UNGROUPED TOXINS

Methylazoxymethanol (MAM)

Core data

Common sources: cycads in the genera

- *Cycas*
- *Macrozamia*

Animals affected: ruminants, dogs (humans)
Mode of action: MAM metabolised by hepatic drug-metabolising enzymes to a highly reactive methylating agent
Poisoning circumstances: ingestion of seeds (leaves to lesser extent)
Main effects:

- acute hepatic periacinar necrosis
- vascular damage (cirrhosis, fibrosis of central veins, veno-occlusion)
- necrotic gastroenteritis

Diagnosis: pathology + plant access
Therapy: nil
Prevention: deny access

Chemical structure:

MAM is the aglycone of the glycosides cycasin and macrozamin.

Sources:

Cycads:

***Cycas* spp.** [DM43](Australasia/Pacific Island/Indian origin; cultivated). See section on "zamia staggers" for full listing of plants. Those known to produce liver damage include:

Cycas media R.Br. [= *C. kennedyana* F.Muell. , *C. normanbyana* F.Muell.] (zamia, zamia palm, tree zamia)

Cycas megacarpa K.D.Hill (Qld)

Cycas ophiolitica K.D.Hill (Qld)

Note on toxicity of *C. media*: The plants associated with field cases in cattle in Queensland and used for feeding experiments there have all been referred in the literature to *C. media*, but reclassification of the plants in this taxon by Hill (1996) means that plants in the newly-recognised species *C. megacarpa* and *C. ophiolitica* as well as *C. media* in the currently-accepted sense and hybrids between these taxa have probably all been involved.

Feeding experiments in cattle with seeds of *C. media* (*sensu lato* [= in the broad sense]) resulting in putative liver damage:

- 2.3 kg whole seeds fed to an 18 month-old heifer over 3 days induced blood-stained faeces in 3 days, followed by anorexia, weight loss and death in 38 days (Mulhearn 1938)
- 5.5 kg mature seeds dosed to a steer through a rumen fistula over 9 days (0.18% body weight/day) induced fatty change in hepatocytes seen in a liver biopsy on day 10, followed by death from haemorrhage from the biopsy site on day 12 (Hall 1956)
- a single dose of 0.6 kg immature seeds (0.16% body weight) fed to a steer induced anorexia, progressive weight loss and death on day 23 (Hall 1961)

**Cycas revoluta* Thunb. (Japanese origin) – dogs eating seeds of cultivated plants have been poisoned in South Africa (Botha *et al.* 1991), North America (Florida) (Albretsen *et al.* 1998) and Australia (D Schull & RA McKenzie, unpublished data 2001)

***Macrozamia* spp**. [DM43] (Australian origin; cultivated) (sheep – Seddon *et al.* 1931 (*M. heteromera*), Gabbedy *et al.* 1975 (*M. riedlei*); dog – Mills *et al.* (1996) (*M. riedlei*))

Bowenia spp. [DM42] (Australian origin; cultivated)

Lepidozamia spp.[DM43] (Australian origin; cultivated)

**Zamia* spp. (North American origin; cultivated) – dog - Senior *et al.* (1993) (*Z. integrifolia*)

Toxicity:

Domestic ruminants, dogs (see above)

See the section on "zamia staggers" for details of the MAM glycoside content of seeds of various species of cycads.

Human toxicity

Humans are susceptible to toxicity from ingestion of cycad seeds. Australian aboriginal people used *Cycas* spp. and *Macrozamia* spp. seeds as a carbohydrate source, but only after prolonged preparation including leaching of mashed seeds in water and baking.

Early European explorers suffered from intoxications including

- Dutch members of de Vlamingh's 1697 expedition at the Swan River (present-day Perth) in Western Australia were violently ill after eating seeds of *Macrozamia riedlei* (Gardner & Bennetts 1956, Low 1987, Jones 1993)
- members of James Cook's 1770 expedition at the Endeavour River in northern Queensland ate *Cycas media* seeds and developed violent diarrhoea (Hall 1987, Jones 1993)
- French sailors of the La Perouse expedition ate seeds of *Macrozamia communis* at Botany Bay in 1788 and became violently ill (Gardner & Bennetts 1956, Jones 1993)
- members of Matthew Flinders' expedition ate seeds of *Macrozamia dyeri* in 1801 at Lucky Bay near present-day Esperance in Western Australia and developed violent vomiting (Gardner & Bennetts 1956, Jones 1993)
- members of Sir George Grey's expedition ate seeds of *Macrozamia riedlei* in Western Australia in 1839 and were violently ill (Gardner & Bennetts 1956, Jones 1993)
- members of John McDouall Stuart's expedition in central Australia in 1860 ate seeds of *Macrozamia macdonelli* and were violently ill (Jones 1993)

Mode of action:

MAM absorbed, metabolised by hepatic drug-metabolising enzymes (microsomal cytochrome P450 mixed function oxygenases) → highly reactive methylating agent → acute hepatic periacinar necrosis, vascular damage (cirrhosis, fibrosis of central veins, veno-occlusion), necrotic gastroenteritis

Conditions of poisoning:

Ingestion of cycad **seeds**

dogs with access to cycad seeds (Botha *et al.* 1991, Senior *et al.* 1993, Mills *et al.* 1996, Albretson *et al* 1998)

sheep accustomed to being fed pelleted feed, then given access to cycad plants carrying seed (Seddon *et al.* 1931)

Some liver damage occurs from ingestion of cycad **leaves** in some cattle affected by the spinal cord damage syndrome (*q.v.*)

Clinical signs: See acute hepatic necrosis chapter

Pathology: See acute hepatic necrosis chapter

Diagnosis: See acute hepatic necrosis chapter

Therapy: See acute hepatic necrosis chapter

Prevention & control: See zamia staggers section

References:

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Seddon HR, Belschner HG, King ROC (1931) Poisoning of sheep by the seeds of burrawang (*Macrozamia spiralis*). *Vet. Res. Rpt. New South Wales Dept. Agric.* No.6, pp.70-80. [These plants are now regarded as *M. heteromera*.]

Senior DF, Sundlof SF, Buergelt CD, Hines SA, O'Neil-Foil CS, Meyer DJ (1993) Cycad intoxication in the dog. *J. Am. Anim. Hosp. Assoc.* **21**:103-109. [2 dogs, Florida, *Zamia floridana* = *Z. integrifolia* seeds]

☑ Stypandrol

Core data

Common sources: Stypandra glauca
Animals affected: sheep, goats, cattle, horses
Mode of action: intralamellar myelin oedema
Poisoning circumstances: grazing young shoots or flowering plant
Main effects: optic nerve & retinal atrophy
Diagnosis: access + histopathology
Therapy: nil
Prevention: deny access

Chemical structure:

Stypandrol is a bisnaphthalene tetrol. There is variation in stypandrol content in various populations of *S. glauca.*

Plant sources: Family Liliaceae

Stypandra glauca R.BR. (blind grass, Candyup poison, nodding blue lily) [includes *S. imbricata* R.Br. & *S. grandiflora* Lindley]. Australian native plant growing in the southern half of the continent (temperate areas of WA, NSW, Vic, Qld) (Henderson 1987).

Hemerocallis spp. (day lilies). Widely-grown perennial garden plants of Asian origin. Rhizomes have been used as herbal medicines and cases of toxicity are recorded in humans. Stypandrol was apparently first isolated from *H. thumbergii* by Wang *et al.* (1989), but assigned the incorrect structure on the basis of ambiguous degradation studies (Colegate & Molyneux 1993).

Dianella revoluta R.Br. (blue flax lily, blueberry lily, black-anther flax-lily, spreading flax-lily). Australian native plant. Only trace amounts of toxin are present, so this plant is not a poisoning hazard.

Toxicity:

sheep, goats, cattle, horses, poultry

Poisoning cases have been almost exclusively recorded from south-western WA, with 1 case reported in goats from central western NSW.

Mode of action: essential lesion = intralamellar myelin oedema

Conditions of poisoning (*S. glauca*):

grazing young green shoots after winter rain (WA)
grazing flowering plants (NSW)

Clinical signs:

acute death
blindness
incoordination
death in 5 days

survival with **permanent blindness**
high-stepping gait
head carried close to ground
traumatic injuries to eye and head
pupils dilated
pupillary light reflexes absent
focal hypertrophy of retinal pigment epithelium
multifocal ↑ tapetal reflectivity (retinal atrophy)

Pathology:

vacuolation (oedema) of CNS white matter → resolves in 6-8 weeks
optic nerve axonal degeneration → complete **atrophy**, sclerosis

12 weeks → **retinal atrophy**
Diagnosis: access + histopathology (eye, optic nerve, brain)
Therapy: nil
Prevention & control: deny access
References:

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Wang JH, Humphreys DJ, Stodulski JBJ, Middleton DJ, Barlow RM, Lee JB (1989) Structure and distribution of a neurotoxic principle, hemerocallin. *Phytochem.* **28**:1825.

☑ Galegine

Core data

Common sources:

- *Galega officinalis*
- *Verbesina encelioides*
- *Schoenus asperocarpus*
- *Schoenus rigens*

Animals affected: ruminants, pigs
Mode of action: ↑ pulmonary vascular permeability → fibrin-rich effusion
Poisoning circumstances: hungry stock + dense plant population
Main effects: hydrothorax, pulmonary oedema
Diagnosis: access + pathology
Therapy: nil
Prevention: deny access

Chemical structure:

Galegine is an isoprenoid guanidine derivative - (3-methyl-2-butenyl) guanidine – related to urea

Sources:

- *Galega officinalis* (goat's rue, French lilac, honeysuckle) [Fabaceae] - Europe, North America, NZ (Tanret 1914, Keeler *et al.* 1986)
- ***Verbesina encelioides*** (crownbeard) [Asteraceae] - NT, SA, Q, NSW, V [DM70] (Anderson 1936, King 1937a,b, Eichholzer *et al.* 1982, Oelrichs *et al.* 1985)
- ***Schoenus asperocarpus*** (poison sedge) [Cyperaceae] – WA (Royce 1952, Nairn *et al.* 1971, Huxtable *et al.* 1993, Colegate *et al.* 1994)
- *Schoenus rigens* [Cyperaceae] - WA (Colegate *et al.* 1994)

Toxicity:

- sheep, goats, cattle, pigs
- toxicity of *Verbesina encelioides* from Argentina confirmed in sheep; oral toxic dose 5 g dried plant/kg [plant dry matter 17.9%] (Lopez *et al.* 1996)

Mode of action:

- ↑ pulmonary vascular permeability → fibrin-rich effusion

Conditions of poisoning: hungry stock with access to dense plant populations
Clinical signs: dyspnoea, rapid death
Pathology:

- fluid from nostrils
- **severe pulmonary oedema** & **hydrothorax**
- thoracic fluid clots rapidly on exposure to air

Diagnosis: access + pathology
Therapy: nil

Prevention & control: deny access

References: Se143

Anderson RH (1936) Crown beard (*Verbesina encelioides*). *Agric. Gaz. N.S.W.* **47**:496. [cited by Hurst 1942]

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☑ *Tetrahydrocannabinol* - Cannabis sativa *(marijuana)*

Core data

Common sources:

- human illicit drug in most jurisdictions
- cultivated plant

Animals affected:

- dogs, cats
- cattle

Mode of action: may relate to changes in biogenic amine concentrations in CNS

Poisoning circumstances:

- pets eat or fed *C. sativa* products or breathe smoke from *C. sativa* cigarettes
- livestock browse cultivated plants

Main effects: depression (somnolence), ataxia, incoordination, sudden falling

Diagnosis:

- access history (often unavailable)
- detect plant in vomitus/rumen
- some labs assay for tetrahydrocannabinol (THC)

Therapy:

- detoxification (emesis, activated charcoal, cathartics)
- control excitement if required (diazepam, xylazine)

Syndrome name: 'stoned'

Chemical structure:

Tetrahydrocannabinol (THC)

THC content of *C. sativa* varies from 1 to 6%, is highest in leaves & flowering tops and highest in warm climates. Fibre-producing cultivars of *C. sativa* have little THC content

Sources:

Cannabis sativa L. (hemp). Classified in Family Cannabaceae [which contains one other genus with one species in Australia - *Humulus lupulus* (hops)]

Illicit drug in most jurisdictions; cultivated plant, sparingly naturalised in all Australian states, native to central Asia (Pearce 1989). Note that low-THC cultivars of this species are projected for cultivation within Australia as a source of plant fibre.

Alternative names include:

marijuana, Indian hemp, pot, grass, sinsemilla = dried leaves & flowers of *C. sativa*

hashish, hash, bhang = resin extracted from *C. sativa*

Toxicity:
- death from marijuana exposure is not expected (dog oral lethal dose > 3g/kg)
- mode of action may relate to changes in biogenic amine concentrations in CNS
- THC is toxic to lepidopteran larvae (Harborne & Baxter 1996, p.355)

Conditions of poisoning:
- dogs (cats less likely) may spontaneously ingest (or be deliberately fed) marijuana cigarettes, butts or baked products
- smoke blown into the nostrils of pets or passively inhaled (Schwartz & Riddile 1985)
- livestock may gain access to cultivated plants (Cardassis 1951, Driemeier 1997)

Clinical signs:

Dogs, cats
- signs may persist 36-48 hr
- most common: **depression (somnolence), ataxia, incoordination, sudden falling** (rapid arousal to normal from somnolence is common)
- ± marked CNS signs - alternating depression & excitement
- ± hallucinations (dogs: barking & agitation for no apparent reason, snapping at thin air - "fly-catching"; cats: "strange facial expressions")
- ± biting or aggressive behaviour
- ± tremor
- ± dilated pupils
- ± vomiting, dry mucosae
- ± hyperthermia or hypothermia, tachypnoea

Cattle, Horses (Cardassis 1951, Driemeier 1997)
- moderate neurological signs (muscle tremor, mydriasis, incoordination)
- ± gastroenteritis with diarrhoea
- ± abundant salivation
- ± dyspnoea, froth from the mouth (pulmonary oedema)

Pathology: Nil

Diagnosis:
- history often incomplete or misleading
- ± identify plant in gastric contents
- ± assay plasma, urine for THC (only certain laboratories)

Therapy (dogs, cats):
- detoxification - emesis [Note: THC has antiemetic properties], activated charcoal, cathartics
- keep patient in warm, dark, quiet and secure environment
- control excessive excitement or agitation with diazepam or xylazine; CNS drugs should not be given unless required to save life

References:

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Schwartz RH, Riddile M (1985) Marijuana intoxication in pets (letter). *J. Am. Vet. Med. Assoc.* **187**:206.

Dendrocnide *spp. (stinging trees)*

Chemical structure:
- haemolytic saponins (Oelrichs & Robertson 1970) and a bicyclic octapeptide (moroidin) (Leung *et al.* 1986; Kahn *et al.* 1989) have been isolated

Sources:
- 5 species in Australia, 27 in Eastern Malesia, Australia and South Pacific (Chew 1989)
- Australian species (previously included in *Laportea*) all growing in and on edges of rainforest and growing in abundance in clearings
- *Dendrocnide corallodesme* (mango-leaved stinger) – Cape York Peninsula (Iron & McIlwraith Ranges)
- *Dendrocnide moroides* (gympie, gimpi-gimpi, mulberry-leaved stinger, stinger) – eastern Q, NSW
- *Dendrocnide cordata* (stinger) – Cape York Peninsula

Dendrocnide photinophylla (shining-leaved stinger, shiny leaf stinging tree) – Cape York to Nepean region, NSW

Dendrocnide excelsa (giant stinger, giant stinging tree) – Bunya Mountains (Q) to Kiama (NSW)

Toxicity:

intensity of effect: *D. moroides, D. cordata* > other species

contact with plants → intense pain from irritant toxin/s injected through the skin by hollow plant hairs

human timber workers and bush walkers affected

horses are particularly vulnerable and may be driven into a frenzy of agony, leading to self-destruction or necessitating euthanasia (Everist 1981)

pain may persist for several weeks

dried plant retains toxicity (herbarium specimens >40 years)

no satisfactory method of relief

Clinical effects (humans) (Robertson & McFarlane 1957):

intense pain at the site of contact

local sweating, piloerection and erythema

References:

Se49

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