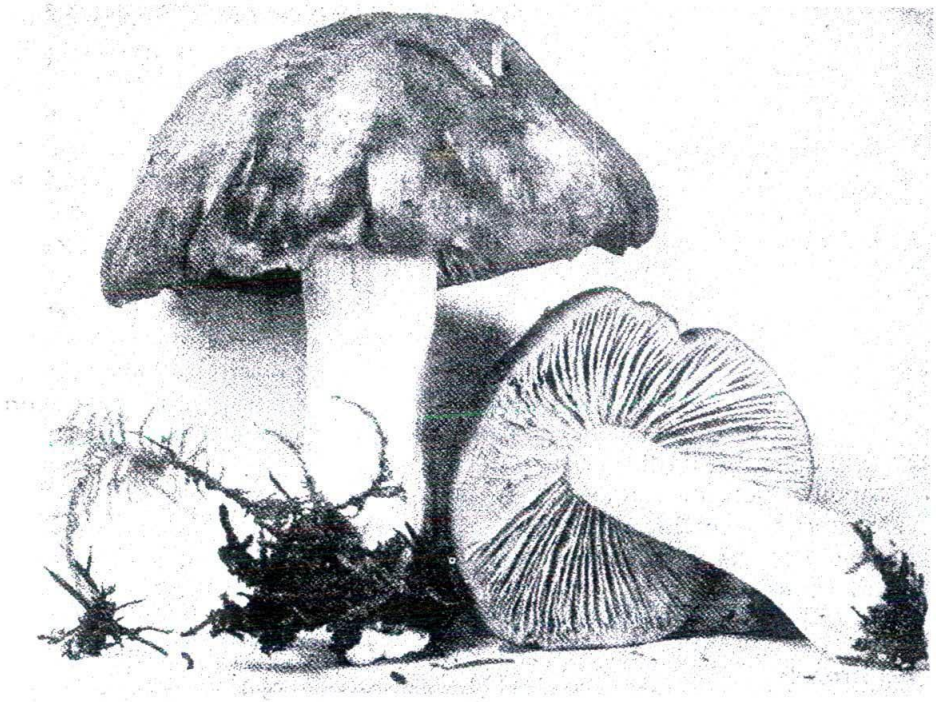


Fig. 15–12. *Rhodophyllus lividus* (Mérat) Quélet carpophores produce gastrointestinal upsets with associated hepatotoxicity. (Photo courtesy of D.E. Stuntz.)

tabolism is thereby retarded and acetaldehyde concentrations in the blood remain abnormally high.

Symptoms, which occur within one half to 2 hours following consumption of the mushroom and alcohol, include flushing, palpitations, dyspnea, hyperventilation, and tachycardia. Vomiting and diarrhea are usually absent. Recovery is ordinarily spontaneous and complete, but severe cases may require gastric lavage and symptomatic care.

READING REFERENCES

Ammirati, J.F., Traquair, J.A., and Horgen, P.A.: *Poisonous Mushrooms of the Northern United States and Canada*, Minneapolis, University of Minnesota Press, 1985.

Baskin, E.: *The Poppy and Other Deadly Plants*, New York, Delacorte Press, 1967.

Benedict, R.G.: Mushroom Toxins Other Than *Amanita*. In *Microbial Toxins*, Vol. VIII, Kadis, S.A., Ceigler, A., and Ajl, S.J., eds., New York, Academic Press, Inc., 1972.

Blohm, H.: *Poisonous Plants of Venezuela*, Cambridge, Harvard University Press, 1962.

Brady, L., and Catalfomo, P.: Mushroom Toxicity and Medical Treatment. In *Mushrooms and Man*. Walters, T., ed., Albany, Oregon, Linn-Benton Community College, 1977.

Christensen, W.I.: Milk Sickness: A Review of the Literature, Econ. Botany, *19*(3):293, 1965.

Der Marderosian, A.: Poisonous Plants In and Around the Home, Am. J. Pharm. Ed., *30*(1):115, 1966.

Dreisbach, R.H.: *Handbook of Poisoning*, 9th ed., Los Altos, Lange Medical Publications, 1977.

Everist, S.L.: *Poisonous Plants of Australia*, Sydney, Australia, Angus and Robertson (Publishers) Pty Ltd., 1974.

Evers, R.A., and Link, R.P.: *Poisonous Plants of the Midwest and Their Effects on Livestock*, Special Publ. 24, Urbana-Champaign, University of Illinois, 1972.

Fochtman, F.W., Manno, J.E., Winek, C.L., and Cooper, J.A.: Toxicity of the Genus *Dieffenbachia*, Toxicol. Appl. Pharmacol., *15*(1):38, 1969.

Francis, D.F., and Southcott, R.V.: *Plants Harmful to Man in Australia*, Adelaide, Botanic Garden, 1967.

Fröhne, D., and Pfänder, H.J.: *A Colour Atlas of Poisonous Plants*, London, Wolfe Publishing Ltd., 1984.

Hardin, J.W., and Arena, J.M.: *Human Poisoning from Native and Cultivated Plants*, 2nd ed., Durham, North Carolina, Duke University Press, 1974.

Hatfield, G.M., and Brady, L.R.: Toxins of Higher Fungi, Lloydia, *38*(1):36, 1975.

Howard, R.A., DeWolf, G.P., Jr., and Pride, G.H.: Poisonous Plants, Arnoldia, *34*(2):41, 1974.

Keeler, R.F.: Toxins and Teratogens of Higher Plants, Lloydia, *38*(1):56, 1975.

Kinghorn, A.D., ed.: *Toxic Plants*, New York, Columbia University Press, 1979.

Kingsbury, J.M.: *Poisonous Plants of the United States and Canada*, Englewood Cliffs, New Jersey, Prentice-Hall, Inc., 1964.

Kingsbury, J.M.: *Deadly Harvest*, New York, Holt, Rinehart & Winston, 1965.

Lampe, K.F., and Fagerström, R.: *Plant Toxicity and Dermatitis*, Baltimore, The Williams & Wilkins Co., 1968.

Lampe, K.F., and McCann, M.A.: *AMA Handbook of Poisonous and Injurious Plants*, Chicago, American Medical Association, 1985.

Lincoff, G., and Mitchel, D.H.: *Toxic and Hallucinogenic Mushroom Poisoning*, New York, Van Nostrand Reinhold Co., 1977.

McKenny, M., and Stuntz, D.E.: *The Savory Wild Mushroom*, rev. ed., Seattle, University of Washington Press, 1971.

Morton, J.F.: Poisonous and Injurious Plants and Fungi. In *Forensic Medicine*, Vol. III, Tedeschi, C.G., Eckert, W.G., and Tedeschi, L.G., eds., Philadelphia, W.B. Saunders Co., 1977.

Morton, J.F.: *Plants Poisonous to People in Florida and Other Warm Areas*, 2nd ed., Miami, Author, 1982.

Muenscher, W.C.: *Poisonous Plants of the United States*, New York, The Macmillan Co., 1951.

North, P.M.: *Poisonous Plants and Fungi*, London, Blandford Press, 1967.

O'Leary, S.B.: Poisoning in Man from Eating Poisonous Plants, Arch. Environ. Health, *9*(8):216, 1964.

Rumack, B.H., and Salzman, E., eds.: *Mushroom Poisoning: Diagnosis and Treatment*. West Palm Beach, Florida, CRC Press, Inc., 1978.

Schwarting, A.E.: Poisonous Plants. In *Toxicology, Mechanisms and Methods*, Vol. II, Stewart, C.P., and Stolman, A., eds., New York, Academic Press, Inc., 1961.

Schwarting, A.E.: Poisonous Seeds and Fruits, Prog. Chem. Toxicol., *1*:385, 1963.

Smith, A.H.: *Mushrooms in Their Natural Habitats*, Portland, Oregon, Sawyer's Inc., 1949.

Smith, A.H.: *The Mushroom Hunter's Field Guide*, rev. ed., Ann Arbor, University of Michigan Press, 1971.

Tyler, V.E., Jr.: Poisonous Mushrooms, Prog. Chem. Toxicol., *1*:339, 1963.

Walter, W.G.: *Dieffenbachia Toxicity*, JAMA, *201*:(2)154, 1967.

Watt, J.M., and Breyer-Brandwijk, M.G.: *The Medicinal and Poisonous Plants of Southern and Eastern Africa*, Edinburgh, E. & S. Livingstone, Ltd., 1962.

Wieland, T., and Wieland, O.: The Toxic Peptides of *Amanita* Species. In *Microbial Toxins*, Vol. VIII, Kadis, S.A., Ciegler, A., and Ajl, S.J., eds., New York, Academic Press, Inc., 1972.

Youngken, H.W., Jr., and Karas, J.S.: *Common Poisonous Plants of New England*, Washington, D.C., U.S. Department of Health, Education and Welfare, Public Health Service Publication No. 1220, 1964.