A Small Dose of Animal and Plant Toxins
Or
An Introduction to the Health Effects of Animal and Plant Toxins

A book chapter of
A Small Dose of Toxicology - The Health Effects of Common Chemicals

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Supporting web sites
web: www.asmalldoseof.org - "A Small Dose of Toxicology"
web: www.toxipedia.org - Connecting Science and People

Dossier – Animal Toxin

Name: Animal Venoms and Poisons
Use: medicinal uses
Source: spiders, insects, snakes, lizards, fish, and frogs
Recommended daily intake: none (not essential)
Absorption: varies but can be very fast, e.g. bites
Sensitive individuals: children (small size), previously sensitized
Toxicity/symptoms: varies
Regulatory facts: none
General facts: long history of use and desire to avoid, often accompanied by fear of the animal
Environmental: global distribution, concern about expanding distribution to new areas
Recommendations: follow precautions for avoiding contact

Dossier – Pant Toxin

Name: Plant
Use: medicinal uses
Source: wide variety of plants
Recommended daily intake: none (not essential)
Absorption: intestine, skin
Sensitive individuals: children (small size), previously sensitized
Toxicity/symptoms: varies
Regulatory facts: none
General facts: long history of use and desire to avoid
Environmental: global distribution, concern about expanding distribution to new areas
Recommendations: generally avoid; know the poisonous plants in area

Case Studies

Puffer Fish

About 100 species of puffer fish use the powerful tetrodotoxin to discourage consumption by predators. Tetrodotoxin is found in all organs of the fish but is highest in liver, skin and intestine. The origins of the toxin are not clear, but one possibility is that the fish come in contact with bacteria that produce tetrodotoxin. Puffer fish may also have elevated levels of saxitoxin, a neurotoxin responsible for paralytic shellfish poisoning. Saxitoxin is produced by dinoflagellates (algae) and most often contaminates mussels, clams, and scallops. Both saxitoxin and tetrodotoxin are heat stable so cooking does not reduce toxicity. Tetrodotoxin causes paralysis by affecting the sodium ion transport in both the central and peripheral nervous system. A low dose of tetrodotoxin produces tingling sensations and numbness around the mouth, fingers, and toes. Higher doses produce nausea, vomiting, respiratory failure, difficulty walking, extensive paralysis and death. As little as 1 to 4 mg of the toxin can kill an adult. Saxitoxin has a very different chemical structure than tetrodotoxin but similar effects on transport of cellular sodium, and produces similar neurological effects but is less toxic that tetrodotoxin. Some people, particularly in Asia, consider the puffer fish a fine delicacy providing, it is carefully prepared by experienced chefs. The trick is to get just a small dose to feel mild tingling effects but not the more serious symptoms of tetrodotoxin poisoning. In the United States tetrodotoxin poisoning is rare but a recent report by the U.S. CDC described several case studies of people catching and consuming puffer fish containing elevated levels of these toxins and suffering the ill effects (MMWR, 2002).

Jimson Weed

Jimson Weed is the common name of one plant in a family of plants recognized since ancient times for their interesting effects on the nervous system. The deadly nightshade plant (*Atropa belladonna*) was used in the Roman Empire and during the Middle Ages both as cure and a poison. Women used preparations from this plant to dilate their pupils as a sign of allure and beauty. Some say the name belladonna refers to beautiful Italian women with dilated pupils. The drug responsible for these effects is called atropine, from the other part of the scientific name for deadly nightshade. We are commonly given a form of atropine (homatropine) to dilate our pupils during our eye examination. This is a short-acting form of atropine that keeps your eyes dilated for a few hours rather than the seven or more days that results from atropine. Atropine is also the same drug you take to counteract the effects of pesticides and chemical warfare agents that act by inhibiting acetylcholinesterase. In addition to atropine, this family of plants contains scopolamine and other belladonna alkaloids. They act by inhibiting the actions of acetylcholine at central and peripheral nerves. Besides dilation of the pupils, exposure to the belladonna alkaloids stops salivation, causing a dry mouth and difficulty swallowing and irregular heart rate. A larger dose causes central nervous system effects such as hallucinations, loss of memory, and confusion. Jimson Weed, part of the belladonna family of plants, is a common weed in North America. The easy availability of Jimson Weed combined with its ability to alter the nervous system leads to youth experimentation with the plant.

Unfortunately, the consequences, especially when combined with other drugs, can be very serious and even lead to death (MMWR, 1995).

Mushroom Poisoning

Worldwide, the most dangerous mushrooms are the "death cap" mushroom (*Amanita phalloides*) or the "death angel" (*Amanita ocreata*). The greatest number of deaths occurs in children less than 10 years of age, but adults are also susceptible. Often it is difficult to associate symptoms with eating the mushrooms because there is a 10-12 hour delay before symptoms become apparent. The initial symptoms are nausea, vomiting, diarrhea and irregular heart rate. Ultimately the toxin, amatoxin, damages the liver cells resulting in liver and kidney failure and possibly death. The amatoxin binds to RNA and inhibits protein synthesis. Amatoxin is very potent: ingestion of only 0.1 to 0.3 mg/kg of body weight results in death. For a child weighting 10 kg (or about 22 lbs) only 1 mg of amatoxin could result in a fatal poisoning. In 1997 the U.S. CDC reported that 2 out of 4 people who picked and consumed the death angel mushroom died of liver failure. This report clearly demonstrates that care is necessary in consuming wild mushrooms (MMWR, 1997).

Introduction and History

The creatures of the world, both animals and plants, produce a wide range of biologically active substances. Biologically active substances produced by animals or plants that cause an adverse effect are called toxins. Toxins refers only to toxic agents produced by animals and plants, not toxic substances such a lead or pesticides. The classification of a substance as a toxin tends to be in the eye of the beholder. Is caffeine, a naturally occurring agent in many plants, a toxin or just a pharmacologically active compound or both?

The study of plant and animal toxins is truly fascinating. Toxins offer many lessons in dose/response as well as a window into the struggle for growth and survival in hostile environments. They are used offensively to aid in gathering food or defensively to ward off predictors. To accomplish these tasks, toxins must interact with biological tissue. The study of their biological activity has provided us with important drugs and greatly improved our understanding of the mechanisms of biology. Much as this work has advanced only since the 1970s, when the sensitive instrumentation necessary to separate these venomous mixtures became available. The toxins of the world are really the medicine chest of nature. Pharmaceutical companies explore the world looking for new plants or animals that might be naturally producing a new drug. We have come to depend upon many of the substances produced by animals and plants. On the other hand, we all learn to avoid the sting of bees, and we know that even some of our houseplants are toxic. Mushrooms are a classic example of species that can be good to eat, deadly poisons, or, when used judiciously, produce hallucinations that some find desirable. Foxglove and

lily-of-the-valley contain a compound called digitalis that lowers blood pressure and prevents heart attacks. On the other hand, digitalis is quite toxic and the plants themselves are considered poisonous.

In the following sections we can only take brief look at this fascinating subject.

Animal Toxins

Animal toxins are roughly divided into venoms and poisons. Venoms are offensive, used in the quest for food. Snakes produce toxins that can immobilize or kill prey for food. The venom of spiders paralyzes insects to allow the spider to feed on the victim's body fluids. While the venoms may also be used defensively, their primary purpose is in the quest for food. Most venom is delivered from the mouth, as in snakes and spiders, but there are exceptions like the scorpion that uses its tail.

Poisons are primarily defensive, designed as protection against predators. Poisons are often sprayed or delivered with a stinger to penetrate the skin. Some fishes for example have poisons spines. Toxins can also be on the skin or be part of the meat of the animal, thus making them poisonous to touch or eat. Some poisonous animals develop very colorful marking to advertise their undesirable qualities.

The purpose of the venom is offensive while that of a poison is defensive, which in turn influences the characteristics of the toxin. Venoms, either large or small molecules, are usually variants of essential biological molecules such as lipids, steroids, histamines or other proteins. They are often mixtures with a specific mechanism of action such as paralyzing the nervous system. Poisons are designed to teach a predator that this is not a good meal. They usually cause more localized pain to discourage a predator but depending on the dose and sensitivity of the individual the poison can be deadly.

There are some unique challenges for the animal that produces toxin, particularly venoms. The toxin must be concentrated and stored in large enough dose to be effective but without being toxic to the animal that produces it. After a quick delivery, the toxin must be rapidly absorbed and act quickly to defeat that prey's response. These properties, along with precise action, make toxins the envy of the drug developers.

Arthropods

Insects, spiders, scorpions, craps, centipedes, millipedes, and even plankton are all arthropods, the largest and most diverse animal phylum. Some are capable of producing very powerful toxins as an aid in the quest for food. Humans come in contact with these toxins, usually by accident or as a result of the animal defending itself. Some insects, mosquitoes and ticks for example, are capable of transmitting other organisms to humans that cause disease. While these organisms may be toxic to humans, they are not toxins and will not be discussed in this chapter.

Arachnids (Scorpions, Spiders, Ticks)

Scorpions

There are approximately 1000 species of scorpions but only around 75 are clinically important. In some parts of the world scorpion stings are common and for the most part treated like bee or wasp stings, producing no long-lasting effects. There are a few scorpions with venom potent enough to harm humans, particularly children. The most potent venoms are low molecular weight proteins that affect the nervous system. There is usually immediate pain at the site of the sting, with elevated or irregular heart rate one of the first clinical signs. Most adults recover within 12 hours, but because of their low weight children are vulnerable to more serious and long-lasting clinical effects.

Spiders

Spiders or arachnids use their venom to paralyze prey while they feast on the victim's body fluids. They primarily feed on insects and other spiders. The venom of about 200 out of the 30,000 species of spiders represent a risk to humans. The venom of spiders is a complex mixture of neuroactive proteins and other chemicals. Researchers have studied venoms both to understand the mechanism of their effects but also in search of new drugs. If spiders were bigger they would be truly dangerous. Fortunately they are small, with only a very small about of venom. Because of our much larger size we receive only a small dose, but when a spider bites another insect it delivers a very large dose indeed.

In the United States one of the infamous venomous spiders is the black widow spider, but there are many similar species found around the world in temperate or tropical climates. It has a number of common names depending on the region of the world and ranges in color from brown to gray to black. The black widow species is shiny black and on the belly of the females is a red hourglass. Both the male and females are venomous, but only the female has fangs large enough to penetrate human skin. The venom of this species is made up of large proteins thought to affect the transmission of calcium ions of nervous system cells. The initial sting of the bite is followed by muscle cramps, sweating and possibly decreased blood pressure. There is no adequate treatment but the bite is seldom fatal.

Another globally distributed venomous spider is the brown recluse or violin spider. It too comes in numerous varieties depending upon the region of the world. The spider has a range of colors but most unique are its six eyes. The venom of the brown recluse contains a range of proteins designed to dissolve the victim's cellular proteins, but the most active agent affects the red blood cells. The effects of the venom vary, but a in the worst case there is serious necrosis of tissue at the center of the bite, with a surrounding area becoming red and swollen. The venom has literally dissolved the cells of the skin and surrounding tissue, which of course triggers the body's own defensive reactions. Significant tissue damage can occur particularly if the bite is on the face, but the bites are almost never fatal. There is no effective treatment for the venom other than supportive care.

The best protection is to avoid activities that may lead to spider bites, especially those of dangerous spiders. It is important to recognize which kinds of spiders are potentially dangerous, since most are harmless and shouldn't be needlessly killed.

Ticks

Ticks have a bad reputation for good reasons. Not only are they carriers of a number of diseases, the saliva of some can cause paralysis. North American natives were aware of tick paralysis, but the condition was officially noted as a disease of both animals and humans in 1912. The bites of at least 60 species of ticks can cause paralysis, which often does not appear until several days after the bite. The first indication is redness and swelling around the site of the bite. This is followed by neuromuscular weakness and difficulty in walking. If the tick is not removed, speech and breathing are affected, with eventual respiratory paralysis and death. Fortunately, removal of the tick results in a quick recovery of function. The exact mechanism of paralysis is not known but it appears to come from a substance the affects the neuromuscular junction. While not related to the venom of the tick saliva, the tick can also transmit diseases such as Lyme disease, Rocky Mountain spotted fever, Q fever, typhus and others.

Table 17.1 Arachnids (Scorpions, Spiders, Ticks)

Class	Examples	Delivery & Venom	Comments
Arachnids (scorpions & spiders & ticks)	Scorpions	Stinger - neurotoxin, no enzymes	Localized pain, mostly dangerous to children
	Latrodectus – Widow spiders (back, brown red-legged spider)	Bite – neurotoxin – large molecular proteins	Localized pain, sweating, muscle cramps, decreased blood pressure
	Loxosceles - Brown or Violin Spiders	Bite – complex mixture of enzymes	Serious tissue damage & attacks blood cells
	Ticks	Bite – saliva neurotoxin – transmit other diseases	Tick paralysis – weakness & difficulty walking – Remove tick

Insects

Some moths and caterpillars produce irritating substances or fend off predators with substances that do not taste good and are thus avoided.

A much more aggressive group of insects, with great power for their size, that almost all of us have come in contact with, are ants. Ants produce poisonous or irritating substances as a means of defense. Most ants have a stinger, and some can spray substances onto skin or the wound created by their powerful jaws. There are thousands of species of ants, and

the poisonous substances they produce vary enormously. Some ants create substances with large amounts of proteins that can cause an allergic response. Others ants produce formic acid, which is very irritating on the skin. Fire ants, common in the United States, produce a substance rich in alkaloids, which can cause localized tissue destruction and necrosis. Multiple bites can be dangerous and even life threatening for both humans and animals. Multiple stings can cause nausea, vomiting, difficulty breathing, coma and death.

Bee Stings

A honey bee has about 150μg of poison, but only a small fraction is typically injected. The faster the stinger is removed the less the response.

The stings from bees, wasps, hornets and related insects are well known to many people. Humans have collected honey for at least 6000 years. Honeybees sting when threatened and to protect their hive and honey from both humans and other predators, including yellow jackets. Yellow jackets are attracted to the smell of a hive's honey and will attempt to steal the honey. Watching the honeybees defend their hive from yellow jackets illustrates their need for a stinger. The stinger of a honeybee is barbed and usually left behind in the skin, literally ripped out of a bee that will soon die. Left behind also is a complex substance of many different proteins including histamine, dopamine and a substance that breaks down tissue. When stung, it is advisable to remove the stinger as soon as possible to reduce exposure. Some people advise putting a meat tenderizer on the site of the sting. This may help because a meat tenderizer is designed to digest protein and soften meat. In the event of a bee sting, the tenderizer is used to digest the bee protein. Response to bee stings varies enormously from almost nothing to life threatening. Usually there is localized swelling as the body rushes to wipe out the foreign protein that has invaded the body. Some people are highly allergic to bee stings (about 1 or 2 per 1000 people), and for them the response is not localized and results in a massive response that can lead to death. Even for those not allergic, multiple stings can cause breathing problems, decreased blood pressure, shock and death.

Wasp stings tend to contain less protein and more formic acid related substance that produces an intense burning.

Table 17.2 Insects

Examples	Poison or Venom	Comments

Moths and caterpillars	Irritating substance	Designed so they do not taste good
Ants	Variable - proteins, formic acid and other	Variable response – irritation, allergic response, tissue damage
Honey bees	Complex proteins	Swelling, allergic reaction
Wasps	Formic acid	Irritating

Reptiles

Lizards

Humans are a far bigger threat to lizards than they are to us. Lizards are generally slow moving and nocturnal, with few enemies other than humans. The venom is a complex mixture that contains serotonin, a neurotransmitter, but lacks many of the other protein-degrading enzymes. Clinical effects are minor unless you are small and receive a large dose.

Snakes

Snakes occupy a unique place in our collective imagination. The primary function of snake venom is to immobilize or kill prey for food. A secondary function of the venom is defensive or protective, but clearly snakes are not capable of eating large animals, such as humans. Often venomous snakes will strike but not release venom, which conserves a resource valuable to them. Approximately 400 of the more than 3,500 species of snake are sufficiently venomous to be a threat to humans and other large animals.

Worldwide, there are an estimated 300,000 to 400,000 venomous snakebites per year with about 10% (or 30,000) resulting in death. In the United States, there are approximately 7,000 venomous bites per year but only 1 in 500 deaths, testifying to the value of prompt medical treatment.

The most common venomous snakebites in North America are from vipers. This class of snakes has the most advanced venom delivery system. The venom is delivered through hinged tubular fangs that can be folded into the snake's mouth. The venom is quickly injected into the victim. The pit vipers, such as rattlesnakes, have a head sensor located between their nostril and eyes, which is thought to guide the strike even in the dark. The venom from vipers is a very complex enzymatic-based substance, which quickly causes localized swelling and tissue destruction (necrosis). The protein-based venom causes an allergic-type reaction leading to hemorrhage of body fluids, decreased blood pressure, shock, fluid in the lungs and death.

Table 17.3 Reptiles

Class	Examples	Venom & Delivery	Symptoms

Vipers (Viperidae)	Rattlesnakes Water moccasins Copperheads Bushmasters	Very complex enzymatic based, advanced delivery – hinged tubular fangs	Swelling & necrosis at site, affects blood cells, hemorrhage, decreased blood pressure, shock
Elapidae	Cobras Kraits Coral Snakes	Neurotoxin (some very potent) Fixed fangs, usually low dose	Nervous system effects, paralysis, numbness, respiratory failure

The second most common venomous snakes are the Elapidae, of which cobras and coral snakes are well known. These snakes deliver their venom from fixed fangs and must hold onto the victim while the venom is released. These snakes tend to be smaller than vipers and deliver a smaller dose of poison. But what they lack in size they make up in potency. The venom of these snakes predominately affects the nervous system, causing paralysis and numbness. Death is usually the result of respiratory failure from nervous system effects.

Marine Animals

Shellfish

Shellfish such as mussels, clams, oysters and scallops are not naturally toxic but can become so after feeding on plankton contaminated with a toxin. When visible, the blooming of the plankton (dinoflagellate) is called the red tide and can cause significant death among marine animals. There are several types of toxins, mostly affecting the nervous system. The newest, domoic acid, first appeared in 1987 off Prince Edward Island in Canada. This neurotoxin caused confusion and memory loss particularly in the elderly. Several elderly people died following seizures and coma. Domoic acid is heat stable, so cooking does not affect the toxin. Government agencies now monitor for contaminants of shellfish and move quickly to restrict harvesting. The domoic acid incident clearly indicates the importance of ongoing monitoring of the food supply.

The puffer fish is the probably the best known neurotoxic fish. Several related species of fish, as well as other marine life, such as some frogs, starfish, octopus and others, contain tetrodotoxin. Many people consider this fish a delicacy despite the occasional reported death from poor preparation. Tetrodotoxin is heat stable but water soluble, so careful preparation is necessary to limit neurological effects. Symptoms of poisoning include a rapid onset of numbness in the lips and mouth, which then extends to the fingers and toes, followed by general weakness, dizziness and respiratory failure, leading to death. The mechanism of action is similar to that of saxitoxin and affects sodium channel permeability.

It should also be remembered that fish high in the food chain, such as tuna, swordfish, and shark accumulate toxic substances like mercury or PCBs. Mercury affects the nervous system and is a proven reproductive hazard.

Table 17.4 Marine Animals

Animal Class	Examples	Toxin	Symptoms	Comment
Shellfish (filter-feeding mollusks)	Mussels, clams, oysters, scallops	Several kinds of toxin taken up from plankton (dinoflagellate)	See below	
	Paralytic Shellfish Poisoning (PSP)	saxitoxin in their muscles	Numbness, respiratory paralysis	Na channel permeability
	Diarrheic Shellfish Poisoning (DSP)	high molecular weight polyethers	Nausea, vomiting, diarrhea	Usually mild but annoying
	Neurotoxic Shellfish Poisoning (NSP)	brevetoxins	Numbness of mouth, muscular aches, dizziness,	
	Amnesic Shellfish Poisoning (ASP)	domoic acid	Confusion, memory loss, seizure, coma	Affects elderly
Coelenterates	Jelly fish, anemona, coral	nematocyst	sting, muscle cramps	
Fish	Sea Snail (cigua) and some fish, oysters and clams	Ciguatera, scaritoxin and maitotoxin	Numbness, salivation, cardiovascular effects, respiratory paralysis	inhibits acetyl cholinesterase
Fish	Puffer Fish (fugu, blowfish, toadfish … some frogs, starfish, octopus	tetrodotoxin	Nervous system Numbness, paralysis, respiratory failure, death	Decreased Na channel permeability
Fish	Tuna, shark, sword fish	Mercury (toxicant)	Neurotoxic, reproductive effects	Not produced by fish itself, concentrated in muscle

Plant Toxins

In the battle to survive, plants have developed a wide array of defensive measures. Plants produce a range of chemicals designed to fend off predators or discourage consumption by insects or animals. We will look at the chemicals that plants produce from a human prospective, that is, how they affect us when we eat or come in contact with the plant. For thousands of years humans have experimented with plants in a search for food, as treatment for illness, and even to alter one perception of the world. Wide ranges of drugs are derived from plants, and the search continues by the world's leading pharmaceutical companies. Others promote the use of plants as herbal or natural medicine. This section will focus only on the toxicity of some of the better-known plants, organized by organ system affected.

The tables below summarize the most important facts. The text provides additional information only if necessary to clarify a particular point. We can only scratch the surface of this fascinating area of biology.

Skin

One of the best protections for a plant is to make skin contact painful. This is done through either an allergic antibody-mediated response or through direct-acting chemicals. For an allergic type response it is not the first contact that produces the reaction but rather the next contact. Poison ivy produces a class of chemicals called urushiol that cause a very variable allergic response in about 70% of people exposed. Although not a direct protection for the plant, pollen of ragweed, mugwort or grasses cause an allergic response in many people.

Dieffenbachia or dumb cane, a common houseplant, produces a juice that is released when a stem is broken or chewed and causes a painful rapid swelling and inflammation of the tongue and mouth. The symptoms can take several days to resolve and are caused by oxalate crystals coated with an irritating protein. Stinging nettles (*Urtica*) releases histamine, acetylcholine, and serotonin from fine tubes with bulbs at the end that break off in the skin causing an intense burning or stinging sensation.

Table 17.5 Effects on Skin

Organ System	**Symptoms**	**Plant Examples**	**Toxin / Comment**
Skin	Allergic Dermatitis – Plant Rashes, itchy skin	Philodendron, poison ivy, cashew, bulbs of daffodils, hyacinths, tulips,	Antibody mediated after initial sensitization, very variable response. Allergens located on outer cells of plant
	Allergic Dermatitis – Pollen Sniffles & sneezing, runny eyes	Ragweed (North America), Mugwort (Europe), grasses	Antibody mediated – Pollen widely distributed in air. Very common, can be debilitating
	Contact Dermatitis Oral – Swelling and inflammation of mouth Skin – pain & stinging sensation	Dumb cane (Dieffenbachia) Nettles (Urtica)	Calcium oxalate crystals coated with inflammatory proteins Fine tubes contain histamine, acetylcholine and serotonin

Gastrointestinal System

For the plant, another good way to stop consumption by an animal is to make the animal sick to the stomach. This approach is used by a number of plants, but the mechanism of action varies. The first approach is direct irritation of the stomach lining to induce nausea and vomiting. The induction of mild vomiting is useful in some situations. The "sacred bark" of the California buckthorn produces cascara that is used to induce mild vomiting (a purgative).

Other approaches to induce gastrointestinal discomfort have far more serious toxic effects. The chemical colchicine stops cell division (an antimitotic), producing severe nausea, vomiting, and dehydration, which can lead to delirium, neuropathy and kidney failure. On the other hand, colchicine is used in the treatment of gout and studied as an anticancer agent because it stops cell division. Most toxic of all are plants that produce lectins, and the most toxic of these is the chemical ricin produced by castor beans. Only 5 to 6 seeds are necessary to kill a small child. Fortunately, following oral consumption much of the ricin is destroyed in the stomach. Ricin is extremely effective at stopping protein synthesis, so much that direct exposure to only 0.1 μg/kg can be fatal.

Table 17.6 Gastrointestinal System

Organ System	**Symptoms**	**Plant Examples**	**Toxin / Comment**
Gastrointestinal	Direct stomach irritation - Nausea, vomiting and diarrhea	California buckthorn (sacred bark), tung nut, horse chestnut, pokeweed ….	Emodin & esculine (toxins); Oil from seeds, nuts; some medical uses Children are most often affected
	Antimitotic (stops cell division) – Nausea, vomiting, confusion, delirium	Lily family, glory lily, crocus, may apple	Colchicine (gout treatment)
	Lectin toxicity – nausea, diarrhea, headache, confusion, dehydration, death	Wisteria, castor bean (Ricinus communis)	Lectins bind to cell surfaces Ricin – block protein synthesis, very toxic: 5 to 6 beans can kill a child

Cardiovascular system

The medically important drug cardiovascular digitalis was derived from foxglove (*Digitalis purpurea*). At medically useful doses, digitalis slows and stabilizes the heart rate, but at high dose it produces an irregular heart rate and decreased blood pressure. The Greeks first reported, "mad honey poisoning" almost 2500 years ago, and honey poisoning still affects people around the world, when bees gather nectar from rhododendrons and take it back to their hives. The cardiovascular effects are caused by

grayanotoxin, which is produced in the leaves and nectar of rhododendrons. The bees concentrate the toxin in the honey. Goats and sheep are also affected when they consume the leaves of rhododendron or some lily plants. The cardiovascular effects of consuming mistletoe contributed to some thinking it had either holy or demonic powers. The first more scientific observations on the cardiovascular effects of consuming mistletoe berries were in 1597.

Table 17.7 Cardiovascular System

Organ System	**Symptoms**	**Plant Examples**	**Toxin / Comment**
Cardiovascular	Digitalis-like glycosides – cardiac arrhythmias	Foxglove (*Digitalis purpurea*), squill, lily of the valley	Contain glycosides that are similar to digitalis:scillaren, convallatoxin
	Heart nerves – decreased heart rate and blood pressure, general weakness	Lily, hellebore, death camas, heath family, monkshood, rhododendron	Alkaloids, aconitum, grayanotoxin (concentrated in honey)
	Blood vessel constriction (vasoconstriction)	Mistletoe (berries contain toxin)	Holy or demonic – effects on heart first described in 1597. Toxin is called phoratoxin.

Nervous system

There are many plants that produce a wide variety of substances that can affect the nervous system. We have exploited the nervous system effects of plants for thousands of years and we continue to derive great value from some plants. In 399 B.C. Socrates died from a dose of the Greek state poison extracted from hemlock. An interesting story possibly about a poison found in hemlock is found in the Bible, Book of Numbers, 11:31-33. Hungry Israelites died after eating quail blown in from the sea. Some have speculated that the quail had consumed seeds from hemlock that contained coniine. The quail are not affected by coniine, but it is stored in their tissue making them deadly for humans to eat. The production and sale of coffee is a large international business solely designed to satisfy the demand for caffeine (see Chapter 4), the most widely consumed stimulant in the world. Mushrooms present another interesting challenge. Every year people are sickened and even die from eating poisonous mushrooms, while others consume them for their hallucinogenic effects.

Below is a brief look at some of the plants produce neuroactive substances.

Table 17.8 Nervous system

Organ System	Symptoms	Plant Examples	Toxin / Comment
Nervous System	Seizures	Water hemlock, (parsley family), mint family [particular species?]	Cicutoxin – affects potassium channels. Monoterpenes in mint oils
	Stimulation – Excitatory Amino Acids – headache, confusion, hallucinations	Red alga (red tide), Green alga Mushrooms– *Amanita* family (fly agaric), Flat Pea (*Lathyrus*)	Kainic acid, domoic acid-concentrated in shell fish, Ibotenic acid, muscarinic, (hallucinations) Latthyrism – motor neuron degeneration
	Aberrant behavior, very excitable, muscle weakness, death	Locoweed - Australian & Western U.S. plant	Swainsonine toxin – liver enzyme inhibitor - well known to affect cattle
	Stimulation	Coffee bean, tea, cola nut,	Caffeine, most widely consumed stimulant in the world
	Neurotoxic – death	Poison hemlock (*Conium maculatum*)	Coniine – neurotoxic alkaloid – Poison used by Socrates
	Paralysis – demyelination of peripheral nerves	Buckthorn, coyotillo, tullidora (U.S., Mexico)	Anthracenones – attack the myelin that surrounds the peripheral nerves
	Atropine-like effects – dry mouth, dilated pupils, confusion, hallucinations, memory lose	*Solanaceae* family – jimsonweed, henbane, deadly nightshade (*Atropa belladonna*), angles trumpet (atropine and scopolamine)	Clinical effects of many of the plants recognized since ancient times. Deaths are rare but children vulnerable. Hallucinations from muscarine & psilocybin
	Neuromuscular – mild stimulation to muscle paralysis, respiratory failure (curare), death	Tobacco – South American – *Strychnos* family (curare) Blue green alga	Nicotine –blocks acetylcholine receptors Curare – used as a hunting poison very potent receptor blocker

		(anatonin A)	

Liver

Fungi produce two of the most potent toxins affecting the liver. The "death cap" and "death angel" mushrooms from the *Amanita* family kill several people every year when mistakenly consume these mushrooms (see case study example). There are also a number of fungi and molds that grow on nuts or grain. High humidity and poor storage conditions encourage the growth of a fungus on nuts that produces aflatoxin, a very potent toxin that causes liver cancer. People with prior liver disease such as hepatitis are particularly susceptible.

Table 17.9 Liver

Organ System	**Symptoms**	**Plant Examples**	**Toxin / Comment**
Liver	"Hepatitis" and cirrhosis of liver – From contaminated grain	Ragwort or groundsel	Pyrrolizidine alkaloids – attack liver vessels – effects humans, cattle but some species resistant
	Liver failure and death	Mushrooms – "Death cap" (*Amanita phalloides*)	Amatoxin and phalloidin effects RNA and protein synthesis
	Liver cancer	Fungus that grows on peanuts, walnuts, etc…	Alfaltoxins– produced by fungus in poorly stored grain

Reproductive Effects

Reproductive and developmental toxins are primarily a concern for livestock. A high rate of fetal malformations in sheep offspring occurs following grazing on *Veratrum californicum* growing in the mountains of North America. Plants that induce abortion, such as bitter melon seeds have a long history of use of in humans.

Table 17.10 Reproductive Effects

Organ System	**Symptoms**	**Plant Examples**	**Toxin / Comment**
Reproductive Effects	Teratogen – malformations in offspring (sheep)	*Veratrum californicum* – native to North America	Veratrum – blocks cholesterol synthesis – seen offspring of mountain sheep
	Abortifacients – cause fetal abortions	Legumes (*Astrogalus*) Bitter melon seeds	Swainsonine toxin – stops cell division Lectins - halt protein

		(*Momordica*)	synthesis– used by humans

Regulatory Standards

Government regulatory agencies monitor some toxins as potential food contaminants. For example, agencies routinely monitor shellfish for several toxins and when necessary issue restrictions on harvesting. Many of the naturally occurring toxins are unregulated and the consumer must be aware of the potential hazards. It is really up to you, for example, to know what mushroom you consuming if you don't buy it at a store.

Note that some governments regulate noxious weeds, including some poisonous plants, but others are sold at garden stores.

Recommendation and Conclusions

Children, because of their small size, are often the most susceptible to many of the naturally occurring toxins, just as they are to other toxicants. The caffeine from a can of cola will have a much bigger effect on a small child than it will on an adult. Health status and age, both young and old, also influence the response. Aflatoxin from contaminated nuts has a greater likelihood of causing cancer in some with a liver disease such as hepatitis. It is important to develop a knowledge of which plants and animals can be dangerous and learn how to avoid dangerous contact with them.

More Information and References

Slide Presentation

- A Small Dose of Animal and Plant Toxins presentation material and references online: http://www.toxipedia.org or http://www.toxipedia.org/wiki/display/toxipedia/Animal+Toxins+Overview. Web site contains presentation material related to the health effects of animals and plant toxins.

European, Asian, and International Agencies

- Amphibians and Reptiles of Europe. Online: < http://www.herp.it/> (accessed: 16 June 2009).
  A large sample of European Amphibians and Reptiles.

North American Agencies

- Society For The Study Of Amphibians And Reptiles (SSAR). Online: < http://www.ssarherps.org/> (accessed: 16 June 2009).
  SSAR, a not-for-profit organization established to advance research, conservation, and education concerning amphibians and reptiles.

- Health Canada - Natural Health Products Directorate. Online: < http://www.hc-sc.gc.ca/dhp-mps/prodnatur/index-eng.php > (accessed: 16 June 2009).
  Natural Health Products Directorate works to "ensure that all Canadians have ready access to natural health products that are safe, effective, and of high quality, while respecting freedom of choice and philosophical and cultural diversity".

- U.S. Food and Drug Administration Center for Food Safety and Applied Nutrition. Online: <http://www.cfsan.fda.gov/seafood1.html> (accessed: 16 June 2009).
  Site has information on seafood health and safety issues.

- Northwest Fisheries Science Center's (NWFSC) Harmful Algal Bloom Program . Online: < http://www.nwfsc.noaa.gov/hab/index.html > (accessed: 16 June 2009).
  NWFSC Harmful Algal Bloom Program, part of the U.S. National Oceanic and Atmospheric Administration, provides information related to algal blooms.

- U.S. Food & Drug Administration Center for Food Safety & Applied Nutrition Foodborne Pathogenic Microorganisms and Natural Toxins Handbook – The "Bad Bug Book". Online: <http://www.cfsan.fda.gov/~mow/intro.html> (accessed: 16 June 2009).
  The "Bad Bug Book" contains extensive information on natural toxins either on the web or book can be downloaded.

Non-Government Organizations

- Natural Toxins Research Center (NTRC) - Texas A&M University System. Online: < http://ntrc.tamuk.edu/> (accessed: 16 June 2009).
  NTRC provides global research, training, and resources that will lead to the discovery of medically important toxins found in snake venoms.

- Cornell University Plants Poisonous to Livestock. Online: <http://www.ansci.cornell.edu/plants/index.html> (accessed: 16 June 2009).
  This is "includes plant images, pictures of affected animals and presentations concerning the botany, chemistry, toxicology, diagnosis and prevention of poisoning of animals by plants and other natural flora (fungi, etc.)".

- Alternative Medicine Foundation, Inc, HerbMed®. Online: <http://www.herbmed.org/> (accessed: 16 June 2009).
  "HerbMed® - an interactive, electronic herbal database – provides hyperlinked access to the scientific data underlying the use of herbs for health. It is an

evidence-based information resource for professionals, researchers, and general public."

- American Association of Poison Control Centers (AAPCC). Online: <http://www.aapcc.org/> (accessed: 16 June 2009).
  The AAPCC is a United States based organization of poison centers and interested individuals that coordinates information on common poisons.

- The Vaults of Erowid. Online: <http://www.erowid.org/> (accessed: 16 June 2009).
  The Vaults of Erowid web site contains information on wide variety of natural plants and chemicals.

References

Handbook of Clinical Toxicology of Animal Venoms and Poisons
by J. Meier (Editor), Julian White (Editor), Informa HealthCare, 768 pages, 1995.

Venomous and Poisonous Animals: A Handbook for Biologists, Toxicologists and Toxinologists, Physicians and Pharmacists. by Dietrich Mebs, Medpharm 360 pages, 2002.

MMWR (1997). Amanita phalloides Mushroom Poisoning – Northern California, June 6, 1997, Vol 46(22), p 489-491. Online: <http://www.cdc.gov/mmwr/preview/mmwrhtml/00047808.htm> (accessed: 16 June 2009).

MMWR (2002). Neurologic Illness Associated with Eating Florida Pufferfish, 2002., April 19, 2002, Vol 51(15), p 321-323. Online: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5115a1.htm> (accessed: 16 June 2009).

MMWR (1995). Epidemiologic Notes and Reports Jimson Weed Poisoning -- Texas, New York, and California, 1994 . January 27, 1995, Vol 44(3), p 41-44. Online: <http://www.cdc.gov/mmwr/preview/mmwrhtml/00035694.htm> (accessed: 16 June 2009).