

Casarett & Doull's Essentials of Toxicology, 2e >

Chapter 27. Toxic Effects of Plants, Fungi, and Algae

Stata Norton

Key Points

- Different portions of the plant (root, stem, leaves, and seeds) often contain different concentrations of a chemical.
- The age of the plant contributes to variability. Young plants may contain more or less of some constituents than mature plants.
- Climate and soil influence the synthesis of some chemicals.
- Plants contain chemicals that may exert toxic effects on skin, lung, cardiovascular system, liver, kidney, bladder, blood, central and peripheral nervous systems, bone, and the reproductive system.
- Contact dermatitis and photosensitivity are common skin reactions with many plants.
- Gastrointestinal effects range from local irritation to emesis and/or diarrhea.
- Cardiac glycosides in the leaves or seeds of many plants cause nausea, vomiting, and cardiac arrhythmias in animals and humans.

Toxic Effects of Plants, Fungi, and Algae: Introduction

Of the many species of plants that contain toxic chemicals, only a few are described here. Selection has been based on three considerations: frequency with which contact occurs, importance and seriousness of toxic effect, and scientific understanding of the nature of the action of the chemical.

Toxic effects of the same species of plant may vary with differences in production of the toxic chemical by plants. The reasons for variability in concentration of toxic chemicals are several:

1. Different portions of the plant (root, stem, leaves, and seeds) often contain different concentrations of a chemical.
2. The age of the plant contributes to variability. Young plants may contain more or less of some constituents than mature plants.
3. Climate and soil influence the synthesis of some chemicals.
4. Genetic differences within a species may alter the ability of individual plants to synthesize a chemical. Synthesis of related toxic chemicals often is found in taxonomically related species as a characteristic of a genus and sometimes as a familial characteristic.

Toxic Effect by Organ

Skin

Contact Dermatitis

Many plants common to temperate regions worldwide contain compounds that produce irritation on contact with the intact plant. Several species of *Ranunculus* (buttercup) cause contact dermatitis. These plants contain ranunculin, which releases toxic protoanemonin, also present in *Anemone*, another genus of the buttercup family. Protoanemonin is readily converted to anemonin, which has marked irritant properties. Ingestion of plants containing protoanemonin may result in severe irritation of the gastrointestinal tract.

Contact of the eye or tongue to the juice of the *Dieffenbachia* plant results in pain and rapid development of edema and inflammation, which may take days or weeks to subside. The toxicity is due to: (1) release of a histamine- or serotonin-like chemical that may be involved in the immediate pain and (2) release of raphides, the needle-like crystals of irritating calcium oxalate that are coated with a trypsin-like inflammatory protein, from ampule-

shaped ejector cells throughout the surface of the leaf.

Contact with the trichomes of species of *Urtica* (nettles) causes pain and erythema after penetration of the skin. In the stinging nettles, *Urtica urens* and *Urtica dioica* (family Urticaceae), the trichomes covering the leaves and stems consist of fine tubes with bulbs at the end that break off in the skin and release fluid containing histamine, [acetylcholine](#), and serotonin, causing the acute response.

Allergic Dermatitis

Most people are familiar with allergic dermatitis caused by plants such as poison ivy. Species of both *Philodendron* (family Araceae, arum family) and *Rhus* (Anacardiaceae, cashew family) cause allergic contact dermatitis. *Philodendron scandens* is a common houseplant, while *Rhus radicans* (poison ivy) is native to North America. In addition to poison ivy, the toxicodendron group of plants contains *Rhus diversiloba* (poison oak) and *Rhus vernix* (poison sumac). The active ingredients in *P. scandens* are resorcinols. In *R. radicans*, the allergenic component is a mixture of catechols called urushiol. Allergic dermatitis also develops with repeated exposures to the sap of mango fruit, because the skin of the fruit contains oleoresins that cross-react with allergens of poison ivy.

Flower growers and other individuals who handle bulbs and cut flowers of daffodils, hyacinths, and tulips sometimes develop dermatitis from contact with the sap. The rashes are due to irritation from alkaloids (masonin, lycorin, and other alkaloids) or to needle-like crystals of calcium oxalate in the bulbs. One alkaloid, tulipalin-A, which causes “tulip fingers,” has allergenic properties.

The major allergen in natural rubber latex from the rubber tree, *Hevea brasiliensis*, is prohevein, a chitin-binding polypeptide. Individuals sensitive to latex rubber may be sensitized to several fruits containing a chitinase, including banana, kiwi, tomato, and avocado.

Pollen from several genera in the family Asteraceae (e.g., mugwort, *Artemisia vulgaris*, in Europe, and ragweed, *Ambrosia artemisiifolia*, in North America) contains allergens causing summer rhinitis. Immunoglobulin antibodies produced by sensitized individuals cross-react with mugwort and ragweed pollen. The cross-reactive allergen is a highly conserved 14-kDa protein, profilin.

Photosensitivity

Poisoning of livestock from *Hypericum perforatum* (St. John's wort) results in development of edematous lesions of the skin, especially in areas not well covered with hair, including the ears, nose, and eyes. The toxic principle hypericin causes photosensitization, and lesions appear after exposure to sunlight. Photosensitization in humans is a rare event after consumption of St. John's wort.

Respiratory Tract

Allergic Rhinitis

Rhinitis from inhalation of plant pollens, also known as “hay fever” or pollinosis, is a seasonal problem for many individuals.

Cough Reflex

Workers who handle *Capsicum annuum* (cayenne pepper) and *Capsicum frutescens* (chili pepper) have an increased incidence of cough during the day. The major irritants in *Capsicum* are [capsaicin](#) and dihydrocapsaicin. Capsaicin-sensitive nerves in the airway are involved in the irritation and cough. Sensory endings of C fibers are part of the cough reflex, and the principal neurotransmitter for these fibers, the neuropeptide substance P, is depleted by [capsaicin](#). [Capsaicin](#) activates a subtype of the vanilloid receptor found in the airway, spinal cord, dorsal root ganglion, bladder, urethra, and colon. Individuals handling the peppers may experience irritation and vesication.

Cell Death

Laboratory rats are highly susceptible to monocrotaline from seeds of *Crotalaria spectabilis* (showy rattlebox, legume family) and develop a condition resembling pulmonary hypertension. Monocrotaline is converted by rat liver into an active pyrrolic metabolite responsible for the cardiopulmonary lesions. Apoptosis of arterial endothelial cells may be involved early in the onset of pulmonary hypertension. Monocrotaline elicits hepatitis as the primary toxicity in most species.

Gastrointestinal System

Direct Irritant Effects

The most common outcome of ingestion of a toxic plant is gastrointestinal disturbance (nausea, vomiting, and diarrhea) from irritation of the gut. Many different kinds of chemicals are responsible for this. Some have found a place in medicine as mild purgatives, such as cascara sagrada (“sacred bark”). Cascara is obtained from the bark of *Rhamnus purshiana* (California buckthorn). The active ingredient is emodin.

Tung nut (*Aleurites fordii*) is grown worldwide. The seeds, from which commercially useful oil is expressed, are the most toxic part. Ingestion of ripe nuts causes abdominal pain, vomiting, and diarrhea. Outbreaks of poisoning are most common in children.

Buffalo bean or buffalo pea (*Thermopsis rhombifolia*) is a legume growing wild in the western United States. Loss of life of livestock has been reported from consumption of the mature plant with seeds. Children develop nausea, vomiting, dizziness, and abdominal pain from eating the beans. The active toxic substances are quinolizidine alkaloids.

Aesculus hippocastanum (horse chestnut) and *Aesculus glabra* (Ohio buckeye) are common trees with attractive panicles of flowers in the spring. Nuts of both trees contain a glucoside called esculin. When eaten by humans, the main effect is gastroenteritis. Esculin is poorly absorbed from the gastrointestinal tract of humans. In cattle the glucoside may be hydrolyzed in the rumen, releasing the aglycone to cause systemic effects of a stiff-legged gait and, in severe poisoning, tonic seizures with opisthotonus.

Antimitotic Effects

Podophyllum peltatum (May apple) contains the toxic purgative podophyllotoxin, especially in foliage and roots. In low doses, mild purgation predominates. Overdose results in nausea and severe paroxysmal vomiting. Podophyllotoxin inhibits mitosis by binding to microtubules.

Colchicine is an antimitotic agent that blocks formation of microtubules causing subsequent failure of the mitotic spindle. **Colchicine** is the major alkaloid in the bulbs of *Colchicum autumnale* (autumn crocus, lily family). Severe gastroenteritis (nausea, vomiting, diarrhea, and dehydration) follows ingestion of the bulbs. Systemic effects may develop, including confusion, delirium, hematuria, neuropathy, bone marrow aplasia, and renal failure. Additional toxic effects may be due to lectins in the plant. These lectins are potent inducers of a gelatinase from mononuclear white blood cells. High circulating levels of gelatinase have been shown to be present in circulatory shock.

Protein Synthesis Inhibition

The seeds of *Wisteria floribunda* (family Leguminosae) contain a lectin with affinity for *N*-acetylglucosamine on mammalian neurons. Consumption of a few seeds can result in headache, nausea, and diarrhea within hours, followed by dizziness, confusion, and hematemesis.

Ricinus communis (castor bean) is a member of the family Euphorbiaceae. If the seeds are eaten, adults and children experience no marked symptoms of poisoning for several days. Loss of appetite, nausea, vomiting, and diarrhea develop gradually. Then, gastroenteritis becomes severe, with persistent vomiting, bloody diarrhea, dehydration, and icterus in fatal cases. Death occurs in 6 to 8 days. The fatal dose for a child can be 5 to 6 seeds; it is about 20 seeds for an adult. Fatality is low in individuals who eat the seeds—less than 10% when a “fatal” dose is consumed—because the toxic protein is largely destroyed in the intestine. Death from castor beans is caused by two lectins, ricin I and ricin II, which inhibit protein synthesis. Similar toxic lectins are found in the seeds of *Abrus precatorius* (jequirity bean). Abrin-a, one of the four isoabrinins from the plant, is the most potent inhibitor of protein synthesis.

Ricin-type lectins with both A and B chains are potentially deadly if they pass, even in small quantities, through the gastrointestinal tract. Plants that produce only A chains offer much less risk when ingested. Young shoots of pokeweed (*Phytolacca americana*) are sometimes used in the spring as a salad green. Mature leaves and berries may cause gastrointestinal irritation with nausea and diarrhea. The plant produces three isozymes of single-chain lectins (PAP, PAPII, and PAP-S) that can inhibit protein synthesis in cells by inactivating rRNA. Single-chain, ribosome-inhibiting proteins do not enter intact cells readily, but if the cell membrane has been breached by a virus, they may enter the cell. Lectins that bind strongly to the cells lining the small intestine and are endocytosed by them may be “nutritionally toxic” if they are consumed over a long period. Experimentally, reduction in weight gain has been the major finding from the presence of high quantities of some lectins in the diet. A correlation between strength of binding to the brush border of the jejunum and effectiveness as an antinutrient has been reported.

Cardiovascular System

Cardioactive Glycosides

Plants containing species with cardioactive glycosides include *Digitalis purpurea* (foxglove, Scrophulariaceae family) containing digitalis, *Scilla maritima* (squill) containing scillaren, *Convallaria majalis* (lily of the valley) containing convallatoxin in the bulbs, *Asclepias* species (milkweeds) containing 6'-O-(E-4-hydroxycinnamoyl) desglucouzarin, *Nerium oleander* (bay laurel) containing oleandrin and nerium, and *Thevetia peruviana* (yellow oleander) containing thevetin A. Animals and humans eating the leaves or seeds present with nausea, vomiting, and cardiac arrhythmias.

Action on Cardiac Nerves

Veratrum viride (American hellebore, lily family), *Veratrum album* (European hellebore), and *Veratrum californicum* have similar alkaloids, including protoveratrine, veratramine, and jervine. After ingestion, the alkaloids cause nausea, emesis, hypotension, bradycardia, and sometimes muscle spasm. Cardiac arrhythmias are common with higher exposures. Several species of *Zigadenus*, including *Zigadenus nuttallii* (death camas), contain *Veratrum*-like alkaloids. The plants grow throughout North America and the white bulbs may be mistaken for wild onions. All parts of the plant are toxic.

Aconitum species have been used in Western and Eastern medicines for centuries. The European plant, *Aconitum napellus* (monkshood, Ranunculaceae family), is a perennial grown in gardens for its ornamental blue flowers. The roots of *Aconitum kusnezoffii* (chuanwu) and *Aconitum Carmichaeli* (caowu) are in the Chinese *Materia Medica*. Poisoning may occur from intentional or accidental ingestion, and the concentration of the alkaloids—aconitine, mesaconitine, and hypoaconitine—varies depending on species, place of origin, time of harvest, and processing procedure. The alkaloids cause a prolonged sodium current in cardiac muscle and nerve fibers with slowed repolarization. Hypotension, gastrointestinal upset, numbness of the mouth, and paresthesias in the extremities may be observed.

Grayanotoxins are produced exclusively by several genera of Ericaceae (heath family). They have been isolated from *Rhododendron ponticum* and *Kalmia angustifolia*. The grayanotoxins are present throughout the plants, including leaves, flowers, pollen, and nectar. The toxin gets into honey from nectar collected by bees from the flowers. Poisoning from consumption of leaves or contaminated honey produces a syndrome consisting of marked bradycardia, hypotension, oral paresthesias, weakness, and gastrointestinal upset. In severe poisoning, there is respiratory depression and loss of consciousness. Grayanotoxin I (acetyl-andromedol) slows both the opening and closing of sodium channels in nerves.

Vasoactive Chemicals

Mistletoe is a parasitic plant on trees that is poisonous. American mistletoe, *Phoradendron tomentosum*, is a member of the same family as European mistletoe (*Viscum album*, Loranthaceae family). Viscotoxins are basic polypeptides that produce hypotension, bradycardia, negative inotropic effects on heart muscle, and vasoconstriction of the vessels of skin and skeletal muscle. Serious poisoning from the plants is rare and includes gastrointestinal distress and hypotension.

Vasoconstriction is a primary toxic effect of *Claviceps purpurea* (ergot), a fungus parasitic on grains of rye. The main toxic effect of ergot alkaloids is vasoconstriction, primarily in the extremities, followed by gangrene. Abortion in pregnant women is also common after ingestion of contaminated rye flour. The alkaloids [ergotamine](#) and [ergonovine](#) have been used in therapeutics.

The fungus, *Acremonium coenophialum*, grows symbiotically on the forage grass tall fescue (*Festuca arundinacea*) and produces some ergot alkaloids and other lysergic acid derivatives. The fungus causes “fescue toxicosis” in cattle grazing on infected plants. The condition in cattle includes decreased weight gain, decreased reproductive performance, and peripheral vasoconstriction. In the southwestern United States, *Stirpa robusta* (sleepy grass) also is infected with an *Acremonium* fungus. Horses grazing in areas where the infected perennial grass grows become somnolent, presumably as a result of ingesting lysergic acid amide, [ergonovine](#), and related alkaloids produced by the fungus.

Liver

Hepatocyte Damage

Senecio (ragwort or groundsel, aster family), *Echium* (bugloss), *Cynoglossum* (hound's tongue), *Heliotropium*, and *Symphytum* have species containing the pyrrolizidine alkaloids responsible for hepatic venoocclusive disease. Animal species susceptible to pyrrolizidine alkaloids are rats, cattle, horses, and chickens, whereas guinea pigs, rabbits, gerbils, hamsters, sheep, and Japanese quail are resistant. Damage to hepatocytes may be due to the microsomal formation of pyrrole metabolites, with cross-linking of DNA strands by the metabolites. Resembling cirrhosis and some hepatic tumors, the clinical condition may be described as a Budd-Chiari syndrome, with portal hypertension and obliteration of small hepatic veins.

Mushroom Toxins

Many of the nonedible mushrooms may cause gastrointestinal distress, but most are not life-threatening. Most deaths from mushroom poisoning worldwide are due to liver damage following consumption of *Amanita phalloides* (death cap), *Galerina*, and *Lepitota*. *Amanita ocreata* (death angel) is equally dangerous. *A. phalloides* contains two types of toxic chemicals: phalloidin and amatoxins. Phalloidin is a cyclic heptapeptide that combines with actin in muscle cells to interfere with muscle function, which contributes to some of the diarrhea that develops 10 to 12 h postingestion. Readily absorbed amatoxins are bicyclic peptides, and the most toxic, alpha-amanitin, has a strong affinity for hepatocytes where it binds to RNA polymerase II, thus inhibiting protein synthesis. Serious clinical signs begin about the third day after ingestion. Treatment in severe cases may require liver transplant. Renal proximal tubular lesions are found in cases of severe amanita poisoning.

Mycotoxins

Various fungi present during harvest, or subsequent storage of food, produce toxins. Most notable toxins are aflatoxins from *Aspergillus* species in stored grain, ochratoxin A, an immunosuppressant chemical produced by *Aspergillus* and *Penicillium* molds, and zearalenone, a mycotoxin produced by *Fusarium* and *Gibberella* species.

Fumonisin are toxins produced by the fungus *Fusarium*, primarily by *Fusarium moniliforme* and *Fusarium proliferatum* growing on corn. Ingestion by horses of corn contaminated with *Fusarium* mold causes “moldy corn poisoning,” or equine leukoencephalomalacia. The signs in affected horses are lethargy, ataxia, convulsions, and death. Fumonisin are structurally similar to sphingosine, and their toxicity is related to their blockade of sphingolipid biosynthesis.

Lantadene Toxicity

Lantana camara (Verbenaceae family) has been described as 1 of the 10 most noxious weeds in the world. Cattle, rabbits, and guinea pigs develop hyperbilirubinemia and cholestasis. One triterpenoid that induces hepatotoxicity is lantadene A.

Kidney and Bladder

Carcinogenic Chemicals

Bracken fern (*Pteridium aquilinum*) grows worldwide and is the only higher plant known to cause epithelial and mesenchymal neoplasms of the bladder in animals under natural conditions of feeding. The carcinogen ptaquiloside alkylates adenines and guanines of DNA. Human consumption of young bracken fern shoots may increase the incidence of esophageal and stomach cancers.

Kidney Tubular Degeneration

Species of *Xanthium* (cocklebur, aster family) induce toxicosis in livestock (pigs, sheep, cattle, horses, and fowl) in pastures where two- and four-leaf seedlings are present. Clinical signs are depression and dyspnea. Pathological findings include renal tubular necrosis and hepatic centrilobular necrosis. The active ingredient is carboxyatractyloside, which causes microvascular hemorrhages in multiple organs.

Acute renal failure causes death in poisoning from *Cortinarius* species of woodland fungi, found especially in northern conifer forests. Species vary widely in habit and in edibility. Renal biopsy in poisoned patients showed acute degenerative tubular lesions with inflammatory interstitial fibrosis.

Blood and Bone Marrow

Anticoagulants

Fungal infections in sweet clover (*Melilotus alba*) silage and hay have caused serious toxicity and death in cattle. Deaths are from hemorrhages caused by dicumarol, a fungal metabolite that causes prothrombin deficiency.

Bone Marrow Genotoxicity

Some species of poppy, such as *Argemone* (Papaveraceae), produce sanguinarine, a benzophenanthridine alkaloid that intercalates DNA. Humans may be exposed to argemone oil as an adulterant of mustard oil. A single low dose has been shown to increase chromosomal aberrations in bone marrow cells in mice.

Cyanogens

Cyanogens are constituents of several different kinds of plants. Amygdalin is present in the kernels of apples, cherries, peaches, and the bitter almond *Prunus amygdalus*, var. *amara*. Amygdalin is not present in the seeds of the sweet almond, the nut used for food. In the stomach, amygdalin releases hydrocyanic acid, which combines with ferric ion in methemoglobin or cytochrome oxidase. Ingestion of several bitter almond seeds causes classic cyanide poisoning and asphyxiation.

Cassava is a staple food starch from *Manihot esculenta* (Euphorbiaceae family) that contains linamarin, a cyanogenic glucoside. Processing of the root for human consumption removes the cyanogen. If local processing is inadequate, then chronic ingestion of linamarin in cassava may cause konzo, a form of tropical myelopathy with sudden onset of spastic paralysis. Degeneration of the corticospinal motor pathway may be caused by production of thiocyanate from linamarin and stimulation of neuronal glutamate receptors by thiocyanate.

Nervous System

Some of the most useful drugs have been plant-derived chemicals that act on the nervous system. However, some unintended serious neurotoxic syndromes may result from ingestion of certain plants. Permanent damage to the nervous system is a serious consequence of excessive neuronal stimulation.

Epileptiform Seizures

The fleshy tubers of *Cicuta maculata* (water hemlock) may cause fatal poisoning, characterized by tonic-clonic convulsions. The toxic principle, cicutoxin, binds to GABA-gated chloride channels.

Several members of the mint family (Labiatae), such as pennyroyal (*Hedeoma*), sage (*Salvia*), and hyssop (*Hyssopus*), contain monoterpenes, which in high doses can cause tonic-clonic convulsions.

Excitatory Amino Acids

Excitatory amino acids (EAAs) from plants may act on one or more glutamate receptor subtypes, and excessive stimulation may result in death of the neurons. Kainic acid is present in the marine red alga *Digeniasimplex*. Under some climatic conditions, the algae reproduce rapidly, causing a “red tide.” Filter-feeding mussels eat the algae and humans may be poisoned by eating the mussels. The green alga *Chondria aranta* produces domoic acid, a tricarboxylic amino acid, as does the marine diatom *Nitzschia pungens*. Consumption of domoic-acid-containing mussels produces gastrointestinal distress, headache, hemiparesis, confusion, and seizures. Prolonged effects were severe memory deficits and sensorimotor neuropathy.

The fungi *Amanita muscaria* (fly agaric) and *Amanita pantherina* (panther agaric) contain EAA, ibotenic acid, and possibly its derivative, muscimol. The effects are somewhat variable: central nervous system depression, ataxia, hysteria, and hallucinations. Myoclonic twitching and seizures sometimes develop.

EAAs are also found in flowering plants. The pea family (Leguminosae) contains several species that produce EAAs in the seeds. Willardiine, isolated from *Acacia willardiana*, *Acacia lemmoni*, *Acacia millefolia*, and *Mimosa asperata*, acts as an agonist on specific glutamate receptors. The seeds of *Lathyrus sylvestris* (flat pea) contain 2,4-diaminobutyric acid and beta-N-oxalylamino-L-alanine, which induce an acute neurologic condition in sheep that begins with weakness and progresses to tremors and prostration, and seizures. Chronic poisoning with seeds of *Lathyrus sativus* (chickling pea) induces lathyrism. Affected individuals have corticospinal motor neuron degeneration with severe spastic muscle weakness and atrophy but little

sensory involvement.

Motor Neuron Demyelination

Anthracenones are found in the seeds of *Karwinskia humboldtiana*, family Rhamnaceae (buckthorn, coyotillo, and tullidora). In human and livestock poisonings, the clinical syndrome that develops after a latency of several days is ascending flaccid paralysis, beginning with demyelination of large motor neurons in the lower legs and leading to fatal bulbar paralysis.

Cerebellar Neurons

Swainsonine, an indolizidine alkaloid found in *Swainsonia canescens*, *Astragalus lentiginosus* (spotted locoweed), and *Oxytropis sericea* (locoweed), causes aberrant behavior with hyperexcitability and locomotor difficulty. Swainsonine inhibits liver lysosomal and cytosomal alpha-mannosidase and Golgi mannosidase II, resulting in abnormal brain glycoproteins and accumulation of mannose-rich oligosaccharides.

Parasympathetic Stimulation

Some mushrooms of the genera *Inocybe*, *Clitocybe*, and *Omphalotus* contain significant amounts of muscarine, and consumption of toxic species causes diarrhea, sweating, salivation, and lacrimation, all referable to stimulation of parasympathetic receptors.

Parasympathetic Block

The belladonna alkaloids (l-hyoscyamine, [atropine](#), d,l-hyoscyamine, and [scopolamine](#)), present in several genera of plants of the family Solanaceae (the nightshades), are best known for their block of muscarinic receptors. Other plants containing anticholinergics include: *Datura stramonium* (jimsonweed)—scopolamine; *Hyoscyamus niger* (henbane)—l-hyoscyamine; *Atropa belladonna* (deadly nightshade)—atropine; *Duboisia myoporoides* (pituri)—l-hyoscyamine. Modest doses induce muscarinic block, presenting with tachycardia, dry mouth, dilated pupils, and decreased gastrointestinal motility. Large doses affect the central nervous system, causing confusion, bizarre behavior, hallucinations, and subsequent amnesia. Deaths are rare, although recovery may take several days.

The brilliant orange-red seeds of *Solanum dulcamara* (woody nightshade, bittersweet) contain solanine, a glycoalkaloid, responsible for the acute toxicity, including tachycardia, dilated pupils, and hot, dry skin, as in [atropine](#) poisoning.

Sensory Neuron Block

[Capsaicin](#) found in species of *Capsicum* (*C. annuum*, sweet pepper, and *C. frutescens*, red pepper, Solanaceae) produces a burning sensation on VR1 sensory endings, but also desensitizes the transient potential vanilloid 1 receptor (TRPV1) of sensory endings of C-fiber nociceptors to stimuli. This long-term sensory neuron-blocking effect has therapeutic use in chronic pain.

Skeletal Muscle and Neuromuscular Junction

Neuromuscular Junction Block

Block of the neuromuscular junction of skeletal muscle may result from block of postsynaptic [acetylcholine](#) (nicotinic) receptors by either an antagonist or an agonist, causing excessive stimulation of the receptor followed by prolonged depolarization. [Nicotine](#), for which the receptor is named, stimulates autonomic ganglia as well as the neuromuscular junction. An isomer of [nicotine](#), anabasine (C₁₀H₁₄N₂), present in *Nicotiana glauca* (tree tobacco), produces prolonged depolarization of the junction. Consumption of the leaves of the plant has caused severe, generalized muscle weakness and respiratory compromise, following flexor muscle spasm and gastrointestinal irritation. Curare, the South American arrow poison, is a potent neuromuscular blocking agent for skeletal muscle and kills by stopping respiration. Paralysis is due to block of [acetylcholine](#) receptors at the postsynaptic junction. Curare is obtained from tropical species of *Strychnos* and *Chondrodendron*. In warm weather, blooms of blue-green algae, *Anabaena flos-aquae*, in pond water produce a neurotoxin, anatoxin A, which depolarizes and blocks both nicotinic and muscarinic receptors, causing death in animals that drink the pond water within minutes to hours from respiratory arrest.

Methyllycaconitine is a norditerpenoid present in *Delphinium barbeyi* (tall larkspur) and some related species. Poisoned cattle show muscle tremors,

ataxia, and prostration and die from respiratory failure. The alkaloid has a high affinity for the neuromuscular nicotinic [acetylcholine](#) receptor and causes death by blocking [acetylcholine](#) at the neuromuscular junction.

Skeletal Muscle Damage

Mature seeds of the poisonous species of *Thermopsis* (family Leguminosae) contain quinolizidine alkaloids, principally anagryne and thermopsine. Young children eating seeds present with abdominal cramps, nausea, vomiting, and headache that lasts up to 24 h.

Bone and Tissue Calcification

Bone and Soft Tissue

Consumption of *Solanum malacoxylon* (nightshade family, Solanaceae), which contains a water-soluble vitamin D-like substance, induces calcification of the entire vascular system, especially the heart and aorta. Joint cartilage, lungs, and kidney may also be affected. Sheep and cows are both affected by ingestion of the plant. Consumption of *Cestrum diurnum* (day-blooming jasmine) and *Cestrum laevigatum* also causes hypercalcemia and extensive soft tissue calcification in animals.

Reproductive System and Teratogenesis

Abortifacients

In addition to actions on the nervous system, swainsonine in the legumes *Astragalus* and *Oxytropis* frequently causes abortions when locoweeds are ingested by pregnant livestock. Two genera of tropical legumes, *Leucaena* and *Mimosa*, contain a toxic amino acid, mimosine. In large amounts in the foliage and seeds of *L. leucocephala*, *L. glauca*, and *M. pudica*, mimosine causes incoordinated gait, goiter, and reproductive disturbances including infertility and fetal death.

A lectin from bitter melon seeds (*Momordica charantia*, family Cucurbitaceae) has been shown to have antifertility, abortifacient, and embryotoxic actions. The lectins are alpha- and beta-momorcharins, single-chain glycoproteins that are known to induce midterm abortion in humans.

Teratogens

Birth defects occurring in cows and goats grazing on *V. californicum* can be produced experimentally in chickens, rabbits, rats, mice, hamsters, and rainbow trout embryos. The alkaloids, jervine, 11-deoxojervine, and 3-*O*-glucosyl-11-deoxojervine, are responsible for the defects. The *Veratrum* alkaloids block cholesterol synthesis and thus the response of fetal target tissue to the sonic hedgehog locus, which has a role in developmental patterning of head and brain. Loss of midline facial structures and malformations involve cyclopia, exencephaly, and microphthalmia.

A cluster of fetal malformations characterized by deformation of limbs and spinal cord is found in cattle grazing on *Lupinuscaudatus* and *Lupinus formosus* (lupines), *N. glauca* (tree tobacco), and *Conium maculatum* (poison hemlock) during sensitive gestational periods. The active alkaloids identified in these plants, anagryne (*L. caudatus*), ammodendrine (*L. formosus*), anabasine (*N. glauca*), and coniine (*C. maculatum*), may depress fetal movements during susceptible gestational periods and in this way cause malformations.

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