Vickery PJ, Wheeler JL, Mulcahy C (1987) Factors affecting the hydrogen cyanide potential of white clover (*Trifolium repens* L.). *Aust. J. Agric. Res.* **38**:1053-1059.
Webber JJ, Roycroft CR, Callinan JD (1985) Cyanide poisoning of goats from sugar gums (*Eucalyptus cladocalyx*). *Aust. Vet. J.* **62**:28.
Winks WR (1940) *Qd. Agric. J.* **54**:364-366.

Cardiac glycosides

Core data

Common sources:

- Important Plants
  - *Nerium oleander* (oleander)
  - *Cascabela thevetia* [=*Thevetia peruviana*] (yellow oleander)
  - *Cryptostegia grandiflora* (rubber vine)
  - *Bryophyllum* spp. (mother-of-millions)
  - *Homeria* spp. (cape tulips)
  - *Adonis microcarpa* (pheasant's eye)
  - *Digitalis purpurea* (foxglove)
  - *Corchorus olitorius* (jute)
- Pharmaceuticals
  - Digoxin

Animals affected: cattle, horses

Poisoning circumstances:

- garden clippings (oleanders, foxglove)
- in hay or seeds in feed grain (cape tulips, pheasant's eye, jute)
- hunger or lack of other feed (mother-of-millions)
- overdose of digoxin

Main effects:

- sudden death
- cardiac arrhythmia
- diarrhoea with blood
- azotaemia
- focal myocardial necrosis

Diagnosis:

- access
- cardiac arrhythmia
- myocardial histopathology

Therapy:

- activated charcoal + electrolyte replacement fluid PO
- + atropine
- + propranolol

Syndrome names:

Two syndromes are associated with intoxication by cardiac glycosides:

- **acute cardiac glycoside poisoning** – discussed in this section
- cotyledonosis or krimpsiekte [Afrikaans = "twisted disease"] due to certain bufadienolides in particular plants and confined to southern Africa – discussed in the following separate section

Chemical structure:

A cardiac glycoside is any plant-derived steroid glycoside with cardiotonic activity. This activity depends on the presence in the aglycone of an unsaturated lactone ring and a hydroxyl group in a specific spatial relationship. Some 400 such compounds have been identified. [adapted from Lewis' Dictionary of Toxicology 1998]. There are some structural affinities with cucurbitacins (*q.v.*) and some similarities of pathological effect.

Cardiac glycosides consist of a steroidal aglycone linked to a sugar or sugars. There are two groups of cardiac glycosides, **cardenolides** with 23-carbon aglycones (5 member lactone ring) and **bufadienolides** with 24-carbon aglycones (6 member lactone ring).

Sources:

Human & veterinary medicaments (cardiac inotropic agents) based on cardenolides derived from *Digitalis* spp. plants, e.g. digoxin (Lanoxin®), or from *Strophanthus* spp. plants, e.g. proscillaridin (Talusin®)

Cardioactive steroids of *Bufo* spp. toads (*q.v.*) have close affinities with cardiac glycosides

Plants in **Australia** known or suspected to contain cardiac glycosides

Toxicity & toxin types are indicated by data in square brackets, thus [*=poisoning reported; toxin type: B=bufadienolide, C=cardenolide, unlabelled=unknown]

Family Apocynaceae (native and naturalised plants in Australia are reviewed by Forster & Williams 1996)

Nerium oleander (oleander)[*C] [DM131]

Cascabela thevetia (L.) Lippold [=*Thevetia peruviana* (Pers.) K.Schum.] (yellow oleander)[*C] [DM132]

**Acokanthera oblongifolia* (bushman's poison, winter sweet)[C]

**Allamanda cathartica* (yellow allamanda)

**Allamanda neriifolia*

Carissa ovata (currant bush, blackberry, burrum bush, conkberry) [C]

Cerbera manghas (sea mango)[C]

Cerbera odollan [C]

**Plumeria rubra* (frangipani)

Nerium oleander (oleander flowers and seed pods [RAM Photo]

Cascabela thevetia (yellow oleander) [RAM Photos]

Family Asclepiadaceae (native and naturalised plants in Australia are reviewed by Forster & Liddle 1996)

Cryptostegia grandiflora (rubber vine)[*C] [DM116] (Marohasy & Forster 1991); listed as a Weed of National Significance for Australia; toxicity (McGavin 1969)

**Cryptostegia madagascariensis* [C] (Marohasy & Forster 1991)

**Araujia sericiflora* [= *A. hortorum*] (white moth plant)[*]

**Asclepias curassavica* (red cotton)[*C] [DM103]

**Gomphocarpus physocarpus* (balloon cotton)[*] [DM104] (Bailey & White 1916)

**Gomphocarpus fruticosus* (balloon cotton)[*C]

**Calotropis procera* (calotrope, rubber bush, kapok tree, king's crown, cabbage tree)[C]

Cryptostegia grandiflora (rubber vine) flowers and seed pod [RAM Photo]

Family Celastraceae

Euonymus europaeus (spindle)[C]

Family Crassulaceae

Bryophyllum daigremontianum* x *B. delagoense (hybrid mother-of-millions)[*B] [DM84]

***Bryophyllum delagoense* [=*B. tubiflorum*]** (mother-of-millions)[*B] [DM85]

Bryophyllum pinnatum (live-leaf, resurrection plant)[*B]

Bryophyllum daigremontianum [B]

Bryophyllum fedtschenkoi [B]

Bryophyllum proliferum [B]

Bryophyllum beauverdii [a climber, naturalised in a few small localities around Brisbane]

Cotyledon orbiculata (pig's ears)[B]

Crassula spathulata [*]

Bryophyllum delagoense [RAM Photo]

Bryophyllum daigremontianum x *B. delagoense* hybrid (left); *Bryophyllum pinnatum* (right) [RAM Photos]

Family Iridaceae (native and naturalised plants in Australia are reviewed by Cooke 1986)

***Homeria flaccida** (breyniana)* (one-leaf cape tulip)[*B]
Homeria miniata (two-leaf cape tulip)[*B]
**Diplarrena moraea* (butterfly flag)[*B]
**Gynandriris setifolia* [B]
**Iris foetidissima* (stinking iris)
**Iris germanica*
**Iris pseudacorus* (yellow flag)
**Moraea aristata* [B]
**Moraea bellendenii* [B]
**Moraea vegeta* [B]
Sisyrinchium iridifolium (blue pigroot)[B]
Sisyrinchium sp.A (*micranthum*) (scour weed)[*B]

Homeria flaccida (one-leaf cape tulip) [left]; *Homeria miniata* (two-leaf cape tulip) [right] [RAM Photos]

Family Liliaceae

**Convalaria majalis* (lily-of-the-valley)[C]

**Ornithogalum thyrsoides* (chinkerinchee, star of Bethlehem) [*] (Hall 1953, Forshaw 1999)

Family Melianthaceae

**Melianthus comosus* (cape honey flower)[B] (Anderson & Koekemoer 1969)

**Melianthus major* (tall cape honey flower)[B]

Family Moraceae

Antiaris toxicaria Leschen. var. *macrophylla* (R.Br.) Corner (umpas tree) [C] - distributed in Top End Northern Territory and Cape York Peninsula Qld. as

well as in south-east Asia; the latex is toxic if injected, but less toxic by ingestion (Chew 1989).

Family Ranunculaceae

Adonis microcarpa [= *Adonis annua*] (pheasant's eye)[*C – convallatoxin, convalloside]

**Helleborus niger* (Christmas rose)[B]

Family Scrophulariaceae

Digitalis purpurea (foxglove)[C]

Digitalis purpurea (foxglove) inflorescence [RAM Photo]

Family Tiliaceae

Corchorus olitorius (jute)[*C – seeds contain strophanthidin (Soliman & Saleh 1950, Hamaguchi *et al.* 1998) and olitoriside (Turakhozhaev *et al.* 1970); young leaves used as human food in Egypt and Japan (Azuma *et al.* 1999)]

Corchorus olitorius (jute) flowering plant and seeds [Brock Photo (left); RAM Image (right)]

Major plants containing cardiac glycosides overseas (number of toxic species per genus given in parenthesis)

Southern Africa (Kellerman *et al.* 1988)

Family Apocynaceae - *Acokanthera* spp.(2), *Adenium multiflorum*, *Nerium* spp.(2), *Strophanthus* spp.(3), *Thevetia peruviana*

Family Asclepiadaceae - *Cryptostegia* spp.(2)

Family Crassulaceae (plakkies) - *Cotyledon orbiculata*, *Tylecodon* spp.(3), *Kalanchöe* spp.(5) [*K. lanceolata* – Masvingwe & Mavenyengwa 1997]

Family Iridaceae (tulp) - *Homeria* spp.(3), *Moraea* spp.(3)

Family Liliaceae (slangkop [Afrikaans, = snake's head]) - *Urginea* spp.(6), *Ornithoglossum viride*, *Lidneria clavata*, *Scilla natalensis*, *Bowiea volubilis, Ornithogalum nanodes* (Bamhare 1998), *Ornithogalum umbellatum*

Family Melianthaceae - *Melianthus* spp.(2), *Bersama abyssinica* [B – hellibrigenin 3-acetate (Kupchan 1969)]

Family Santalaceae - *Thesium* spp.(2)

Northern America

Family Asclepiadaceae - *Asclepias* spp.(9)

Family Apocynaceae - *Nerium oleander* (Galey *et al.* 1998)

Europe

Family Apocynaceae - *Nerium oleander* (native of the Mediterranean region)

Asia

Family Moraceae – *Antiaris toxicaria* (umpas tree) [C – convallatoxin, convalloside]

Toxicity:

There are 2 forms of cardiac glycoside poisoning - acute (described here) and cotyledonosis (only in southern Africa & described separately below)

Ruminants, pigs, horses, dogs and humans are susceptible. Birds are relatively resistant.

Plants retain toxicity when dried

Toxic doses (for example):

- Horse lethal dose of *Nerium oleander* leaf for adults = 15-30 g (10-20 leaves)
- Cattle LD_{50} *Bryophyllum delagoense (tubiflorum)* flower heads = 7 g wet weight/kg; leaf & stem = 40 g wet weight/kg (McKenzie & Dunster 1986)

Radunz *et al.* (1984) demonstrated lack of toxicity for cattle and sheep from *Calotropis procera* of Northern Territory origin. Reports from Queensland are that cattle can eat the plant without ill effect in the dry season, but if they are stressed (e.g. mustered) they may die suddenly (Anon 2001).

Australian records of cardiac glycoside toxicity:
Horses: *Nerium oleander* (Hughes *et al.* 2002); *Cryptostegia grandiflora* (Cook *et al.* 1990)
Cattle: *Nerium oleander* (RA McKenzie, unpublished data 1994, 1995); *Corchorus olitorius* (McKenzie *et al.* 1992); *Bryophyllum* spp. (McKenzie & Dunster 1986, 1987; McKenzie *et al.* 1987, 1989); *Cryptostegia grandiflora* (McGavin 1969); *Homeria* spp.
Pigs: *Adonis microcarpa* (Davies & Whyte 1989)

Mode of action:

Cardiac glycosides inhibit cardiac Na^+-K^+-ATPase, the sodium pump. The binding site on the enzyme molecule for cardiac glycosides or their aglycones is in the extracellular portion of the α-subunit (Kaplan 2002). This enzyme is involved in the maintenance of membrane potential of cardiac muscle fibres and in the active transport of Na and K ions across the cell membrane. Mechanisms of alimentary, respiratory (bronchoconstrictive) and nervous effects (cotyledonosis) are unclear.

Conditions of poisoning:

Plants

Cardiac glycoside-containing plants are **usually not palatable** (exception: cattle, *Cryptostegia grandiflora*), but they **retain toxicity when dried** and may be more palatable in the dried state.

The toxin content of the plants may vary with stage of the life cycle, e.g. *Bryophyllum* spp. are most toxic when flowering (May-October).

The vehicles for delivery of toxic quantities of cardiac glycosides to animals include

- **garden waste**, e.g. oleanders, foxgloves, with toxic material mixed with wholesome material
- weeds harvested as contaminants **in hay** e.g. cape tulips, pheasant's eye
- **seeds in feed grains** or screenings e.g. jute (Johnson & Toleman 1982, McKenzie *et al.* 1992, Samanta *et al.* 1992, Hamaguchi *et al.* 1998), pheasant's eye

Hunger or lack of alternative feed promotes ingestion of toxic amounts of these plants e.g. *Bryophyllum* spp.

Cattle browsing *Cryptostegia grandiflora* or *Calotropis procera* are reported to be usually affected only when exercised (Anon. 2001). Exercise may cause sudden death (heart failure) in apparently normal or slightly affected cattle after ingestion of a number of cardiac glycoside-containing plants.

Medicaments

Accidental overdose of digoxin (Ward 1999)

Clinical signs:

organ systems affected = cardiovascular, alimentary, nervous and respiratory systems
sudden death (particularly with exertion)
diarrhoea ± with blood in faeces
cardiac arrhythmia - tachycardia; bradycardia; heart block

vomiting (monogastric animals)
dyspnoea (poor prognosis)
ruminal atony
abdominal pain (colic in horses)

Pathology:

increasing plasma urea, creatinine and glucose concentrations with time after ingestion
cardiomyopathy (multifocal degeneration & necrosis). Lesions can be expected in animals that survive for over 24 hours. Animals dying earlier may not have had time for lesions to develop to a stage that is detectable microscopically.
haemorrhage into alimentary tract or congested, fluid-filled alimentary tract
pulmonary atelectasis (associated with dyspnoeic cases) and/or pulmonary oedema
omasal ulceration (in cases surviving several days - related to uraemia)

Diagnosis:

Access to plants, including seeds
± recognise plant fragments in stomach/rumen contents
Cardiac arrhythmia + diarrhoea + azotaemia
Myocardial histopathology (collect multiple samples: both ventricles, both atria & interventricular septum)
Assay stomach contents/faeces for some toxins [limited availability of chromatographic assay: TLC (Galey *et al.* 1996; Holstege *et al.* 2000), HPLC (Tor *et al.* 1996)]
Radioimmunoassay has been used to confirm the presence of cardiac glycosides in serum of intoxication cases (pigs: Davies & Whyte 1989). In human medicine this technique is used to monitor the therapeutic use of cardenolides and medical laboratories may provide assays in veterinary cases.

Therapy:

Ruminants

prognosis worsens with onset of diarrhoea > heart block > tachycardia > dyspnoea
activated charcoal (absorption of toxin in rumen/intercept enterohepatic circulation)
+ **electrolyte replacement solution** (rehydration/stimulate rumen)
+ **antiarrhythmic drugs**

Therapeutic protocol for cardiac glycoside poisoning (ruminants)

- Activated charcoal @ 5 g/kg by stomach tube in a slurry with electrolyte replacement solution (5 litres/kg charcoal)
- Continue electrolyte replacement solution dosage over next 24 hours (overall daily dose of 150 ml/kg)
- For tachycardia, 5 mg propranolol slowly IV repeated as required (if propranolol not available: 10 ml 2% lignocaine *without adrenalin* slowly IV, stopping if adverse reaction occurs)
- For heart block, 0.5 mg atropine/kg, half IV & half SC, repeated as required.

Horses

activated charcoal
treat abdominal pain with analgesics/antispasmodics → reduced severity of arrhythmias
treat arrhythmias

Outline Therapeutic protocol for cardiac glycoside poisoning in horses (F.D.Galey, personal communication 1998)

- Activated charcoal @ 2 g/kg by stomach tube in a slurry with electrolyte replacement solution every 8 hrs
- Flunixin meglumine (Finadyne®, Flumav®, Flunix®, Flunixil®) in large doses before treating arrhythmias

---

in human medicine, antibodies against cardenolides (digitalis-type glycosides) have been used to treat overdoses of medication; this technique has been applied to dogs (Ward *et al.* 1999). In humans, dialysis, oral activated charcoal and cholestyramine (Roberge & Sorensen 2000) are also used

Intravenous fluids containing calcium should be avoided. They enhance the effect of the toxins on the myocardium (Knight 1988). Potassium should be included only if hyperkalaemia is absent.

Prevention & control:

Cryptostegia grandiflora: biological control agents rubber vine rust fungus (*Maravalia cryptostegiae*) and *Euclasta whalleyi* moth caterpillars have been released in northern Queensland. The rust fungus spores require leaf surfaces to be wet (rain or dew) for 8 hr or more to effect entry to leaf cells. Infection rates are thus determined by seasonal conditions. Rust fungus life cycle takes 7-10 days from infection to spore release (Vitelli 2000).

Corchorus olitorius seeds should not be fed to pigs at more than 0.1 g /kg feed (100 jute seeds weigh 0.6 g) (Takken 1990); poultry can tolerate at least 5.0% jute seed in their diet (Johnson & Toleman 1984).

weed control measures for *Bryophyllum* spp. (fire, herbicides, pasture rehabilitation) are given by McKenzie & Armstrong (1986); there are prospects for biological control of *Bryophyllum* spp. in Australia through insects imported from Madagascar – several insect species identified as capable of damaging the plants; the most promising include *Osphilia tenuipes* (a weevil), *Eurytoma* sp. (a wasp) and an unidentified eumolpine leaf beetle (Witt 2000).

References: Se22

Anderson LAP, Koekemoer JM (1969) Toxic bufadienolides from *Melianthus comosus. J. S. Afr. Chem. Inst.* **22**:S119-S124.

Anon. (2001) Calotrope. *NRM Facts. Pest Series.* PP41 QNRM01258 pp.2.

Azuma K, Nakayama M, Koshioka M, Ippoushi K, Yamaguchi Y, Kohata K, Yamauchi Y, Ito H, Higashio H (1999) Phenolic antioxidants from the leaves of *Corchorus olitorius* L. *J. Agric. Food Chem.* **47**:3963-3966.

Bailey FM, White CT (1916) On two species of *Gomphocarpus* (wild cotton) naturalised in Queensland. *Qd. Agric. J.* **6** (New Series):104-105. [cited by Hurst 1942]

Bamhare C (1998) Suspected cardiac glycoside intoxication in sheep and goats in Namibia due to *Ornithogalum nanodes* (Leighton). *Onderstepoort J. Vet. Res.* **65**:25-30.

Capon RJ, Macleod JK, Oelrichs PB (1985) Structure elucidation of a new bufadienolide toxin from the flowers of *Bryophyllum tubiflorum* Harv. (Crassulacea [*sic*]). *J. Chem. Res. S* **11**:333; *Microfisch* **11**:3666-3685.

Capon RJ, Macleod JK, Oelrichs PB (1986) Bryotoxins B and C, toxic bufadienolide orthoacetates from the flowers of *Bryophyllum tubiflorum* (Crassulaceae). *Aust. J. Chem.* **39**:1711-1715.

Chew WL (1989) Moraceae. *Flora of Australia* **3**:15-68. [*Antiaris* pp.24-26.]

Cook DR, Campbell GW, Meldrum AR (1990) Suspected *Cryptostegia grandiflora* (rubber vine) poisoning in horses. *Aust. Vet. J.* **67**:344.

Cooke DA (1986) Iridaceae. *Flora of Australia* **46**:1-66.

Davies RL, Whyte PBD (1989) *Adonis microcarpa* (pheasant's eye) toxicity in pigs fed field pea screenings. *Aust. Vet. J.* **66**:141-143.

Forshaw D (1999) Chinkerinchee poisoning. *Vet. Path. Report (Newsletter Aust. Soc. Vet. Path.)*, No.53 (September), p.25. [sheep, Tambellup WA, sudden death, ataxia, diarrhoea, cardiomyopathy]

Forster PI, Liddle DJ (1996) Asclepiadaceae. *Flora of Aust.* **28**:197-283.

Forster PI, Williams JB (1996) Apocynaceae. *Flora of Aust.* **28**:104-196.

Galey FD, Holstege DM, Plumlee KH, Tor E, Johnson B, Anderson ML, Blanchard PC, Brown F (1996) Diagnosis of oleander poisoning in livestock. *J. Vet. Diagn. Invest.* **8**:358-364.

Galey FD, Holstege DM, Johnson BJ, Siemens L (1998) Toxicity and diagnosis of oleander (*Nerium oleander*) poisoning in livestock. Chapter 44 in *Toxic Plants and Other Natural Toxicants*, edited by T Garland and AC Barr, CAB International, Wallingford UK, pp. 215-219.

Hall WTK (1953) *Ornithogalum thyrsoides*. Unpublished report, 22 September 1953, Queensland DPI Poisonous Plants Files. [sheep seen eating plant; colic and diarrhoea 2 days later lasting a week]

Hamaguchi Y, Hirai Y, Taniyama A, Aizawa M (1998) [Mulukhiyya seed (*Corchorus olitorius* L.) poisoning in Japanese black cows] *J. Jap. Vet. Med. Assoc.* **51**:407-410. [Japanese with English abstract]

Holstege DM, Francis T, Puschner B, Booth MC, Galey FD (2000) Multiresidue screen for cardiotoxins by two-dimensional thin-layer chromatography. *J. Agric. Food Chem.* **48**:60-64.

Hughes KJ, Dart AJ, Hodgson DR (2002) Suspected *Nerium oleander* (oleander) poisoning in a horse. *Aust. Vet. J.* **80**:412-415.

Johnson SJ, Toleman MA (1982) The toxicity of jute (*Corchorus olitorius*) seed to pigs. *Aust Vet. J.* **58**:264-265.

Johnson SJ, Toleman MA (1984) Apparent lack of toxicity of jute (*Corchorus olitorius*) seed for poultry. *Aust Vet. J.* **61**:124.

Kaplan JH (2002) Biochemistry of Na,K-ATPase. *Ann. Rev. Biochem.* **71**:511-535.

Kellerman TS, Coetzer JAW, Naude TW (1988) *Plant Poisonings and Mycotoxicoses of Livestock in Southern Africa*. Oxford University Press, Cape Town. p.83-108.

Knight AP (1988) Oleander poisoning. *Compendium of Continuing Education for Veterinarians* **10**:262-263.

Kupchan SM (1969) *J. Org. Chem.* **34**:3894. [cited by Harborne & Baxter 1996, p.191]

Marohasy J, Forster PI (1991) A taxonomic revision of *Cryptostegia* R. Br. (Asclepiadaceae: Periplocoideae) *Aust. Syst. Bot.* **4**:571-577.
Masvingwe C, Mavenyengwa M (1997) *Kalanchoe lanceolata* poisoning in Brahman cattle in Zimbabwe: the first field outbreak. *J. S. Afr. Vet. Assoc.* **68**:18-20.
McGavin MD (1969) Rubber-vine (*Cryptostegia grandiflora*) toxicity for ruminants. *Qd. J. Agric. Anim. Sci.* **26**:9-19.
McKenzie RA, Callinan RB, Unger DB, Flanagan MA (1992) Suspected jute seed (*Corchorus olitorius*) poisoning of cattle. *Aust. Vet. J.* **69**:117-118.
McKenzie RA, Armstrong TR (1986) Poisoning of cattle by *Bryophyllum* plants. *Qd. Agric. J.* **112**:105-108.
McKenzie RA, Dunster PJ (1986) Hearts and flowers: *Bryophyllum* poisoning of cattle. *Aust. Vet. J.* **63**:222-227.
McKenzie RA, Dunster PJ (1987) Curing experimental *Bryophyllum tubiflorum* poisoning of cattle with activated carbon, electrolyte replacement solution and antiarrhythmic drugs. *Aust. Vet. J.* **64**:211-214.
McKenzie RA, Franke FP, Dunster PJ (1987) The toxicity to cattle and bufadienolide content of six *Bryophyllum* species. *Aust. Vet. J.* **64**:298-300.
McKenzie RA, Franke FP, Dunster PJ (1989) The toxicity for cattle of bufadienolide cardiac glycosides from *Bryophyllum tubiflorum* flowers. *Aust. Vet. J.* **66**:374-376.
Radunz BL, Wilson G, Beer G (1984) Feeding rubberbush (*Calotropis procera*) to cattle and sheep. *Aust. Vet. J.* **61**:243-244.
Reppas GP (1995) *Bryophyllum pinnatum* poisoning of cattle. *Aust. Vet. J.* **72**:425-427.
Roberge RJ, Sorensen T (2000) Congestive heart failure and toxic digoxin levels: role of cholestyramine. *Vet. Human Toxicol.* **42**:172-173.
Samanta G, Samanta AR, Basak DK, Pal AK (1992) Studies on the pathological changes in broilers fed with jute seed (*Corchorus olitorius*) cake. *Indian Vet. Med. J.* **16**:149-151.
Soliman G, Saleh W (1950 Constituents of the seeds of *Corchorus olitorius* L.. Part I. Corchorin and its identiy with strophanthidin. *J. Chem. Soc.* pp.2198-2200.
Takken A (1990) Toxic weed seeds – pig health. Farmnote F120/May90, Queensland Department of Primary Industries.
Tor ER, Holstege DM, Galey FD (1996) Determination of oleander glycosides in biological matrices by high-performance liquid chromatography. *J. Agric. Food Chem.* **44**:2716-2719.
Turakhozhaev MT, Shamsutdinov MRI, Shakirov TT (1970) The isolation of olitoriside. *Chem. Nat. Compounds* **6**:712-714.
Vitelli M (2000) What colour is your rubber vine? *Northern Muster* [QDPI Beef Industry Institute Northern Newsletter] No.67, p.12
Ward DM, Forrester SD, DeFrancesco TC, Troy GC (1999) Treatment of severe chronic digoxin toxicosis in a dog with cardiac disease, using ovine digoxin-specific immunoglobulin G Fab fragments. *J. Am. Vet. Med. Assoc.* **215**:1808-1812.
Wagner H, Fischer M, Lotter H (1985) New bufadienolides from *Kalanchoe daigremontiana* Hamet et Perr. (Crassulaceae). *Z. Naturforsch.* **40B**:1226-1227.
Wagner H, Lotter H, Fischer M (1986) [The toxic and sedative bufadienolides of *Kalanchoe daigremontiana* Hamet et Perr.] *Helvetica Chimica Acta* **69**:359-367.
Witt A, Palmer B (2000) Prospects for the biological control of mother-of-millions in Queensland. *Proceedings, Queensland Weeds Symposium, Caloundra July 2000*. pp.4.
Yamagishi T, Xiu-Zhen Yan, Rong-Yang Wu, McPhail DR, McPhail AT, Kuo-Hsiung Lee (1988) Structure and stereochemistry of bryophyllin-A, a novel potent cytotoxic bufadienolide orthoacetate from *Bryophyllum pinnatum*. *Chem. Pharmacol. Bull.* **36**:1615-1617. [bryophyllin A = bryotoxin C of Capon *et al.* 1986]
Yamagishi T, Haruna M, Xiu-Zhen Yan, Jer-Jang Chang, Kuo-Hsiung Lee (1989) Antitumor agents, 110. Bryophyllin B, a novel potent cytotoxic bufadienolide from *Bryophyllum pinnatum*. *J. Nat. Prod.* **52**:1071-1079.

Cumulative bufadienolide cardiac glycosides (cotyledonosis)

Syndrome names:

- cotyledonosis
- krimpsiekte (Afrikaans = "twisted disease") in southern Africa
- nenta

This syndrome has been described only from southern Africa. Some of the plants involved are cultivated as garden plants and are sparingly naturalised in Australia, e.g. *Cotyledon orbiculata*.

Chemical structure:

Cumulative bufadienolide cardiac glycosides belonging to 3 classes (defined by Steyn *et al.* 1986b), all with multiple ether bridges between the aglycone and the carbohydrate moiety:

- Class 1 is represented by **tyledoside C** and closely related to a large group of cardenolides e.g. gomphoside (*q.v.*) and originates from a 2α,3β-dihydroxybufadienolide and a 2-oxo carbohydrate moiety. [Note: tyledoside C = cotyledoside B in Anderson *et al.* 1985]
- Class 2 includes **cotyledoside** (van Wyk 1975, Steyn *et al.* 1984) and **tyledosides A, B, D, F and G** (Steyn *et al.* 1986a) and originates from a 2α,3β-dihydroxybufadienolide and a 3-oxo carbohydrate moiety
- Class 3 includes **orbicusides A, B and C** (Steyn *et al.* 1986b) and originates from a 3β-hydroxy-2-oxobufadienolide and a 4,6-dideoxy carbohydrate moiety. [Note: orbicusides A, B & C in Steyn *et al.* 1986b = cotyledosides A, C & D in Anderson *et al.* 1985]

In addition, **lanceotoxins A and B** (Anderson *et al.* 1984) have been described from *Kalanchoe lanceolata*.

Sources:

Family Crassulaceae

Species of *Cotyledon* and *Tylecodon* are known in southern Africa as plakkies. The taxonomy of *Cotyledon* was revised by Toelken (1978) who created the genus *Tylecodon*.

Toxic species in this family include

Cotyledon orbiculata L. (Terblanche & Adelaar 1965, Anderson *et al.* 1985); contains orbicusides (Steyn *et al.* 1986b)

Tylecodon grandiflorus (Burm.f.) Toelken (Anderson *et al.* 1983b, van Rooyen & van der Walt 1990); contains tyledosides (Steyn *et al.* 1986a)

Tylecodon ventricosus (Burm.f.) Toelken (Botha *et al.* 1998a); contains tyledoside D (Botha *et al.* 1998a)

Tylecodon wallichii (Harv.) Toelken ssp. *wallichii* [= *Cotyledon wallichii* Harv.] (Naudé & Schultz 1982); contains cotyledoside (Steyn *et al.* 1984)

Kalanchoe lanceolata (Forssk.) Pers. (Anderson *et al.* 1983a, 1984, Masvingwe & Mavenyengwa 1997); contains lanceotoxins (Anderson *et al.* 1984)

Family Liliaceae

Ornithogalum toxicarium (a chinkerinchee) (Botha *et al.* 2000)

Toxicity:

cumulative poisoning with bufadienolide cardiac glycosides

goats > sheep > cattle > horse

Suni antelope were recorded as poisoned by 'plakkies' (*Cotyledon*) in a fenced enclosure (Fourie *et al.* 1996).

Secondary poisoning occurs in dogs and humans that eat meat from carcases of animals dead from cotyledonosis.

The syndrome has been reproduced by dosing sheep with cotyledoside (Naudé & Schultz 1982, Botha *et al.* 1997)

The concentration of cotyledoside in *Tylecodon wallichii* peaks in winter and spring/early summer, coinciding with field poisoning incidents (Botha *et al.* 2001). The greatest concentration of cotyledoside in *Tylecodon wallichii* is in the flowering stalk (Botha *et al.* 2001).

Mode of action: undescribed

Conditions of poisoning:

known only from southern Africa

Clinical signs:

lag behind flock, head dangling

stand with back arched, feet together

recumbent with head and neck stretched on the ground

torticollis (persists)

paralysis of lower jaw and tongue → drooling saliva, dysphagia [kwylbek krimpsiekte; kwylbek = salivation]

Pathology:

Nervous system lesions appear to be undescribed in natural cases. Anderson *et al.* (1983a) dosed sheep with lanceotoxin B and produced moderate brain oedema in the periventricular white matter, brain stem and cerebellum. Botha *et al.* (1997) dosed sheep with cotyledoside and produced mild oedema and vacuolation of the neuropil and astrocyte swelling in the cerebral and cerebellar grey and white matter, which was particularly pronounced in the white matter of the thalamus. Thalamic sites involved varied between sheep and included the ventrolateral, dorsolateral and ventrorostral nuclei and the optic radiation.

Diagnosis: access + syndrome

Therapy: nil

Prevention & control: deny access

References:

Anderson LAP, Schultz RA, Joubert JPJ, Prozesky L, Kellerman TS, Erasmus GL, Procos J (1983a) Krimpsiekte and acute cardiac glycoside poisoning in sheep caused by bufadienolides from the plant *Kalanchoe lanceolata* Forsk. *Onderstepoort J. Vet. Res.* **50**:295-300.

Anderson LAP, Joubert JPJ, Prozesky L, Kellerman TS, Schultz RA (1983b) The experimental production of krimpsiekte in sheep with *Tylecodon grandiflorus* (Burm.f.) Toelken and some of its bufadienolides. *Onderstepoort J. Vet. Res.* **50**:301-307.

Anderson LAP, Steyn PS, van Heerden FR (1984) The characterization of two novel bufadienolides, lanceotoxins A and B from *Kalanchoe lanceolata* (Forsk.) Pers. *J. Chem. Soc. Perkin Trans.* **1**:1573-1575.

Anderson LAP, Schultz RA, Kellerman TS, Kotzé SM, Prozesky L, Erasmus GL, Labuschagne L (1985) Isolation and characterisation of and some observations on poisoning by bufadienolides from *Cotyledon orbiculata* L. var. *orbiculata. Onderstepoort J. Vet. Res.* **52**:21-24.

Botha CJ, van der Lugt JJ, Erasmus GL, Kellerman TS, Schultz RA, Vleggaar R (1997) Krimpsiekte, associated with thalamic lesions, induced by the neurotoxic cardiac glycoside, cotyledoside, isolated from *Tylecodon wallichii* (Harv.) Toelken subsp. *wallichii. Onderstepoort J. Vet. Res.* **64**:189-194.

Botha CJ, Kellerman TS, Schultz RA, Erasmus GL, Vleggaar R, Retief E (1998a) Krimpsiekte in a sheep following a single dose of *Tylecodon ventricosus* (Burm. f.) Toelken and the isolation of tyledoside D from this plant species. *Onderstepoort J. Vet. Res.* **65**:17-23.

Botha CJ, van der Lugt JJ, Erasmus GL, Kellerman TS, Schultz RA, Vleggaar R (1998b) Krimpsiekte, a paretic condition of small stock poisoned by bufadienolide-containing plants of the Crassulaceae in South Africa. Chapter 80 in Garland T, Barr AC (eds) *Toxic Plants and Other Natural Toxicants.* CAB International, Wallingford. pp. 407-412.

Botha CJ, Schultz RA, van der Lugt JJ, Archer C (2000) A krimpsiekte-like syndrome in small stock poisoned by *Ornithogalum toxicarium* Archer & Archer. *J. S. Afr. Vet. Assoc.* **71**:6-9.

Botha CJ, Rundberget T, Wilkins AL, Mülders MSG, Flåøyen A, van Aardt MP (2001) Seasonal variation in cotyledoside concentration of *Tylecodon wallichii* (Harv.) Toelken subsp. *wallichii* sampled in a krimpsiekte-prevalent region. *Onderstepoort J. Vet. Res.* **68**:1-9.

Fourie N, Basson AT, Basson KM, Ferreira GCH, van den Berg H, Smith JCS, Labuschagne L (1996) Poisoning of wildlife in South Africa. *J. S. Afr. Vet. Assoc.* **67**:74-76.

Kellerman TS, Coetzer JAW, Naude TW (1988) *Plant Poisonings and Mycotoxicoses of Livestock in Southern Africa*. Oxford University Press, Cape Town. p.99-105.

Masvingwe C, Mavenyengwa M (1997) *Kalanchoe lanceolata* poisoning in Brahman cattle in Zimbabwe: the first field outbreak. *J. S. Afr. Vet. Assoc.* **68**:18-20.

Naudé TW, Schultz RA (1982) Studies on South African cardiac glycosides. II. Observations on the clinical and haemodynamic effects of cotyledoside. *Onderstepoort J. Vet. Res.* **49**:247-254.

Steyn PS, van Heerden FR, van Wyk AJ (1984) The structure of cotyledoside, a novel toxic bufadienolide glycoside from *Tylecodon wallichii* (Harv.) Toelken. *J. Chem. Soc., Perkin Trans.* **1**:965-967.

Steyn PS, van Heerden FR, Vleggaar R, Anderson LAP (1986a) Structure elucidation and absolute configuration of the tyledosides, bufadienolide glycosides from *Tylecodon grandiflorus. J. Chem. Soc., Perkin Trans.* **1**:429-435.

Steyn PS, van Heerden FR, Vleggaar R, Anderson LAP (1986b) Bufadienolide glycosides of the Crassulaceae. Structure and stereochemistry of orbicusides A-C, novel toxic metabolites of *Cotyledon orbiculata. J. Chem. Soc., Perkin Trans.* **1**:1633-1636.

Terblanche M, Adelaar TF (1965) A note on the toxicity of *Cotyledon orbiculata* L. *J. S. Afr. Vet. Med. Assoc.* **36**:555-559.

Toelken HR (1978) New taxa and new combinations in *Cotyledon* and allied genera. *Bothalia* **12**:377-393.

Tustin RC, Thornton DJ, Kleu CB (1984) An outbreak of *Cotyledon orbiculata* L. poisoning in a flock of Angora goat rams. *J. S. Afr. Vet. Assoc.* **55**:181-184.

Van Rooyen JM, van der Walt JJ (1990) The toxic effects on cardiac myocytes of tyledoside F, a cumulative neurotoxic cardiac glycoside isolated from *Tylecodon grandiflorus. Onderstepoort J. Vet. Res.* **57**:223-227.

Van Wyk AJ (1975) The chemistry of *Cotyledon wallichii* Harv. III. The partial constitution of cotyledoside, a novel bufadienolide. *J. S. Afr. Chem. Inst.* **28**:281-283.

☑ *Ptaquiloside*

Core data

Syndrome names:

- 'bracken' poisoning (haemorrhagic disease) (worldwide)
- bovine enzootic haematuria (worldwide)
- bright blindness (retinal degeneration) (only sheep in Britain)
- alimentary tract neoplasia (Scotland, South America, New Zealand)

Common sources: ferns:

- *Pteridium esculentum* (bracken),
- *Cheilanthes sieberi* (mulga or rock fern)

Animals affected:

- Cattle
- Sheep (very rare)

Poisoning circumstances:

'Bracken' poisoning

- bracken: young fronds most toxic, 2-4 weeks intake
- mulga fern: first green plants available after drought

Enzootic haematuria: prolonged intake of small amounts of ferns (usually > 3 yr)

Main effects:
'Bracken' poisoning
- thrombocytopaenia, leucopaenia
- multiple haemorrhages ± fever

Enzootic haematuria
- urinary bladder neoplasia, haematuria
- anaemia, wasting

Diagnosis:
'Bracken' poisoning
- live: haematology (blood smears)
- dead: bone marrow histopathology (sternum)

Enzootic haematuria
- live: microurine
- dead: bladder histopathology

Therapy: nil
Prevention:
- prevent prolonged fern intake
- bracken control
  - no burning
  - pasture improvement
  - slash each new frond crop
  - herbicides

Syndrome names:

Ptaquiloside is responsible for 4 distinct poisoning syndromes depending on the dose and duration of exposure, the animal species exposed and a postulated interaction with bovine papilloma viruses. These are

- **'bracken' poisoning** ('acute' ptaquiloside poisoning) of cattle (and rarely sheep) , causing widespread and usually fatal haemorrhages and occurring worldwide.
- **bovine enzootic haematuria**, causing urinary bladder neoplasia in cattle (and rarely sheep) and occurring worldwide
- **bright blindness**, causing retinal degeneration only in sheep in Britain. The syndrome name originates from the reflection of light from the tapetum through dilated pupils.
- **alimentary tract neoplasia** of cattle and sheep in certain areas of the world including Scotland, South America, and New Zealand

Chemical structure:

Ptaquiloside [= aquilide A] is a **norsesquiterpene glycoside** with radiomimetic and carcinogenic (Hirono & Yamada 1987) properties. "Radiomimetic" refers to the suppression of bone marrow, mimicking the effects of ionising radiation (radioactivity). Assay and extraction techniques are available (Oelrichs *et al.* 1995). Concentrations of ptaquiloside in *Pteridium* spp. in Australia are greatest in the temperate zone (southern Australia); Australian ptaquiloside concentrations (μg/g) - *Pteridium esculentum* mean 2115 [range 20-12945], *Pteridium revolutum* mean 619 [36-12358] (Smith *et al.*1994). Concentrations of ptaquiloside in *Cheilanthes sieberi* in Australia & New Zealand have been measured at 150-448 μg/g (Smith *et al.* 1989)

Ptaquiloside is heat-stable with 70-80% remaining after 3 hr at 80°C; it also resists boiling (Smith & Seawright 1995, BL Smith, personal communication 1997).

Sources:
Ferns
Family Dennstaedtiaceae

Pteridium aquilinum (bracken) is the cosmopolitan species (Page 1976). Some botanists recognise a number of separate species. Those in Australia (Brownsey 1989, 1998) are currently classified as

Pteridium esculentum (austral bracken) [DM40] - Australia & New Zealand

Pteridium revolutum (hairy bracken) - Australia (N. Qld + NT only) & China

Pteridium esculentum x *Pteridium revolutum* hybrid (previously classified as *Pteridium yarrabense* and called northern bracken) – Australia (N.Qld + NT only)

Pteridium aquilinum – a small population is recognised in part of South Australia

Bracken is mostly distributed around the eastern, southern and south-western coasts of Australia

Histiopteris incisa (bat's wing fern [Aust.], water fern [NZ]) – Australia & New Zealand, associated with 1 case in cattle in NZ (BL Smith, personal communication 7 April 2000)

Family Adiantaceae

Cheilanthes sieberi (mulga or rock fern) [DM38] - Australia & New Zealand

15 *Cheilanthes* spp. in Australia, *ca.* 180 worldwide (Chambers and Farrant 1998);

Cheilanthes sieberi is known to be toxic with field cases of the haemorrhagic syndrome first recognised in 1969 in cattle in south-eastern Queensland and experimental reproduction following closely (Clark & Dimmock 1971). *C. sieberi* is widely distributed in coastal and inland Australia. See also Thiaminase.

Cheilanthes distans (bristly or woolly cloak-fern) is suspected to be toxic and was involved in a field case in cattle in southern Queensland in 2001 in combination with *C. sieberi* (RJ Newman, JA Taylor & RA McKenzie, unpublished data 2001)

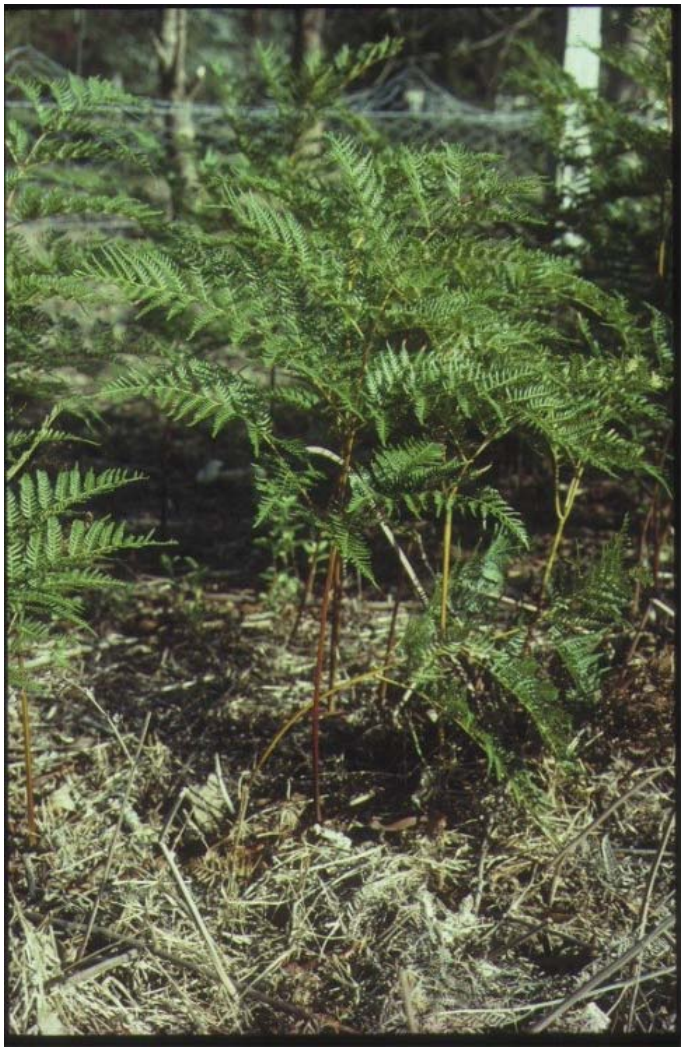
Other fern species reported to contain ptaquiloside include

Onychium contiguum (fuh) – India

Pteris cretica [Saito K (1990) *Phytochemistry* **29**:1475 cited by Harborne & Baxter 1996]

Hypolepsis punctata [Saito K (1990) *Phytochemistry* **29**:1475 cited by Harborne & Baxter 1996]

Dennstaedtia hirsuta [Saito K (1990) *Phytochemistry* **29**:1475 cited by Harborne & Baxter 1996]



Pteridium esculentum (austral bracken). [RAM Photo]

Pteridium esculentum (austral bracken. [RAM Photo]

Cheilanthes sieberi (mulga or rock fern) in habitat. [RAM Photo]

Cheilanthes distans (bristly or woolly cloak-fern). Cultivated specimen. [RAM Photo]

Toxicity:

'Bracken' poisoning:

cattle (Evans *et al.* 1982, Fenwick 1988, Hopkins 1990)

very rarely in sheep (Moon & Raafat 1951, Parker & McCrea 1965, Sunderman 1987)

acute bracken poisoning has been experimentally reproduced in cattle with ptaquiloside (Hirono *et al.* 1984)

The syndrome has been reproduced in cattle by feeding *Cheilanthes sieberi* (Clark & Dimmock 1971): A steer dosed PO with 13.33 g/kg/day for 26 days developed thrombocytopaenia by day 15, prolonged bleeding time after day 22, complete absence of neutrophils by day 23, pyrexia from day 24, anaemia from day 25 and died on day 27. A second steer dosed PO with 8.1 g/kg/day for 16 days developed thrombocytopaenia from day 10, complete absence of neutrophils from day 22 and died on day 23. A bull remained clinically normal while dosed PO with 8.1 g/kg/day for 10 days during which it developed thrombocytopaenia and neutropaenia but then recovered during the next 14 days. It was then dosed PO with 8.1 g/kg/day for a further 10 days during which it again developed a transient neutropaenia, but remained clinically normal.

records of ptaquiloside poisoning of cattle in Australia: Skerman & Newton (1952), Clark & Dimmock (1971)

ptaquiloside poisoning of cattle recorded worldwide: Europe, North & South America, Asia (Miura & Oshima 1961), Africa (Tustin *et al.* 1968)

Bovine enzootic haematuria:

cattle (Hopkins 1986); very rarely sheep (Harbutt & Leaver 1969)

There is a potential carcinogenic risk to humans directly consuming bracken (for example in Japan) or consuming products of cattle eating ferns (Evans *et al.* 1971, Smith & Seawright 1995, Shahin *et al.* 1999). There is an association of gastric neoplasia in South American farmers with dense bracken populations in cattle pastures and ptaquiloside in milk (Alonso-Amelot *et al.* 1996). Where dairying is industrialised, the dilution of ptaquiloside in bulk milk supplies is believed to reduce its concentration below that considered hazardous for humans.

Bright blindness:

progressive retinal degeneration

cases in United Kingdom only

sheep only

peak age incidence 3-4 years, thus 2-3 summers grazing bracken

experimentally produced; 50% bracken in diet for 63 weeks. First case at 28 weeks (Watson *et al.* 1972)

experimentally produced in sheep by IV ptaquiloside (Hirono *et al.* 1993)

Alimentary neoplasia:

Upper alimentary tract neoplasia of cattle is reported from Scotland and South America.

Intestinal adenocarcinoma of sheep is reported from New Zealand and Australia

Mode of action:

'Bracken' poisoning:

The `radiomimetic' action of ptaquiloside causes bone marrow aplasia resulting in thrombocytopaenia and leucopaenia. This leads to widespread haemorrhage and loss of protection against bacterial infection and terminal infections ensue.

Bovine enzootic haematuria:

Put simply, ptaquiloside binds to DNA in alkaline conditions causing neoplastic transformation of cells, bovine urine being normally alkaline. Ptaquiloside alkylates DNA when activated to its unstable dienone form under alkaline conditions (Ojika *et al.* 1987). Ptaquiloside damages DNA causing strand breaks (Kushida *et al.* 1994). Alkylation is considered the first step in chemical carcinogenesis and ptaquiloside alkylates adenine and subsequently causes depurination in codon 61 of the *ras* gene and thus activates the H-*ras* proto-oncogene in bovine ileum and urinary bladder (Prakash *et al.* 1996, Shahin *et al.* 1998, 1999)

Bright blindness:

The pathogenesis of retinal degeneration is undescribed, but it can be induced by intravenous dosing of sheep with ptaquiloside.

Alimentary neoplasia:

Chronic ptaquiloside intake from bracken interacting with bovine papilloma virus infection is suggested as the initiating cause in cattle with neoplasia of the pharynx and oesophagus.

Intestinal adenocarcinomas in sheep are suggested as associated with chronic ptaquiloside intake.

Conditions of poisoning:

'Bracken' poisoning:

bracken

young fronds more toxic

2-4 weeks intake required for induction of clinically-significant bone marrow suppression

most commonly in newly-weaned calves, occasionally in adults

rarely, hay contamination or bracken as bedding

mulga fern

Cheilanthes sp. are abundant widespread ferns adapted to arid zone conditions in Australia. *Cheilanthes sieberi* may be a very prominent component of the ground cover in mulga (*Acaia aneura*) communities. They may be the first green plants occurring in pasture after drought because they are xerophytic ferns (drought tolerant), entering a dormant state under dry conditions and rapidly reviving after rain (within 24 hr).

Bovine enzootic haematuria:

BEH reported from Australia (Dickinson 1940, McKenzie 1978a,b), New Zealand (Kerrigan 1926, Smith & Beatson 1970, Smith & van der Wouden 1972, Smith *et al.* 1988), Europe (Pinto *et al.* 1999), Turkey, China (Xu *et al.* 1984, Zhao *et al.* 1988, Xu 1992), India, North & South America

chronic intake of small quantities of ferns (insufficient to cause bone marrow damage) → **neoplastic changes** in **urinary bladder mucosa** → haematuria

time to onset = years (youngest affected animals usually > 3 yrs old)

Bright blindness:

prolonged grazing of bracken-infested pastures; 2-3 summers exposure required

Alimentary neoplasia:

Prolonged grazing of bracken-infested pastures

Clinical signs:

'Bracken' poisoning:

depression

nasal discharge + blood

free blood in faeces

haemorrhages (petechiae) under visible mucous membranes

mucosal pallor

± haematuria

± fever (superimposed bacterial infection → other signs including those of pneumonia & septicaemia)

Bovine enzootic haematuria:

weight loss progressing to emaciation

haematuria (bloody urine, clots in urine)

anaemia which becomes very severe over the course of the disease

Bright blindness:

pupils dilated

↑ tapetal reflectivity

Alimentary neoplasia:

Pathology:

'Bracken' poisoning: (see Naftalin & Cushnie 1951, 1954)

thrombocytopaenia

leucopaenia

anaemia

multiple haemorrhages (subcutaneous, intramuscular, subserosal, subepicardial *etc.*)

ulceration of intestine (over Peyer's patches)

± oedema of larynx (calves)

± liver septicaemic infarcts

Bovine enzootic haematuria:

anaemia

usually normal leucocyte and platelet numbers
various bladder mucosa lesions: chronic cystitis with various neoplasms. Haemangiomas, haemangiosarcomas or both are usually present. Transitional cell carcinomas, adenomas, adenocarcinomas or other types of neoplasms may also be present.

Bright blindness:
leucopaenia
retinal atrophy (loss of rods & cones)

Alimentary neoplasia:
Squamous cell carcinoma of the pharynx and oesophagus

Diagnosis:

'Bracken' poisoning:
haemorrhagic disease
+ thrombocytopaenia, leucopaenia
live: blood smear assessment
dead: bone marrow histopathology [Hint: take sample from the sternum rather than a rib or long bone]
+ access to above fern species

Bovine enzootic haematuria:
live: access to ferns + clinical syndrome (microurine to differentiate haematuria from haemoglobinuria or other pigments)
dead: bladder pathology

Bright blindness:
Syndrome + chronic bracken access

Alimentary neoplasia:
Syndrome + chronic fern access

Therapy:

There are no effective specific therapies available for any of the syndromes. Antibiotics and blood transfusions may be useful supportive measures in 'bracken' poisoning, but the prognosis is always poor to grave. Batyl alcohol (D-α-octa-decylglycerol ether) is reported to produce bone marrow stimulus and has been suggested as therapy for 'bracken' poisoning, but its effectiveness is doubtful (Evans *et al.* 1957, Dalton 1964, Anon 1966, Philp & Gowdey 1967). In future, the use of such preparations as filgrastim [Neupogen® AMGEN Australia Pty Ltd] (a granulocyte colony-stimulating factor of human origin used in dogs poisoned by 5-fluorouracil (*q.v.*)) to stimulate bone marrow stem cell proliferation and boost circulating neutrophil numbers may be useful.

Prevention & control:

'Bracken' poisoning:
bracken
note that burning tends to increase the population density of bracken
pasture improvement measures + reduction in bracken vigour
slashing each new crop of fronds
herbicides (including possible fungal pathogens/mycoherbicides [McElwee *et al.* 1990])
Cheilanthes sieberi
It may be possible for cattle to survive intake of toxic doses of *C. sieberi* if access is restricted to 10 days or less followed by at least 14 days without access before a further short period of exposure (Clark & Dimmock 1971), but this is based on data from only 1 experimental animal and should be applied with caution.

Bovine enzootic haematuria:
Prevent prolonged access of cattle to ferns
Theoretically, continuous acidification of urine may prevent establishment of bladder neoplasia because ptaquiloside alkylates DNA when activated to its unstable dienone form under alkaline conditions (Ojika *et al.* 1987). There is a dearth of information on achieving permanent acidification of bovine urine, but research into prevention of phosphorus deficiency (e.g. Beighle 2000) and hypocalcaemia may produce effective practical techniques in future.

Reference: Se17

Anon. (1966) Batyl alcohol and fern poisoning. *Nutr. Rev.* **24**:19-21.

Brownsey PJ (1989) The taxonomy of bracken (*Pteridium*: Dennstaedtiaceae) in Australia. *Aust. Syst. Bot.* **2**:113-128.
Brownsey PJ (1998) *Pteridium*. *Flora of Australia* **48**:223-227.
Carrigan M (1990) Rock fern poisoning in cattle. *Vet. Path. Report (ASVP Newsletter)* No.28.p.32.
Chambers TC, Farrant PA (1998) *Cheilanthes*. *Flora of Australia* **48**:271-286.
Clark IA, Dimmock CK (1971) The toxicity of *Cheilanthes sieberi* to cattle and sheep. *Aust. Vet. J.* **47**:149-152.
Dalton RG (1964) The effects of batyl alcohol on the haematology of cattle poisoned with bracken. *Vet. Rec.* **76**:411-416.
Evans WC, Evans IA, Edwards CM, Thomas AJ (1957) Bracken poisoning of cattle – therapeutic treatment. *Biochem. J.* **65**:6P.
Evans WC, Patel MC, Koohy Y (1982) Acute bracken poisoning in homogastric and ruminant animals. *Proc. Roy. Soc. Edinburgh* **81B**:29-64.
Fenwick GR (1988) Bracken (*Pteridium aquilinum*) – toxic effects and toxic constituents. *J. Sci. Food Agric.* **46**:147-173.
Hirono I, Kono Y, Takahashi K, Yamada K, Niwa H, Ojika M, Kigoshi H, Niiyama K, Uosaki Y (1984) Reproduction of acute bracken poisoning in a calf with ptaquiloside, a bracken constituent. *Vet. Rec.* **115**:375-378.
Hopkins A (1990) Bracken (*Pteridium aquilinum*): its distribution and animal health implications. *Br. Vet. J.* **146**:316-326.
McElwee M, Irvine JIM, Burge MN (1990) A mycoherbicidal approach to bracken control. In Bassett C, Whitehouse LJ, Zabkiewicz JA (eds.) *Alternatives to the Chemical Control of Weeds*. Proceedings of an International Conference, Rotorua, New Zealand, July 1989. Ministry of Forestry Forest Research Institute Bulletin 155, pp.74-79.
Miura S, Oshima K (1961) A pathological study on the first cases of bracken poisoning in cows in Japan. *Jap. J. Vet. Sci.* **23**:347-351.
Moon FE, Raafat MA (1951) The experimental production of bracken poisoning in sheep. *J. Comp. Path.* **61**:88-100.
Naftalin JM, Cushnie GH (1951) Pathology of bracken poisoning. *Vet. Rec.* **63**:332.
Naftalin JM, Cushnie GH (1954) Pathology of bracken poisoning in cattle. *J. Comp. Path.* **64**:54-74.
Oelrichs PB, Ng JC, Bartley J (1995) Purification of ptaquiloside, a carcinogen from *Pteridium aquilinum*. *Phytochem.* **40**:53-56.
Page CN (1976) The taxonomy and phytogeography of bracken – a review. *Bot. J. Linnean Soc.* **73**:1-34.
Parker WH, McCrea CT (1965) Bracken (*Pteris aquilina*) poisoning of sheep in the North York moors. *Vet. Rec.* **77**:861-866.
Philp RB, Gowdey CW (1967) Anaemia, thrombocytopenia and reduced platelet adhesiveness in rats fed bracken fern, and protective effects of batyl alcohol. *Nature* **216**:498-499.
Seaman JT, Philbey AW (1987) *Cheilanthes* toxicity in cattle. *Proc. Ann. Conf. Aust. Soc. Vet. Pathol.* pp.B3.1-B3.2.
Skerman KD, Newton LG (1952) Bracken fern poisoning of cattle. *Qd. Agric. J.* **74**:163-167.
Smith BL, Embling PP, Lauren DR, Agnew MP, Ross AD, Greentree PL (1989) Carcinogen in rock fern (*Cheilanthes sieberi*) from New Zealand and Australia. *Aust. Vet. J.* **66**:154-155.
Smith BL, Seawright AA, Ng J, Hertle AT, Thomson JA, Bostock PD (1994) Ptaquiloside in bracken ferns (*Pteridium* spp.) from eastern Australia and from a cultivated collection of bracken from world-wide sources. Chapter 9 in *Plant-Associated Toxins: Agricultural, Phytochemical & Ecological Aspects.* eds. Colegate SM, Dorling PR, CAB International, Wallingford UK, pp.45-50.
Sunderman FM (1987) Bracken poisoning in sheep. *Aust. Vet. J.* **64**:25-26.
Taylor J (1998) Mulga fern (*Cheilanthes sieberi*) poisoning in cattle. *Vet. Path. Report (ASVP Newsletter)* No.50, p.15.
Tustin RC, Adelaar TF, Meldal-Johnsen CM (1968) Bracken poisoning in cattle in the Natal midlands. *J. S. Afr. Vet. Med. Assoc.* **39**:91-99.

BEH

Alonso-Amelot ME. Castillo U, Smith BL, Lauren DR (1996) Bracken ptaquiloside in milk. *Nature* **382**:587.
Beighle DE (2000) Bone, blood and faecal response to an acidogenic lick for range cattle using different concentrations of ammonium chloride. *J. S. Afr. Vet. Assn.* **71**:215-218.
Dickinson CG (1940) *Aust. Vet. J.* **16**:224.
Evans IA, Widdop B, Jones RS, Barber GD, Leach H, Jones DL, Mainwaring-Burton R (1971) The possible human hazard of the naturally occurring bracken carcinogen. *Biochem. J.* **124**:28-29P.
Harbutt PR, Leaver DD (1969) Carcinoma of the bladder of sheep. *Aust. Vet. J.* **45**:473-475.
Hirono I, Yamada K (1987) Bracken fern. Chapter 4 in Hirono I (ed) *Naturally Occurring Carcinogens of Plant Origin – Toxicology, Pathology and Biochemistry.* [Bioactive Molecules Vol. 2] Elsevier, Amsterdam. pp.87-120.
Hopkins NCG (1986) Aetiology of enzootic haematuria. *Vet. Rec.* **118**:715-717.
Kerrigan J (1926) Chronic haematuria affecting cattle. Notes on cases in the South Island west coast district. *N. Z. J. Agric.* **33**:85-87.
Kushida T, Uesugi M, Sugiura Y, Kigoshi H, Tanaka H, Hirokawa J, Ojika M, Yamada K (1994) DNA damage by ptaquiloside, a potent bracken carcinogen: detection of selective strand breaks and identification of DNA cleavage products. *J. Am. Chem. Soc.* **116**:479-486.
McKenzie RA (1978a) An abattoir survey of bovine urinary bladder pathology. *Aust. Vet. J.* **54**:41.
McKenzie RA (1978b) Bovine enzootic haematuria in Queensland. *Aust. Vet. J.* **54**:61-64
Ojika M, Wakamatsu K, Niwa H, Yamada K (1987) Ptaquiloside, a potent carcinogen isolated from bracken fern *Pteridium aquilinum* var. *latiusculum*: structure elucidation based on chemical and spectral evidence, and reactions with amino acids, nucleosides and nucleotides. *Tetrahedron* **43**:5261-5274.
Pinto CA, Lima R, Louza AC, Almeida V, Melo M, Vaz Y, Neto Fonesca I, Lauren DR, Smith BL (1999) Bracken fern induced bovine enzootic haematuria in Sao Miguel Island, Azores. *Proceedings of the IVth International Bracken Conference*, University of Manchester, July 20-23, 1999.
Prakash AS, Pereira TN, Smith BL, Shaw G, Seawright AA (1996) Mechanism of bracken fern carcinogenesis: evidence for H-*ras* activation via initial adenine alkylation by ptaquiloside. *Nat. Toxins* **4**:221-227.
Shahin M, Smith BL, Prakash AS (1999) Bracken carcinogens in the human diet. *Mutation Res.* **443**:69-79.
Shahin M, Moore MR, Smith BL, Seawright AA, Prakash AS (1998) Acute and chronic toxicity induced by activated ptaquiloside in rats: comparison of pathogenesis due to oral and intravenous administrations. Chapter 52 in

Toxic Plants and Other Natural Toxicants. eds Garland T, Barr AC. CAB International, Wallingford. pp. 255-259.
Smith BL, Beatson NS (1970) Bovine enzootic haematuria in New Zealand. *N. Z. Vet. J.* **18**:115-120.
Smith BL, Embling PP, Agnew MP, Lauren DR, Holland PT (1988) Carcinogenicity of bracken fern (*Pteridium esculentum*) in New Zealand. *N. Z. Vet. J.* **36**:56-58.
Smith BL, Embling PP, Lauren DR, Agnew MP, Ross AD, Greentree PL (1989) Carcinogen in rock fern (*Cheilanthes sieberi*) from New Zealand and Australia. *Aust. Vet. J.* **66**:154-155.
Smith BL, Seawright AA (1995) Bracken fern (*Pteridium* spp.) carcinogenicity and human health – a brief review. *Nat. Toxins* **3**:1-5.
Smith BL, van der Wouden M (1972) Bovine enzootic haematuria lesions in cattle passing through a Nelson meatworks. *N. Z. Vet. J.* **20**:56.
Xu L, Wang Y, Wen L, He K, Ma W, You S, Yang K (1984) [Experimental induction of urinary bladder tumours in yellow cattle by feeding *Pteridium revolutum*.] *Acta Vet. Zootech. Sinica* **15**:211-217. [in Chinese, English summary]
Xu LR (1992) Bracken poisoning and enzootic haematuria in cattle in China. *Res. Vet. Sci.* **53**:116-121.
Zhao SZ, Hu WY, Ni BY, Zhu T, Meng XQ, Li ZC, Liu N, Liu LX, Yang HS (1988) [Experimental studies on bladder tumours induced by *Pteridium revolutum* (BL) Nakai in yellow cattle.] *Chinese J. Vet. Med.* **14**:5-8. [in Chinese; Abstract in *Vet. Bull*]

Bright blindness
Se20

Hirono I, Ito M, Yagyu S, Haga M, Wakamatsu K, Kishikawa T, Nishikawa O, Yamada K, Ojika M, Kigoshi H (1993) Reproduction of progressive retinal degeneration (bright blindness) in sheep by administration of ptaquiloside contained in bracken. *J. Vet. Med. Sci.* **55**:979-983.
Watson WA, Barnett KC, Terlecki S (1972) Progressive retinal degeneration (bright blindness) in sheep: a review. *Vet. Rec.* **91**:665-670.
Watson WA, Terlecki S, Patterson DSP, Sweasey D, Hebert N, Done JT (1972) Experimentally produced progressive retinal degeneration (bright blindness) in sheep. *Brit. Vet. J.* **128**:457-469.

Diterpenoid (kaurene) glycosides - atractyloside, carboxyatractyloside, parquin, carboxyparquin & wedeloside

Core data

Common sources:

- *Cestrum parqui*
- *Xanthium occidentale*
- *Wedelia asperrima*

Animals affected: ruminants, pigs
Mode of action: inhibit mitochondrial oxidative phosphorylation
Poisoning circumstances:

- *Xanthium occidentale*: cotyledons or seeds ingested

Main effects: acute liver necrosis
Diagnosis: pathology + plant access
Therapy: nil
Prevention: prevent access

Chemical structure:

Diterpenoid (kaurene) glycosides. Carboxyatractyloside readily undergoes carboxylation to atractyloside.

Sources:

***Cestrum* spp.** (Family Solanaceae)

Cestrum parqui (green cestrum)– an introduced garden plant, naturalised and weedy in Australia, native of South America [Se32,DM125, Descazeaux 1930, Rudd & White 1933, Lopez *et al.* 1978, McLennan & Kelly 1984, Kudo *et al.* 1985, Reit-Correa *et al.* 1986]; parquin & carboxyparquin isolated (Pearce *et al.* 1992, Oelrichs *et al.* 1994)

Cestrum nocturnum - cultivated garden plant in Australia (Hindmarsh 1937)
Cestrum aurantiacum - cultivated garden plant in Australia
Cestrum elegans - cultivated garden plant in Australia
Cestrum laevigatum (Peixoto *et al.* 2000)

Cestrum parqui [RAM Photo]

Cestrum parqui (green cestrum) fruit [RAM Photo]

***Xanthium* spp.** (Family Asteraceae)

Xanthium occidentale *(= X. pungens, X. strumarium* complex*)* (noogoora burr, cockle burr [North America]) [Se147,DM112, Seddon & King 1938, Kenny *et al.* 1950, Cole *et al.* 1980]

Xanthium spinosum (Bathurst burr)

Xanthium cavanillesii burrs contaminating soyabean residues poisoned feedlot cattle in Brazil (Drimeier *et al.* 1999)


Xanthium occidentale (Noogoora burr) leaf, fruit [RAM Photos]

***Wedelia* spp.** (Family Asteraceae)

Wedelia asperrima (sunflower daisy)– native to tropical Australia (Q, NT, WA) [Se145,DM71, Mulhearn 1939, Oelrichs & Muller 1972, Oelrichs *et al.* 1980, Lewis *et al.* 1981, Klingenberg *et al.* 1985]

Wedelia glauca (Obatomi & Bach 1998)

Melanthera biflora [= *Wedelia biflora*] (MacLeod *et al.* 1990)

Atractylis spp. (Family Asteraceae)

Atractylis gummifera– native of Mediterranean countries, not in Australia (carboxyatractyloside isolated – Danieli *et al.* 1972; human toxicity - Hamouda *et al.* 2000)

Atractylis carduus – native of Mediterranean countries, not in Australia

Atractylodes lancea (Family Asteraceae) – native of eastern Asia, not in Australia

Callilepsis laureola (Family Asteraceae) – native of southern Africa, not in Australia

Iphiona aucheri (Family Asteraceae) – native of Africa, not in Australia (Brookes 1983)

Toxicity:

Carboxyatractylosides in cotyledons of *Xanthium* spp. are recognised as **allelochemicals** (Cutler & Cole 1983). Allelopathy is the release by a plant of a chemical that inhibits the growth of near-by plants, thus providing a competitive advantage.

Carboxyatractyloside lethal doses: pigs 0.75-2.0% of body weight; calves 1.0% of body weight (Harborne & Baxter 1996, p.69)

Cestrum parqui

was demonstrated toxic to sheep by Rudd & White (1933) and hepatotoxic to sheep and cattle by Lopez (1978)

was demonstrated toxic to poultry by Newton (1955).

Iphiona aucheri is toxic to camels in North Africa

Mode of action:

inhibit mitochondrial oxidative phosphorylation (Luciani *et al.* 1971, Klingenberg *et al.* 1985)

Conditions of poisoning:

Cestrum parqui

- cattle will eat green cestrum if other feed is scarce, particularly during late winter (Rudd & White 1933)

Xanthium spp.

- only the **cotyledons**, the first 2 leaves emerging from the seed at germination, and thus the **seeds** enclosed in the burrs (2 seeds per burr), are toxic
- mass germination of *Xanthium occidentale* is common on alluvial flats along water courses, thus exposing grazing animals to a palatable concentrated source of toxin
- burrs in feed grains are toxic

Wedelia asperrima

- hungry cattle and sheep introduced to abundant plants in paddocks with poor pasture growth

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:

bioherbicides (fungal plant pathogens, mycoherbicides) are being researched for control of *Xanthium* spp. (*Colletotrichum orbiculare* vs. *X. spinosum*) (Anon. 1999)

References:

Anon. (1999) Bioherbicides and product formulation. *Weed Watch* No.11 (CRC for Weed Management Systems)

Brookes KB (1983) *S. Afr. J. Chem.* **36**:65. [*Iphiona aucheri*]

Cole RJ, Stuart BP, Lansden JA, Cox RH (1980) Isolation and redefinition of the toxic agent from cocklebur (*Xanthium strumarium*). *J. Agric. Food Chem.* **28**:1330-1332.

Cutler HG, Cole RJ (1983) Carboxyatractyloside: a compound from *Xanthium strumarium* and *Atractylis gummifera* with plant growth inhibiting properties. The probable "inhibitor A". *J. Nat. Prod.* **46**:609-613.

Danieli B, Bombardelli E, Bonati A, Gabetta B (1972) Structure of the diterpenoid carboxyatractyloside. *Phytochem.* **11**:3501-3504.

Descazeaux J (1930) Intoxication des ruminants par *Cestrum parqui. Comp. Rend. Soc. Biol., Paris* **3**:240-241.

Drimeier D, Irigoyen LF, Loretti AP, Colodel EM, Barros CSL (1999) [Spontaneous poisoning by the burs of *Xanthium cavanillesii* (Asteraceae) in cattle in Rio Grande do Sul, southern Brazil] *Pesq. Vet. Bras.* **19**:12-18.

Eichholzer JV *et al.* (1981) *Tetrahedron* **37**:1881 [wedeloside]

Hamouda C, Amamou M, Thabet H, Yacoub M, Hedhili A, Bescharnia F, Ben Salah N, Zhioua M, Abdelmoumen S, El Mekki Ben Brahim N (2000) Plant poisonings from herbal medication admitted to a Tunisian toxicologic intensive care unit, 1983-1998. *Vet. Human Toxicol.* **42**:137-141. [*Atractylis gummifera* responsible for 16 deaths from liver damage]

Hindmarsh WL (1937) Plant poisoning of stock 6. *Cestrum nocturnum*: a plant poisonous to stock. *New South Wales Department of Agriculture Veterinary Research Report* No.7 pp.115-117.

Kenny GC, Everist SL, Sutherland AK (1950) Noogoora burr poisoning of cattle. *Qd. Agric. J.* **70**:172-177.

Klingenberg M, Appel M, Oelrichs PB (1985) Wedeloside, a powerful inhibitor and ligand of the mitochondrial ADP/ATP carrier. *FEBS Letters* **189**:245-249.

Kudo K, Kelly WR, Oelrichs PB (1985) Experimental poisoning of mice and sheep with *Cestrum parqui.* In Seawright AA, Hegarty MP, James LF, Keeler RF (eds.) *Plant Toxicology.* Queensland Poisonous Plants Committee, Brisbane. pp.540-553.

Lewis IAS, MacLeod JK , Oelrichs PB (1981) The toxic extractives from *Wedelia asperrima* - II. The structure of wedeloside, a novel diterpenoid aminoglycoside. *Tetrahedron* **37**:4305-4311.

Lopez TA, Spinelli R, Villar JA (1978) Effectos de la dosification de *Cestrum parqui* L'Herit er en ovinos y bovinos. *Gaceta Veterinaria, Buenos Aires* **40**:642-650.

Luciana S, Martini N, Santi R (1971) Effects of carboxyatractyloside, a structural analogue of atractyloside , on mitochondrial oxidative phosphorylation. *Life Sciences* **10**:961-968.

MacLeod JK, Gaul KL, Oelrichs PB (1990) Bifloratoxin; a toxic aminoglycoside of carboxyatractyligenin from *Melanthera biflora. Aust. J. Chem.* **43**:1533-1539.

McLennan MW, Kelly WR (1984) *Cestrum parqui* (green cestrum) poisoning in cattle. *Aust. Vet. J.* **61**:289-291.

Mendez MC, dos Santos RC, Riet-Correa F (1998) Intoxication by *Xanthium cavanillesii* in cattle and sheep in southern Brazil. *Vet. Human Toxicol.* **40**:144-147.

Mulhearn CR (1939) Yellow daisy (*Wedelia asperrima*) - a plant toxic to sheep. *Qd. Agric. J.* **52**:397-400.

Newton LG (1955) *Annual Report, Department of Primary Industries, Queensland.*

Obatomi DK, Bach PH (1998) Biochemistry and toxicology of the diterpenoid glycoside atractyloside. *Food. Chem. Toxicol.* **36**:335-346.

Oelrichs PB, Muller WA (1972) Isolation of the toxic principle from *Wedelia asperrima. Toxicon* **10**:63-66.

Oelrichs PB, Vallely PJ, McLeod JK, Lewis IAS (1980) Isolation of a new potential antitumor compound from *Wedelia asperrima. Lloydia* **43**:414-416.

Oelrichs PB, Pearce CM, Kudo K, Kelly WR (1994) The isolation, structure elucidation and toxicity of the kaurene glycosides parquin and carboxyparquin in *Cestrum parqui.* Chapter 46 in Colegate SM, Dorling PR (eds.) *Plant-associated Toxins. Agricultural, Phytochemical & Ecological Aspects.* CAB International, Wallingford. pp. 251-256.

Pearce CM, Skelton NJ, Naylor S, Kannan R, Kelland J, Oelrichs PB, Sanders JKM, Williams DH (1992) Parquin and carboxyparquin, toxic kaurene glycosides from the shrub *Cestrum parqui*. *J. Chem. Soc., Perkin Trans.* **1**:593-600.

Peixoto PV, Brust LC, Duarte MD, Franca TN, Duarte VC, Barros CSL (2000) *Cestrum laevigatum* poisoning in goats in south-eastern Brazil. *Vet. Human Toxicol.* **42**:13-14.

Rudd JA, White CT (1933) A plant poisonous to livestock (*Cestrum parqui*). *Qd. Agric. J.* **40**:143-144.

Reit-Correa F, Shild AH, Mendez M del C, Pinkiero MH (1986) Intoxicação por *Cestrum parqui* (Solanaceae) em bovinos no Rio Grande do Sol. *Pesq. Vet. Bras.* **6**:111-115.

Seddon HR, King ROC (1938) Noogoora burr (*Xanthium chinense*): poisonous for stock in very early stage of growth. New South Wales Department of Agriculture Veterinary Research Report No.7 pp.101-108.

Plant calcinogenic glycosides (cholecalciferol, vitamin D_3)

Syndrome names:

- **enzootic calcinosis**
- Manchester wasting disease (named after the Manchester plateau of Jamaica)
- espichamento (Brazil)
- enteque seco (Argentina)

Chemical structure:

1,25-dihydroxycholecalciferol (vitamin D_3) and its glycoside (*q.v.*)

Sources:

- plant sources:
  - The Americas
    - *Solanum malacoxylon*
    - *Nierembergia veitchii*
    - *Cestrum diurnum* (day-blooming jessamine)
    - *Stenotaphrum secundatum* (crab grass – Jamaica)
  - Hawaii
    - *Solanum linnaeanum (hermannii, sodomaeum)* (apple of Sodom)
  - New Guinea
    - *Solanum torvum* (devil's fig)
  - Europe
    - *Trisetum flavescens* (yellow or golden oat grass) (Braun *et al.* 2000)
- *Cestrum diurnum*, *Solanum torvum*, *Solanum linnaeanum* and *Trisetum flavescens* occur in Australia, but poisoning of this sort has not been reported.

Toxicity:

- cattle, sheep, goats and horses affected

Mode of action:

- chronic intake → hypervitaminosis D → metastatic calcification of soft tissue

Conditions of poisoning: chronic intake of sources as browse, grazing or in conserved fodder (hay, haylage)

Clinical signs:

- weight loss → emaciation
- reluctance to walk, get up or lie down
- stiff gait
- stand with back arched
- cardiac murmurs
- recumbency → death
- foetuses affected (Gorniak *et al.* 1999)

Pathology:

- serum Ca & P ↑ 20-25%
- anaemia
- anasarca, ascites
- calcification of blood vessels & endocardium, pleura, lungs, tendons & ligaments

Diagnosis: access + pathology

Therapy:

- no effective therapy available
- signs subside if exposure to the plant is prevented, but resorption of the calcium deposits is minimal even after 5 years

References:

Se121
Arnold RM, Fincham IH (1997) Manchester wasting disease: a calcinosis caused by a pasture grass (*Stenotaphrum secundatum*) in Jamaica. *Trop. Anim. Hlth. Prod.* **29**:174-176.
Braun U, Diener M, Camenzind D, Flückiger M, Thoma R (2000) Enzootic calcinosis in goats caused by golden oat grass (*Trisetum flavescens*). *Vet. Rec.* **146**:161-162.
Copland JW (1975) Enzootic calcinosis of cattle in Papua New Guinea. *Aust. Vet. J.* **51**:326.
Gorniak SL, Dagli MLZ, Maiorka PC, Raspantini PC, Jerico MM (1999) Evaluation in rabbits of the fetal effects of maternal ingestion of *Solanum malacoxylon*. *Vet. Res. Commun.* **23**:307-316.

Glucosinolates

Syndrome names:

- Goitre including congenital goitre
- Atypical interstitial pneumonia
- Rumenitis
- Fatty haemorrhagic liver syndrome of poultry (suspected association with glucosinolates)
- Perosis (lateral slipping of tendon from hocks in poultry) (Cheeke 1998)

See sinapine under Amino Acids & Proteins for information on egg taint from rapeseed or canola meal.

Chemical structure:

Glucosinolates are glycosides of β-D-thioglucose (Cheeke 1998). Crushing (including mastication) of fresh glucosinolate-containing plant material releases the enzyme thioglucosidase (myrosinase) which hydrolyses glucosinolates to glucose, hydrosulphuric acid ion and a sulphur-and-nitrogen-containing aglycone (Seawright 1989). Further hydrolysis of the aglycone yields a thiocyanate, an isothiocyanate or an organic nitrile (Seawrigth 1989). Intestinal bacteria also contain thioglucosidase and may contribute to hydrolysis of glucosinolates (Seawright 1989). Each plant contains several different glucosinolates and thus may produce a variety of such products, the amount and type formed depend on the parts of the plants involved and how they are treated (Seawright 1989).

Sources:

Plant sources:

Family Brassicaceae (Cruciferae)

***Brassica* spp.**

Brassica juncea (Indian mustard, leaf mustard) (Ev210, 891)
Brassica napobrassica (swede turnip, rutabaga) (Ev210, 891)
Brassica napus (rape, canola) (Ev210, 891)
Brassica oleracea var. *acephala* (common kale, chou moellier) (Ev212, 891)
Brassica oleracea var. *botrytis* (broccoli, cauliflower) (Ev212, 891)
Brassica oleracea var. *capitata* (cabbage) (Ev212, 891)
Brassica oleracea var. *gemmifera* (Brussels sprouts) (Ev212, 891)
Brassica pekinensis (Chinese cabbage) (Ev213, 891)
Brassica rapa (turnips) (Ev213, 891)
Brassica tournefourtii (wild turnip) (Ev213, 891)

Crambe abyssinica L. (crambe, Abyssinian kale)
Sinapis spp. (mustards) (?)
Sinapis alba [= *Brassica hirta*] (white mustard) (?) (Ev215, 914)
Sinapis arvensis [= *Brassica sinapistrum, Brassica kaber*] (charlock) (?) (Ev215, 914)
Raphanus raphanistrum (wild radish)
Rapistrum rugosum (turnip weed) - contains cheirolin (Stocks *et al.* 1984)

Family Limnanthaceae

Limnanthes alba Hartweg ex Benth. (meadowfoam) - native to western North America

Meals produced as by-products of oil production from seeds ("oil seeds") of *Brassica napus* (rape, canola), *Sinapis* spp. (mustards) and *Crambe abyssinica* (crambe).