Herbicides or poisons?

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Toxicology of plants

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Introduction

A peasant farmer in Russia wrote early this century of collecting mushrooms in the forests near his home *"Although it cannot be compared to the more lively forms of hunting, there is an element of the unknown, of the accidental, there is success or failure and all these things arouse the hunting instincts in Man."*

The excitement of the chase and the find can, especially within the mushroom and toadstool group, produce some fairly alarming results to those inexperienced in identifying the safe versus the dangerous toadstools.

Amanita muscaria, the fly agaric, the common toadstool seen near *Pinus radiata* throughout Victoria and elsewhere is, however, rarely fatal in humans. Its scarlet and white spotted cap surely indicates a warning that it contains several poisonous alkaloids, a group of heterocyclic compounds or aromatic ring structures containing nitrogen. *A. muscaria* contains muscarine, bufotenine (Figure 1), ibotenic acid and muscimole.

In humans, from 0.5 to 3 h after eating *A. muscaria* the patient experiences hallucinations, weeping, mental confusion, salivation, perspiration, gastro-intestinal discomfort, and loss of consciousness. There follows a 3–6 h sleep where the patient wakes up with no recollection of the experience. The death cap *A. phalloides*—a toadstool with a greenish-grey cap and white gills—contains complex sulphur containing cyclopeptides of high molecular weight made up of complex and chemically unusual amino acids. Death cap produces irreversible liver damage where the phallotoxins dismantle the endoplasmic reticulum and the other group of compounds, the amatoxins damage the nucleus of the liver cells. Somewhere between 10–15 h after eating *Amanita phalloides* the patient suffers severe abdominal pain, vomiting, diarrhoea with blood, excessive thirst, urine retention, spasms and extreme pain, screaming and vomiting, prostration, jaundice, cyanosis and after 2–3 days lapses into coma with final convulsions and death.

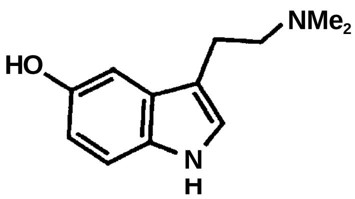


Figure 1. The alkaloid bufotenine.

Some are kinder – *Psilocybe* contains psilocybin, an indol containing relative of LSD producing initially drowsiness, dizziness, then uncontrollable hilarity, difficulty in standing and incoherent speech. Possession of this toadstool is illegal in all states whereas possession of *Amanita* is not!

These more dramatic examples bring up spectres of witchcraft and unexplained death, but illustrate what complex chemists some plants are.

An ancient Egyptian papyrus written some 3500 years ago lists 800 or so cures for common ailments, mostly from plants, some with magical properties; the toxicology of plants is therefore an ancient branch of science.

In the 1st century A.D. the Greek physician Dioscorides produced the Materia Medica; the branch of medicine that corresponds to pharmacology today describing more than 600 plants used in medicine. Galen a century later produced a medical herbal that remained in use for hundreds of years. Monasteries continued the tradition with monks tending cottage gardens. The current interest in traditional and herbal remedies is the same as our current interest in alternative medicine and aromatherapy etc. It has been estimated that 75% of the population of the world today receives health care solely through traditional (herbal) medicine.

It is virtually impossible to tell what toxic principles are in a plant without complex analyses. Cattle and sheep however seem to learn using a more sensitive sense of taste and smell than ours. Native people learn, presumably by drastic trial and error, what plants are toxic and those that are not. When Cook arrived in 1770 his men fed cycad seeds to the pigs they brought with them. They had seen them by aboriginal fires and assumed them to be edible. What the Europeans did not realise was that the Aborigines treated the cycad seeds with heat and complex washing procedures to remove several toxic azoglycosides.

Toxic compounds may be in the vacuoles of cells and distributed differentially throughout the plant. That is to say, the entire plant may contain a toxic principal or only, for example, the leaves may be toxic. Many aromatic compounds are found in glands, either as individual single celled (uni-seriate) hairs or gland cells or in multi-celled (multi-seriate) gland cells. Oils are usually produced as extra cellular compounds where oils accumulate between cells, or in oil ducts as in many seeds (e.g. coriander, cumin) or in oil glands as a result of the death of cells, for example in eucalypts. The amount of any compound accumulated depends on:

i. the species,
ii. the stage of growth,
iii. the season,
iv. the weather and
v. the soil.

Some common poisonous compounds (e.g. cyanides and oxalates) are found in young growing shoots in higher concentrations than in older parts, whereas plants that accumulate nitrate have most in the older basal parts of the plants.

Some plants (e.g. oleander) are toxic at any stage of growth and all parts are toxic. Some dangerous principles are concentrated in leaves, stems, roots, flowers or seeds. Rhubarb has leaves that contain toxic levels of soluble oxalates, whereas the petioles have considerably lower levels.

Seasonal conditions also alter toxicity of plants, particularly toxic weeds or plants of agricultural significance. Drought-stricken animals for example often end up eating lethal amounts of toxic, deep-rooted poisonous shrubs.

Toxins

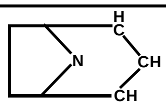
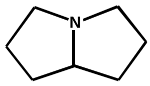
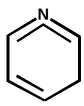
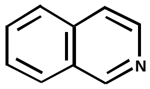
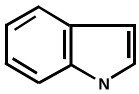
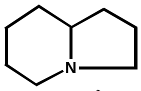
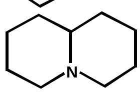
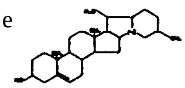
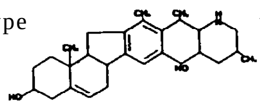
Toxins (following Everist 1974) can be groups as:

i. Metallic toxins
Lead arsenic
Cadmium
Copper
Molybdenum
Selenium

ii. Non-metallic 'mineral' toxins
Fluorine compound
Inorganic nitrogen compounds

iii. Organic compounds
Cyanogenic glycosides
Glucosinolates

Table 1. Basic configurations of major plant alkaloids (from Everist 1974).

Basic configuation		Examples of alkaloids	Examples of plants
Tropane		hyoscine (scopolamine) hyoscyamine	*Datura* spp. *Duboisia myoporoides* *Duboisia leichhardtii*
Pyrrolizidine		senecionine jacobine	*Senecio* spp.
		monocrotaline spectabiline	*Crotalaria* spp.
		heliotrine lasiocarpine	*Heliotropium* spp.
Pyridine		coniine	*Conium* spp.
		nicotine nor-nicotine anabasine	*Nicotiana* spp. *Duboisia hopwoodii*
Isoquiniline		sanguinarine protopine	*Argemone* spp.
		morphine	*Papaver* spp.
Indole		alstonine	*Alstonia* spp.
		dimethylated tryptamines	*Phalaris* spp.
		psilocybin	*Psilocybe* spp.
Indolizidine		swainsonine	*Swainsona* spp.
		slaframine	*Rhizoctonia* spp.
Quinolizidine		lupinine	*Lupinus* spp.
		sparteine	*Cytisus* spp.
Steroid alkaloids			
i. Solanum type		tomatidine	*Lycopersicon* spp.
		solanidine solasodine	*Solanum* spp.
ii. Veratrum type		veratramine	*Veratrum* spp.

- Aliphatic nitro compounds
- Alkaloids
- Polypeptides and amines
- Amino-acids
- Toxalbumins

iv. Non-nitrogenous compounds

- Oxalates
- Organic acids
- Coumarins
- Steroids
- Terpenes
- Phenols
- Alcohols
- Quinones
- Resins and resinoids

Many plant toxins however are complex in their effect and chemical composition. An example is Saponin— a compound that forms a froth when shaken up in water. Ivy and lucerne contain saponins. Chemically a saponin is a glycoside because it is made up of a sugar (solanose) which is bound to an aglycone. During digestion the sugar is split off and the remnants of the molecule (aglycone) is solanidine. Because solanidine contains nitrogen and is basic rather than acidic in its reaction with other compounds, solanidine can be defined as an alkaloid. However part of an alkaloid molecule contains a sterol group so it can also be defined as a sterol. Therefore as Everist (1974) says, solanine can be regarded chemically as a steroidal, alkaloidal glycoside with the properties of a saponin.

Metals

There is often an accumulation of cadmium in crop plants. Cadmium is an 'impurity' within superphosphate used as an agricultural / horticultural fertilizer. Similarly lead can arrive in crops by the proximity of traffic via lead from the tetra ethyl lead of petrol expelled in exhaust fumes.

Copper gets into the food web often via legumes, particularly sub-clover producing a copper complex methhaemoglobin resulting in jaundice in cattle. The necrosis of the liver produces coffee coloured urine and severe damage in cattle. Copper is a rare contaminant in the human food chain but has significant importance to herbivores on which we depend for meat.

Selenium replaces sulphur in some plants especially in the sulphur containing amino acids leading to loss of hair in humans and the shedding of hoofs in sheep and cattle.

Fluorine ends up in organo fluoridated compounds, particularly fluoroacetates. Fluoroacetates are produced in 39 species of Australian plants—usually legumes—*Acacia, Gastrolobium* and *Oxylobium* being common examples.

In these plants the fluoroacetates following digestion are converted to fluorocitrates, which inhibit the enzyme aconitase in the Krebs Cycle and as a result citric acid accumulates in the cells. Toxic levels for fluoroacetates are low (4–7 mg kg^{-1}) for man. Sheep and cattle having ingested fluoroacetates go into respiration distress, and become highly excitable.

Inorganic nitrates are used in the food industry to prevent the darkening of red meat, especially in sausages; potassium nitrate being commonly used in older recipes. Nitrates are accumulated in maize, lucerne and kikuyu grass, mainly in the lower parts of the stems. In ruminants these are converted to nitrites, these in turn converting divalent Fe^{++} to Fe^{+++} in the blood leading effectively to asphyxiation in the animal. Lethal doses, as far as cattle are concerned (1.5% NO_2 DW) are commonly found in capeweed, *Atriplex* spp., *Avena sativa, Beta vulgaris, Brassica rapa, Carduus chenopodium* and *Medicago sativa.*

Gaseous oxides of nitrogen in NO_2 and N_2O_4 express themselves as 'silo fillers disease' and are produced during the fermentation of silage. Nitrogenous organic compounds mainly cyanogenic glycosides are complexes of a CN radicle incorporated into an α-hydroxy nitrile compound complexed to a sugar. Different sugars are present in the different glycoxides of different plants. The glycosides themselves are not toxic but they yield HCN when the cells are damaged or the cells broken down by microbial attack in the gut. Usually the amount produced (e.g. in almonds and apricot kernels) is small and the HCN is rapidly converted to thiocyanate in the liver. If the amount is greater than the detoxification process, the cyanide poisoning develops due to the inhibition of cytochrome oxidase. This results in accelerated and deepened breathing, irregular pulse and a staggering gait. Levels sufficient to produce this can be produced with root tubers of Cassava.

Alkaloids

One of the most complex group of plant toxins are the alkaloids. These contain nitrogen in heterocyclic or aromatic ring structure. Most are bitter to taste and almost all of the important drugs of medicine fall into this category. The best known are the tropane alkaloids. They are all particularly toxic to horses, pigs, dogs, cats, rabbits, sheep, cattle, man, chickens and ostriches. The effect on the dose and the

Table 2. Maximum legal levels of heavy metals in food for sale in Australia.

Metal	Level (mg kg^{-1})
Antimony	1.5
Arsenic	1.0
Cadmium	0.05
Copper	10.0
Lead	2.0
Methyl mercury	0.03
Selenium	1.0
Zinc	150.0

symptoms depend on which part of the plant is eaten. They are found in a wide range of plants. Virtually the whole of the family Solanaceae; *Amsinkia, Echium, Heliotropum, Senecio,* and *Papaver* contain alkaloids. Examples of alkaloids are nicotine, quinine, scopolamine, hyocyamine, morphine, psilocybin, solanidine (Collins *et al.* 1990).

The symptoms of poisoning include thirst, dilation of the pupils, flushing of the skin, delirium; the tendency to pick at imaginary things in the air, weak rapid pulse, convulsions, coma and death. Related compounds, the indole alkaloids (*Phalaris* staggers in sheep and cattle), *Clavieps* (ergot), *Psilocybe* (magic mushroom), *Phalaris aquatica* and steroid alkaloids from the Solanaceae—solasodine—a precursor to the steriodal compounds for oral contraceptive, all fall into this group. Solanaceae also produces solanine, the toxin of green potatoes which produce headaches, and coma if eaten in quantity. The reputation of nicotine from *Nicotiana* sp. does not need any qualification, other than in low concentrations it produces a feeling of well being.

Of all the narcotic substances used by the Australian natives, members of the Solanaceae, in particular *Dubosia hopwoodii, Nicotiana excelsa* and *N. gossii*, were the most used (Cribb and Cribb 1981). These were used as a powder or a plug of

Table 3. Common toxic garden plants.

Common name/s	Botanical name	Toxic part/s	Toxicity
Aconite or monkshood	*Aconitum napellus*	(all parts)	***
Agapanthus or African blue lily	*Agapanthus orientalis*	(sap)	*
Almond	*Prunus dulcis*	(kernel – bitter type)	***
Angel's trumpet	*Datura arborea*	(nectar, seeds)	***
Apple	*Malus* spp.	(leaves, seeds in large amounts)	***
Apricot	*Prunus armeniaca*	(kernels in large amounts)	***
Belladonna lily	*Amaryllis belladonna*	(bulb)	**
Black nightshade or blackberry nightshade	*Solanum nigrum*	(green fruit)	***
Bluebell	*Scilla nonscripta*	(bulb)	**
Buttercups	*Ranunculus* spp.	(all parts)	*
Calla lily or white arum lily	*Zanthedeschia aethiopica*	(all parts, esp. spike)	***
Cape lilac or white cedar	*Melia azedarach*	(fruit, leaf, bark and flowers)	***
Castor oil plant	*Ricinus communis*	(seeds: 2–8)	***
Cherry	*Prunus cerasus*	(kernels)	**
Common privet	*Ligustrum vulgare*	(leaves, fruit, berries)	**
Cotoneaster	*Cotoneaster* spp.	(fruit, flowers)	**
Daffodil	*Narcissus pseudonarcissus*	(sap and bulb)	**’*
Daphne	*Daphne* spp.	(berries)	***’*
English ivy	*Hedera helix*	(all parts, esp. berries)	**’*
Flag iris, flag lily or fleur de lis	*Iris germanica*	(all parts)	**
Foxglove	*Digitalis purpurea*	(all parts)	**
Frangipani	*Plumeria* spp.	(sap)	**’*
Fruit salad or Swiss cheese plant	*Monstera deliciosa*	(ripe fruit)	*
Hyacinth	*Hyacinthus orientalis*	(all parts, esp. bulb)	**
Hydrangea	*Hydrangea* spp.	(flowers)	**
Japanese pepper tree	*Schinus terebinthifolius*	(fruit, large amounts)	**’*
Jonquil	*Narcissus jonquilla*	(sap and bulb)	**’*
Kangaroo apple	*Solanum laciniatum & Solanum vescum*	(green fruit)	**
Lantana	*Lantana camara*	(green fruit)	***
Lily of the valley	*Convallaria majalis*	(all parts)	***
Loquat	*Eriobotrya japonica*	(seeds, [many])	**
Oleander – see also yellow oleander	*Nerium oleander*	(all parts)	***’*
Pear	*Pyrus communis*	(seeds)	**
Potatoes	*Solanum tuberosum*	(green skin)	***
Quince	*Cydonia oblonga*	(seeds, fresh leaves)	**
Rhubarb	*Rheum rhaponticum*	(leaf blade)	***
Scarlet rhus, kuntze or Japanese wax tree	*Toxicodendron succedaneum*	(all parts and smoke)	**’*
Wisteria	*Wisteria floribunda, W. sinensis*	(seeds and pods)	**
Yellow oleander	*Thevetia peruviana*	(all parts, esp. seed in kernel)	***

*** Deaths reported.
** Toxic but no deaths and / or poisonings reported.
* Can cause dermatitis or irritate skin on contact.

Compiled from:
Plants poisonous to people. Division of Health Education and Information, Queensland Health Department.
Poisonous garden and other plants harmful to man in Australia. Western Australian Department of Agriculture.
Poison plants in the garden. Western Australian Department of Agriculture.
Poisonous plants in the home garden. Tasmanian Department of Agriculture.
Poisonous plants of the Northern Territory. Department of Primary Production, Northern Territory.

leaves that were chewed, producing the analgesic effects of nicotine and scopolamine, the latter a component of anti sea sickness tablets. In the plants the alkaloids are bound to organic acids and are released by chewing with wood ash to produce alkaline conditions for the chemical release of the alkaloids.

Ricin from *Ricinus communis* (castor bean) probably is one of the most toxic alkaloid producers. Ricin being lethal at about 10^{-9} body weight.

The cardiac glycosides (e.g. digitalis) act directly on heart muscle and foxgloves have been well known as a heart stimulant for hundreds of years. *Toxicadendron* (rhus) as its generic name suggests contains a wide variety of compounds in stems and leaves which produce severe dermatitis after sensitization to the plant. All parts of the rhus tree are toxic.

Nereium oleander, a native to the Mediterranean region, is notorious as a poisonous, yet very common, garden plant and despite its extreme toxicity (1 leaf, 2 flowers fatal) few poisonings occur. The alkaloids oleandrin and nerium affect the autonomic and central nervous system, the myocardium and gastro-intestinal tract.

Comfry (*Symphytum*), an old world cottage garden plant, has come in for some recent publicity – the leaves being dipped in batter and fried. As much as a healthy tonic of times gone by, the leaves contain the alkaloids eclinatine, heliosupine, and acetylchinatine. 0.7 g ingested over several months has produced chronic liver damage in man.

Cannabis sativa, not quite a garden plant, with some notoriety yet legal protection, contains tetrahydrocanabinol resulting in tremor, vertigo and difficulty with muscular co-ordination. It was removed from the British Pharmacopoea in the 1930s where a tincture of cannabis was an excellent analgesic providing a sense of well being to those in the last stages of a terminal illness.

The family Cruciferae contains many agricultural weeds but also the mustards, cabbages, cauliflowers and broccoli of horticulture.

Large quantities of glucoinolates accumulate in the seeds of *Brassica* sp. Although these compounds are not toxic in themselves they yield isothiocyanates, a group of sulphur and nitrogen containing compounds which are the irritant mustard oils. Despite the presence of a wide range of toxic chemicals in the brassicas they are extensively eaten by man and are used as condiments.

Where would most of us be without a cup of tea or coffee? *Thea sinensis* (*Camelia sinensis*), depending on the treatments following the picking of the leaves, produces green or black tea. Caffeine, an alkaloid, is the central nervous system stimulant, the "pause that refreshes". Caffeine is also produced in the seeds of *Caffea arabica* (coffee) with up to 3% DW being caffeine; the flavour and taste being due to an oil caffeol. However more people are probably 'addicted' to chocolate, the roasted seeds of the cocoa tree (*Theobroma cacao*).

For the sake of completeness, (and it has been impossible to summarize the 3000 or so papers published since 1940 on the toxic chemicals in plants) we should mention the ferns and the algae. *Pteridium aquilinum* var. *esculentum* (bracken) contains 4–5 toxins: thiaminase, shikimic acid, 'bone marrow toxin', the cyanogenic glycoside, pruinase and 'night blindness factor'. These produce a range of sometimes fatal symptoms in sheep, cattle, horses and pigs. Blood in the urine, multiple haemorrhages and tumours in the bladder, all the result of the cacinogenic and mutagenic nature of these compounds in combination with each other. Imported cooked and canned young bracken fronds available in gourmet shops have and can induce carcinomas in rats, mice, quail and guinea pigs.

Some years ago the moulds, especially *Aspargillus flavus*, achieved some measure of publicity. *Aspergillus* grows on stored grains, especially those stored at high temperature and high humidity. The fungus produces oxygenated heterocyclic compounds known as aflatoxins—compounds with an LD_{50} of 1 mg kg^{-1}. Lethal effects include loss of appetite, loss of weight and loss of co-ordination. The major publicity years ago was that significant levels of aflatoxins were found in peanuts and therefore, potentially in peanut butter.

Many of the so called 'health foods' contain potential toxins. Marine algae, for example, accumulate a range of metals (e.g. antimony, arsenic, cadmium, copper, lead, mercury, selenium and zinc).

Several years ago at least one death in the United Kingdom was attributed to poisoning from an overdose of kelp tablets that contained considerable amounts of (naturally accumulated) arsenic.

The National Health and Medical Research Council (1987) adapted the maximum legal levels of heavy metals in food for sale in Australia (Table 2).

A recent survey by Werner (1992) showed that 32 marine algae (seaweeds) from 25 genera, most of which are used for human consumption would not comply with Australian food standards. Some contain ketones related to tear gas.

The Blue green alga *Anacystis cyanea* (Cyanophyta) appearing in the Murray Darling system of recent years produced four toxic compounds—cyclic polypeptides of seven amino acids—causing stock losses in highly contaminated water.

Common toxic garden plants are listed in Table 3.

Plant toxicology is a complex discipline. This paper serves as an introduction to the field of phytochemicals and contains information largely gleaned from the references listed below.

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