

Plants that produce dermatitis, photosensitivity and liver damage



ADVS 5860

Bryan L. Stegelmeier





Festuca arundinacea



Neotyphodium coenophialum









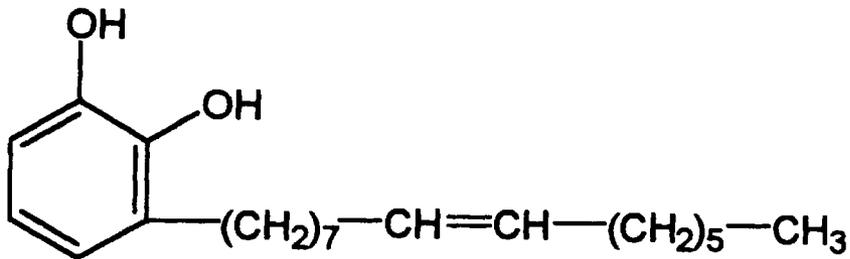
Primary Plant-Induced Skin Lesions

Contact Dermatitis:

- *Toxicodendron diversilobum* (poison oak) N.America, British Columbia, Mexico
- *Toxicodendron radicans* (poison ivy) All US
- *Toxicodendron vernix* (poison sumac) Mississippi river
- Cashew nut tree (*Anacardium occidentale*), Mango tree (*Mangifera indica*), and the Lacquer tree (*Toxicodendrum vernicifluum*)



Urushiol



Urushiol

- Urushiols, oleoresins are oxidized to quinones that bind to proteins



- Repeated exposures increase sensitivity
- Remarkable variability in allergic response
- Animals generally not sensitive
- Oral exposure often induces tolerance

Stinging Netles (*Urtica* spp.)

- Injected mixtures of histamines and platelet activating phospholipids
 - Dose dependent response and recovery
- Other irritants- Leafy spurge (*Euphorbia esula*), Buttercup (*Ranunculus* spp.)



Contact Dermatitis

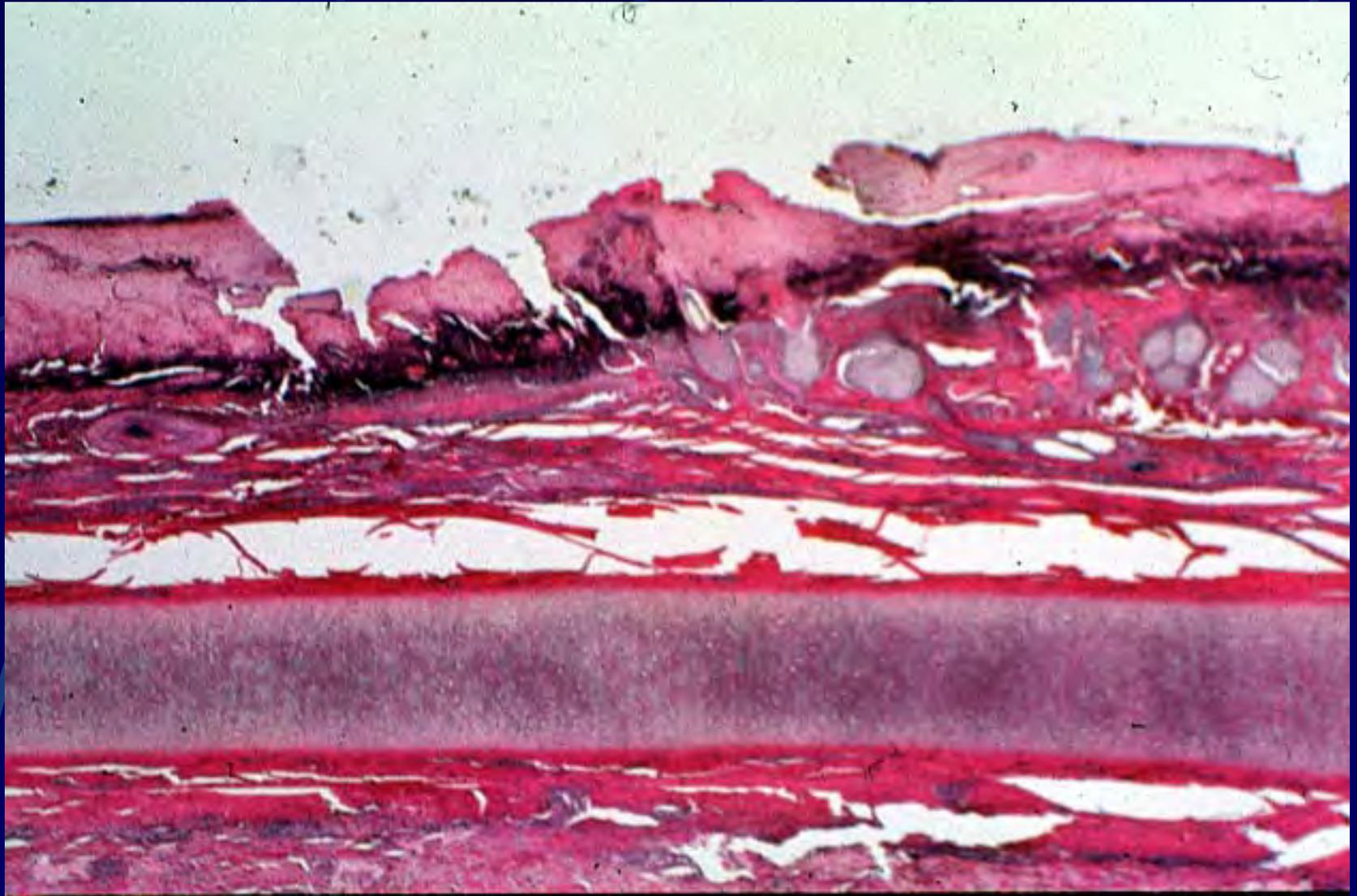


Photosensitization

- Erythema
- Edema
- Intense pruritis (rubbing, scratching, and kicking affected parts)
- Marked exudates
- Necrosis (skin dries and sloughs in desiccated sheets)
- Affects unpigmented, glabrous or lightly haired areas (upper surfaces of ears of sheep, muzzle, eyelids etc.)
- Photophobia and lacrimation.







- **Photodynamic agents** (chromophores) can chemically absorb specific wavelengths of light (UV or visible- activation spectrum) raising it to a metastable triplet state. This may react with adjacent cellular proteins/membranes or nucleic acids or it may react with molecular oxygen. This may produce reactive oxygen intermediates such as superoxide anion, singlet oxygen and hydroxyl radical. This may result in chains of free radical formation resulting in additional protein, nucleic acid or lipoprotein damage.
- **Type I Photosensitization** the photodynamic agent is exogenous
- **Type II Photosensitization** an aberrant endogenous pigment is photodynamic
- **Type III Photosensitization** is produced by phylloerythrin as a result of hepatic dysfunction (hepatoendogenous photosensitization)

Primary Photosensitization

Results from ingestion or direct absorption of photodynamic agents. Most are of plant origin (St John's wort *Hypericum perforatum*, Buckwheat *Fagopyrum* spp., Spring parsley *Cymopterus watsoni*, and *Ammi* spp. Some drugs are also photodynamic- anthelmintic phenothiazine.

St. John's Wort (*Hypericum perforatum*)

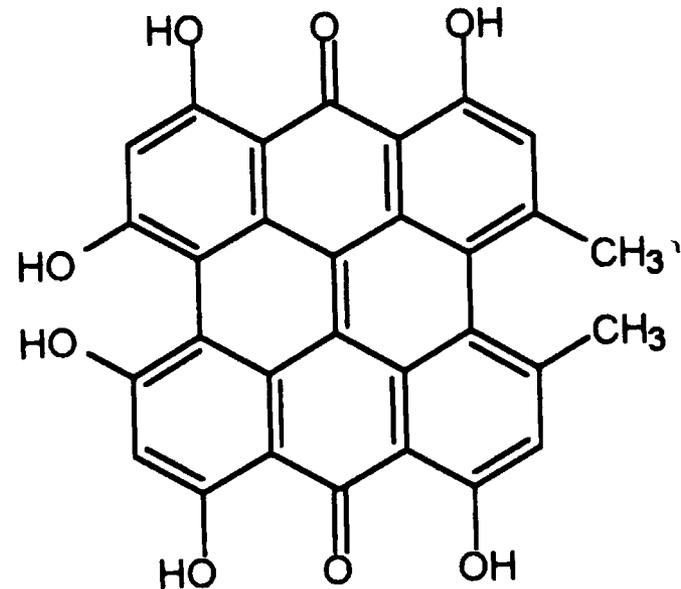
- Perennial that grows along roadsides and in meadows, pastures, rangelands, and waste places.
- Generally it is a 0.5 to 2 tall, smooth-branched, erect plant. The leaves are covered with clear, small dots that contain the toxic substances (hypericin). Five-petaled flowers grow in clusters; they are orange-yellow with occasional black dots along the edges. After maturity, flowers wilt and the entire plant turns brown.
- Pacific Coast states, Europe, Australia, New Zealand, and South America.
- Dry, gravelly, or sandy soils in full sunshine forming dense patches or mixed among other plants.
- Noxious weed in many states





St. John's Wort (*Hypericum perforatum*)

- Pathogenesis: Ingests St. John's wort, hypericin circulates to the skin, sensitizes the skin to sunlight, white or unpigmented areas damaged.



Hypericin



Signs: Lesions itch, become red, swollen, and sore, and the skin may peel or come off in large sheets. Lesions usually appear 2 to 21 days after ingestion.

Most palatable in the spring. Mature plant unpalatable to cattle and sheep, hay containing dry St. Johns wort is poisonous. Cattle poisoned at approximately one percent of their body weight and are then exposed to direct sunshine for 2 to 5 days. Sheep fed 5 percent of their body weight develop symptoms.

St. John's wort has been traditionally used as an herbal medicine and hypericin has been associated with both antiviral and antidepressant activity.



Leaves

Leaves contain antidepressant compounds that regulate levels of dopamine, interleukins, melatonin, monoamine-oxides, and serotonin.

Flowers

Used fresh in olive oil as a treatment for external ulcers, wounds, cuts, and bruises. Flower tea is folk remedy for bladder problems, worms, dysentery, and diarrhea.

Notes:

St John's Wort outsells Prozac 20-to-1 in Germany. Contains compounds such as hypericin and pseudohypericin which may have anti-retroviral activity and are being researched for AIDS effectiveness. Not proven effective treatment for severe depression, and internal or external use may cause skin to be extra sensitive to light.

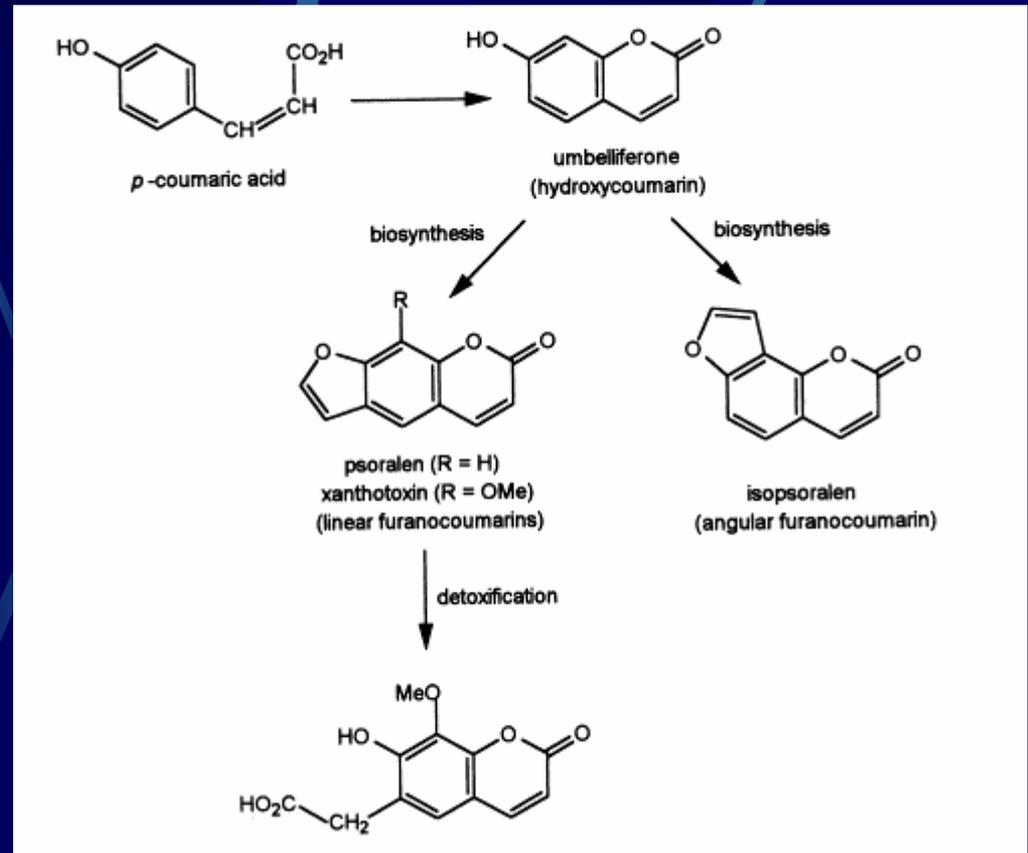
Buckwheat (*Fagopyrum esculentum*)

- Fagopyrin- hypericin with C₆H₁₁ON side chain attached to each methyl group.
- Buckwheat is sometimes grown as a grain or forage
- Reports of sheep photosensitization in Australia



Furocoumarins

- Furan ring fused with a coumarin nucleus (psoralen derivatives)
- Furocoumarins are primary plant cpds and phytoalexins (fungal pathogens)



Spring Parsley (*Cymopters watsonii*)

- Perennial 8-12 cm tall, parsley like leaves, small white or cream-colored flowers in umbrellalike clusters, long taproot (carrot family).
- Poisonous from early spring until they mature and dry in early summer.
- well-drained soils on rolling foothills at 1500 to 3500 meters. Grows in early spring with flowers from late April to June and disappears by early summer.
- Noxious weed that often invades pastures and rangelands.

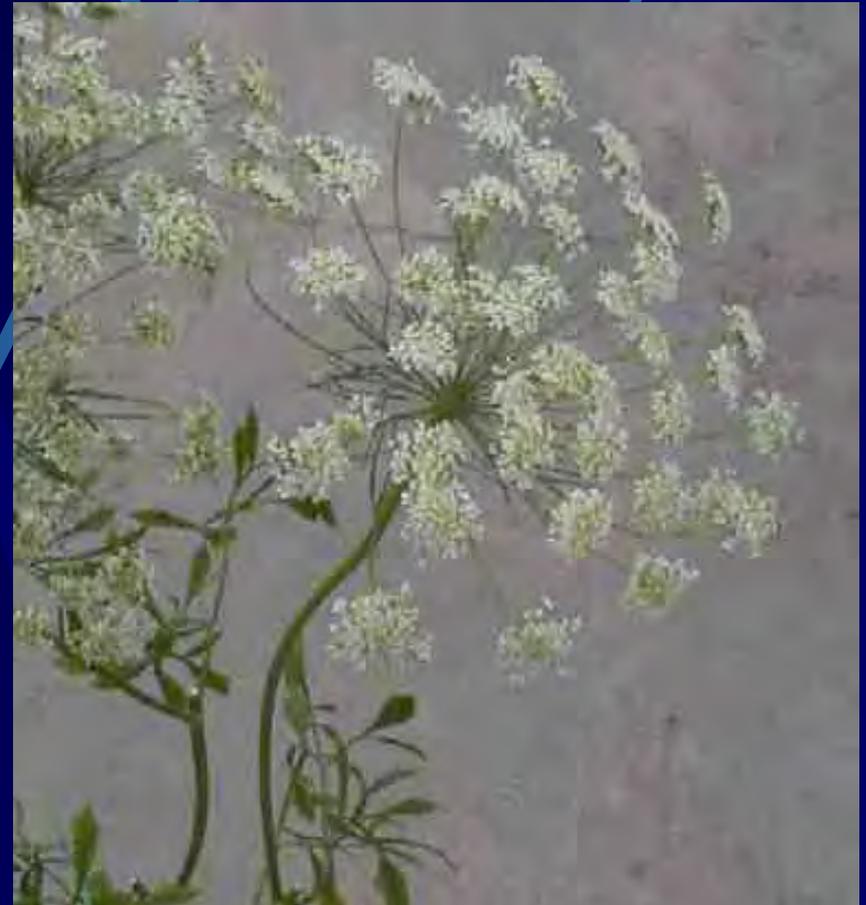


- Reddening and blistering of exposed areas of the body (nose, udder, external genitals), Scabs form after blistering, Ewes and cows may refuse to allow young to nurse.
- Sheep poisoned with 200 gm of the green plant.
- Cattle are affected after eating about one pound of the green plant.
- All recover gradually.



Bishop's Weed (*Ammi majus*)

- Carrot like weed found in central and southern states that is sporadically linked to photosensitivity in cattle and sheep



Dutchman's Breeches (*Thamnosma texana*)

- Perennial weed of the southwest
- 9 psoralens (xanthotoxin and bergapten)
- Affects both cattle and sheep



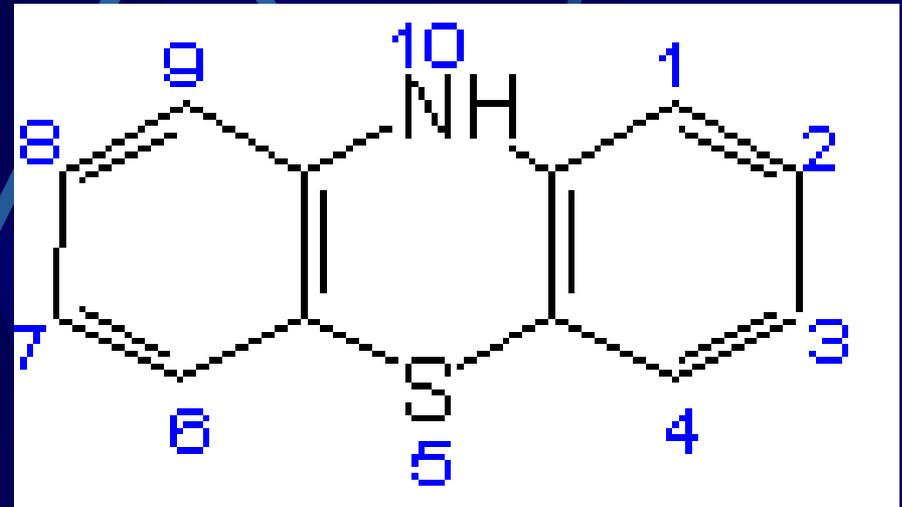
Celery/Parsnip Dermatitis

- Phytoalexins (xanthotoxin and trisoralen) that develop on celery in response to fungal infection.
- Phytophotocontact dermatitis in pigs (New Zealand parsnips and celery)



Phenothiazine photosensitization

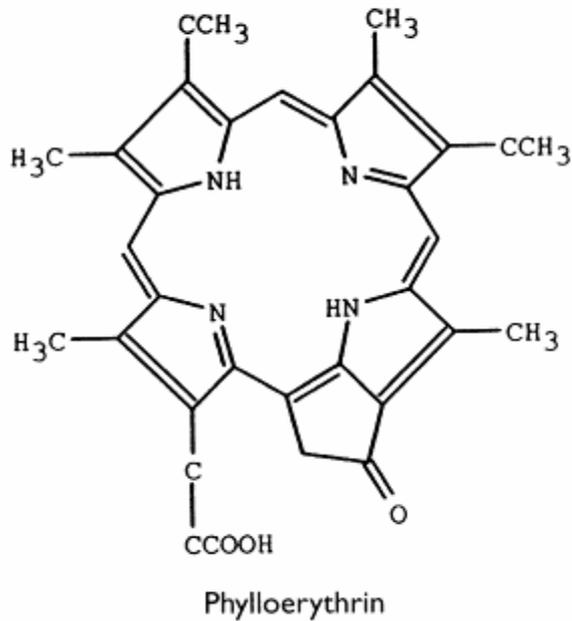
- Corneal edema, keratoconjunctivitis from rumen metabolite-phenothiazine sulfoxide excreted in tears and aqueous humor. Most common in calves but also seen in sheep, swine and birds.
- Sulfonamides and tetracyclines also in humans



Photosensitization Due to Defective Pigment Synthesis

- **Bovine congenital erythropoietic porphyria**
 - Uroporphyrinogen III cosynthetase
 - Simple recessive trait in Shorthorn, Ayrshire, Holstein, and Jamaican Cattle
 - Osteohemochromatosis and pink tooth
 - Porphyrinuria and hematoporphyrinuria
 - Uroporphyrins
- **Bovine erythropoietic protoporphyria**
 - Limousin cattle
 - Ferrochelatase cause photodermatitis (no color abnormalities)

Hepatogenous Photosensitization (Secondary Photosensitization)



- Photosensitization caused by increased circulating phylloerythrin concentrations. This is the most common cause of photosensitization in livestock and it is secondary to hepatic injury altering hepatic phylloerythrin excretion. Phylloerythrin is formed by intestinal degradation of chlorophyll. It is normally excreted in the bile.

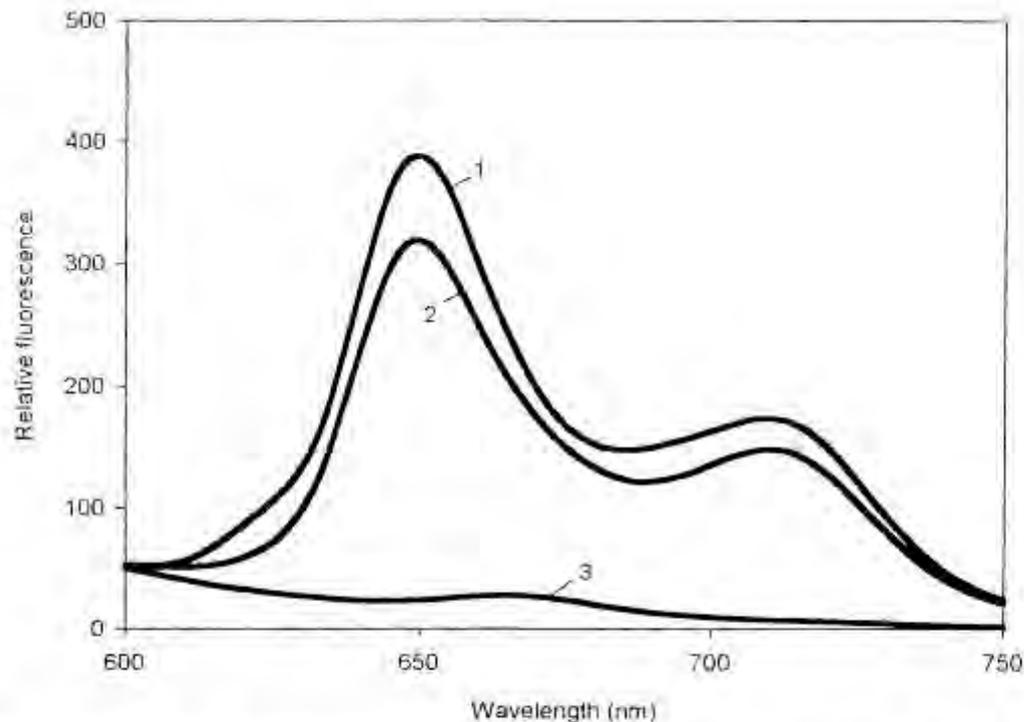


Fig. 23.1. The fluorescence spectra of plasma obtained from a healthy lamb to which phylloerythrin had been added (curve 1), from a photosensitized lamb 17 days after being dosed with $0.25 \text{ mg sporidesmin kg}^{-1}$ bodyweight for 2 consecutive days (curve 2) and from a control (curve 3). The maximum of the shorter wavelength band occurs at 649 nm and the longer at 709 nm. Excitation wavelength was 422 nm for all spectra.

Scheie 2003



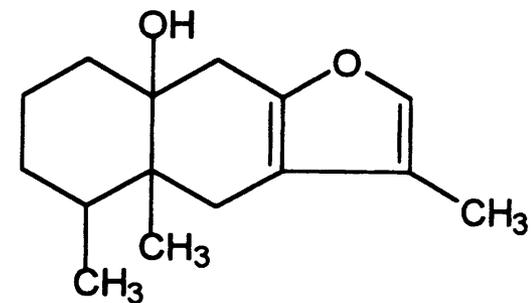
- *Senecio, Amsinckia, Crotolaria, Heliotropium, Cynoglossum and Trichodesma*
- *Tetradymia*
- *Lantana*
- *Ryegrass debris (Sporodesmin)*
- *Xanthium*
- *Phyllanthus*
- *Cassia/Senna*
- *Cestrum*
- *Drymaira*
- *Vicia*
- *Galenia*
- *Tribulus*
- *Agave lechuguilla*

Black sage and (*Tetradymia* spp.) Bighead in Sheep

- Two species of horsebrush that grow in the Great Basin region of the West are poisonous to sheep.
- Littleleaf horsebrush (*Tetradymia glabrada*) is commonly called coal-oil brush and spiny rabbitbrush.
- Spineless horsebrush (*T. canescens*) is also called gray horsebrush



- Furanoeremophilanes (furanosquiterpenes) known as tetradymol.
- Metabolized by hepatic mixed function oxidases and they uncouple oxidative phosphorylation.
- In sheep less than 0.5 kg of the littleleaf brush will cause bighead. Larger amounts may result in death.
- Less toxic, nearly twice as much spineless horsebrush must be eaten to cause similar symptoms.
- Synergy with black sagebrush.

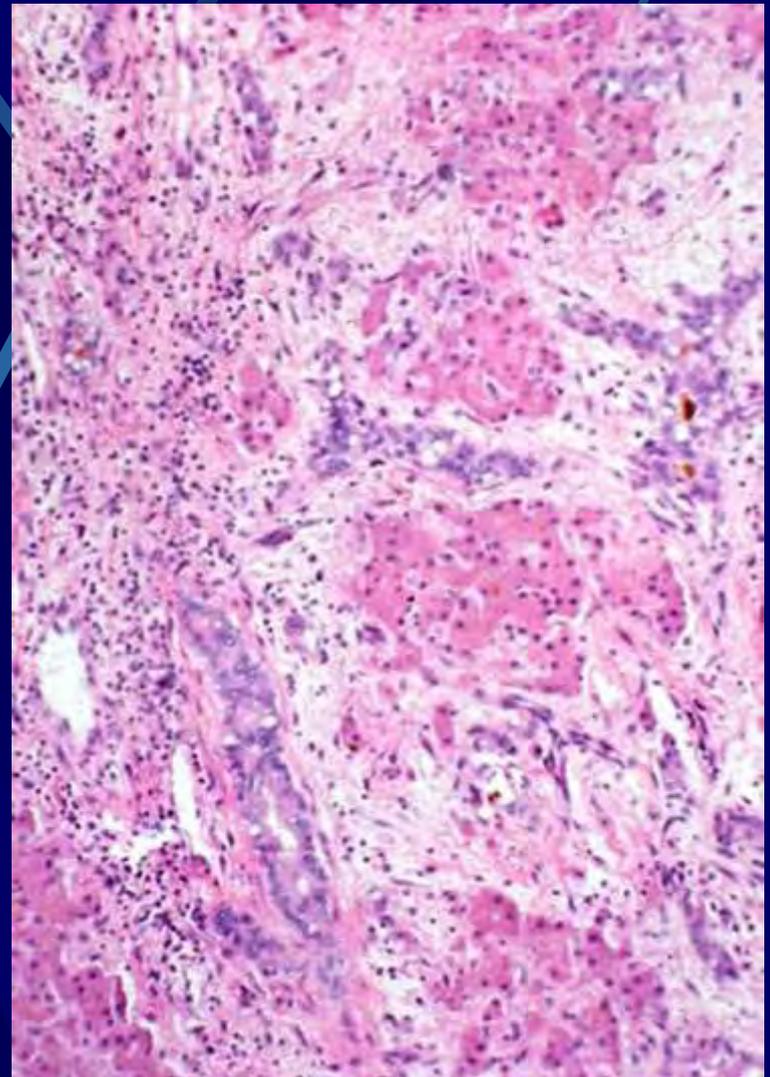


Tetradymol

Loss of appetite, depression, lagging behind the herd, weakness, recumbency, and death, itching and uneasiness, swelling of lips, ears, eyelids and cheeks, serum may ooze from sores and scabs, animals seek shade, peeling of skin from face and ears, abortion may occur, liver swollen, engorged, and often shows severe fatty changes, nephritis, petechial hemorrhages on serosal surfaces



- Severe liver necrosis
- Photosensitization, loss of appetite, depression, lagging behind the herd, weakness, recumbence, and death (within a day or two)
- Itching and uneasiness, swelling of lips, ears, eyelids and cheeks, serum may ooze from sores and scabs, animals seek shade, peeling of skin from face and ears, abortion may occur
- Liver swollen, engorged, and often shows severe fatty changes, nephritis, petechial hemorrhages on serosal surfaces

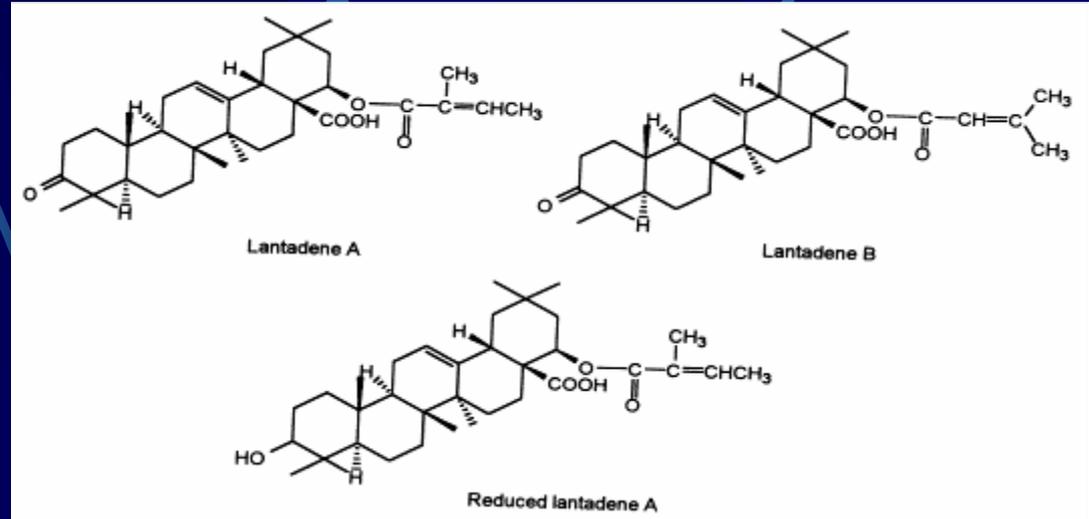


Lantana (*Lantana camara*)

- Oranamental vine native to central and south America. Found as weed in southern US from Florida to California.



Toxins are triterpenoid cpds- Lantadenes A and B are hepatotoxins that are activated by microsomal enzymes and cause intrahepatic cholestasis. Lantadene metabolites damage canaliculi membranes.



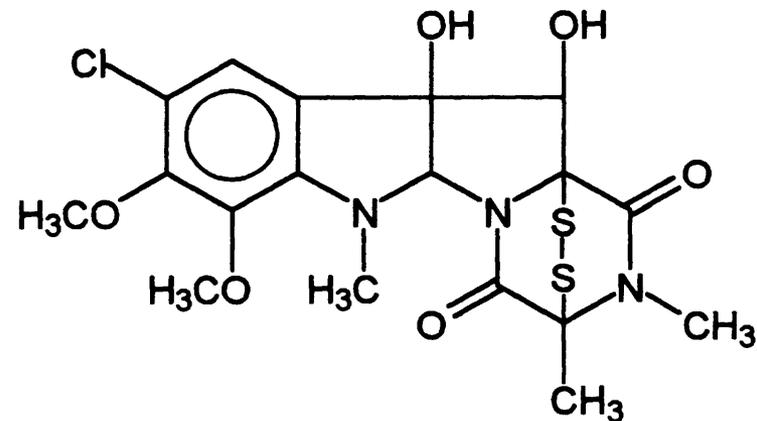
Lantana lesions

- Jaundice, rumen stasis, photosensitization, anorexia, dehydration and death
- Liver is firm, enlarged and yellow
- Acutely toxic at about 1% BW
- Toxicity has been reported in horses



Sporidesmin from *pithomyces chartarum* causing facial edema of Australia, New Zealand and South Africa

- Sporidesmin is an hepatotoxic mycotoxin produced by *Pithomyces chartarum* that grows in dead litter of ryegrass pastures
- Sporidesmin A is most toxic (B,C,D,E,F, G, and H are less toxic). Spore levels rise during warm wet weather. Can be seen as a cloud of black dust if disturbed.
- Disulfide bridge is important for toxicity.



- Sheep stop grazing, become restless, shake their heads and rub their eyes and ears against solid objects. The ears swell and droop. The lips and eyelids may scab. Cattle also affected.
- 20-25 mg/kg zinc oxide or iron supplements may protect sheep
- recently several cases of ryegrass toxicity have been described in the northwest.

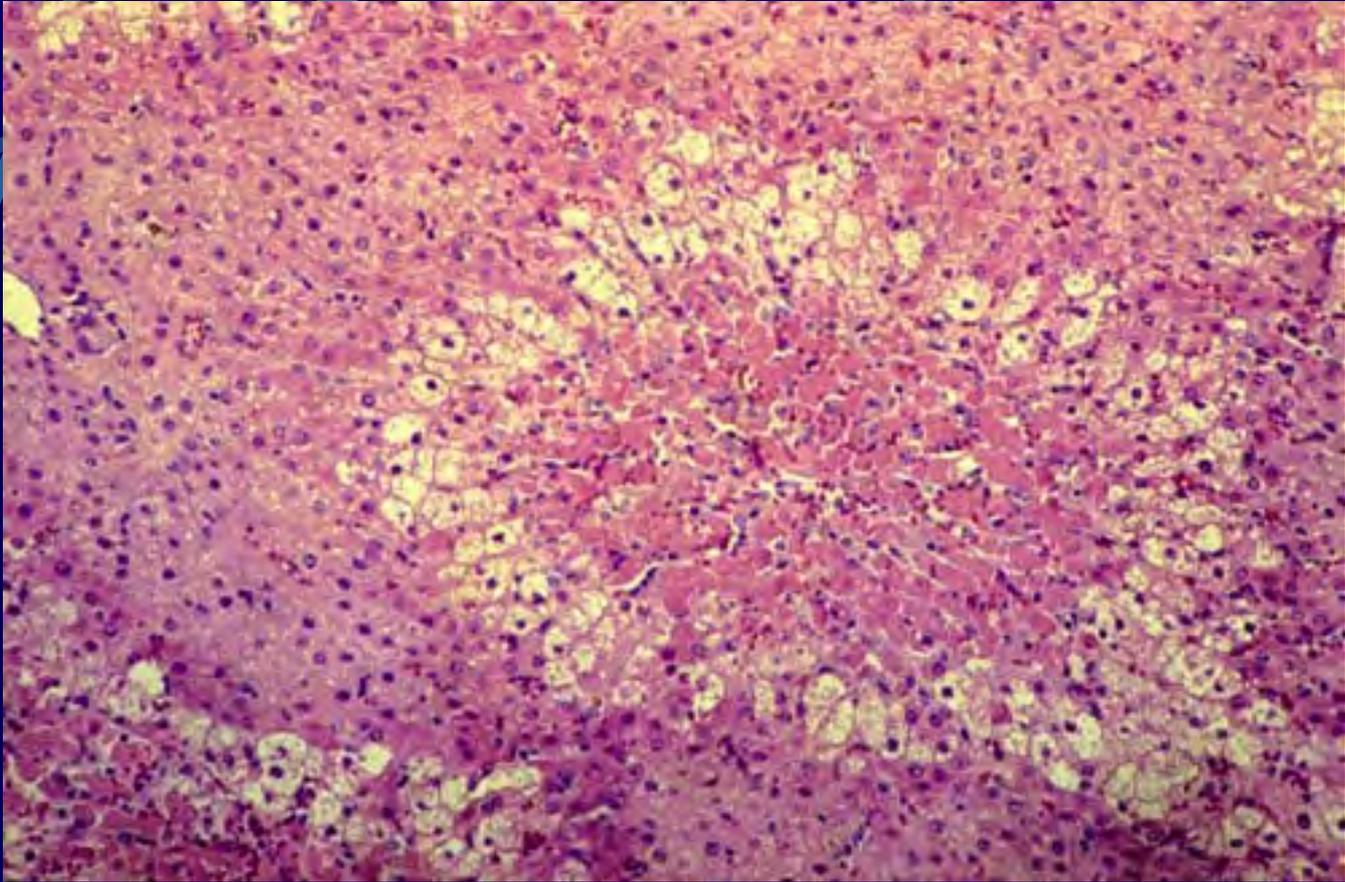


Cocklebur (*Xanthium* spp.)

- Carbosyatractyloside
- Atractyloside
- Kaurene glycoside

- Pigs- periacinar necrosis

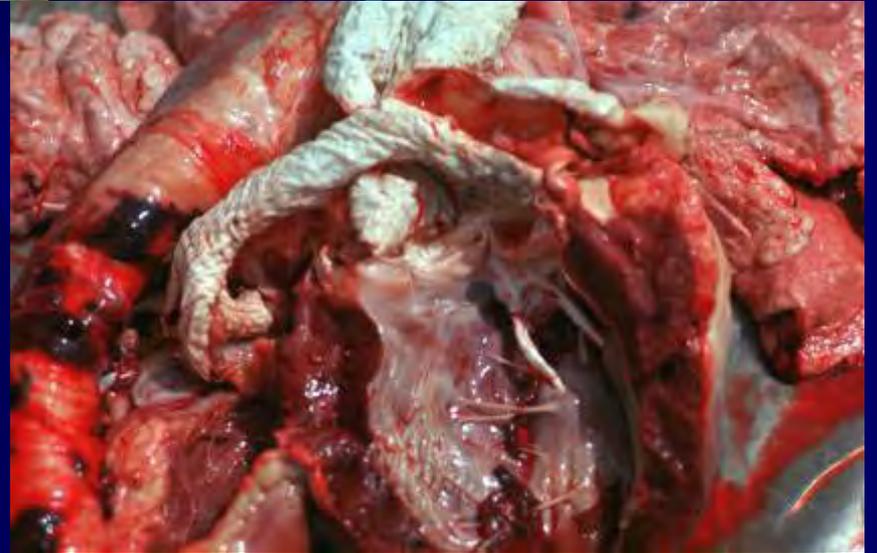


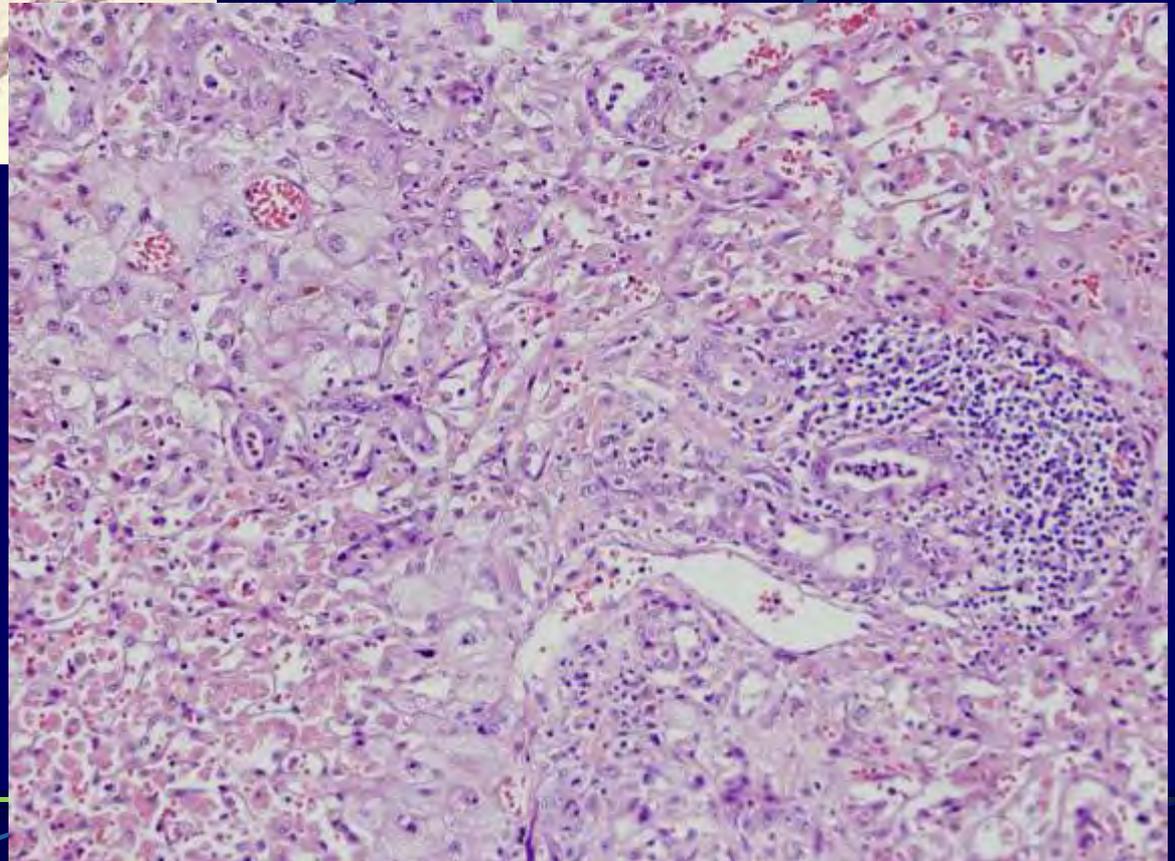
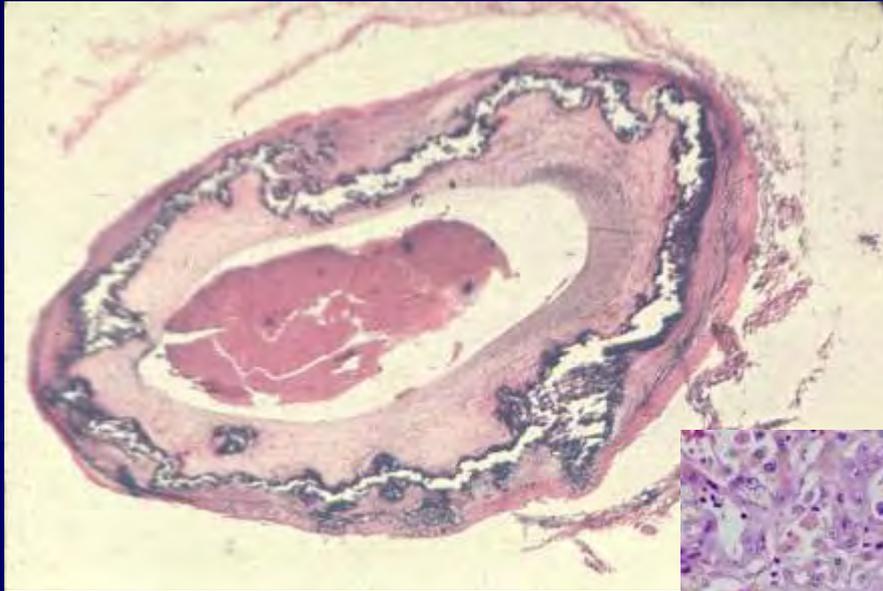


Cestrum diurnum

- 1,25-dihydroxycholecalciferol
- Dystrophic calcification
- Kaurene glycosides-carbox; yparquin and parquin (similar to carboxytractyloside)







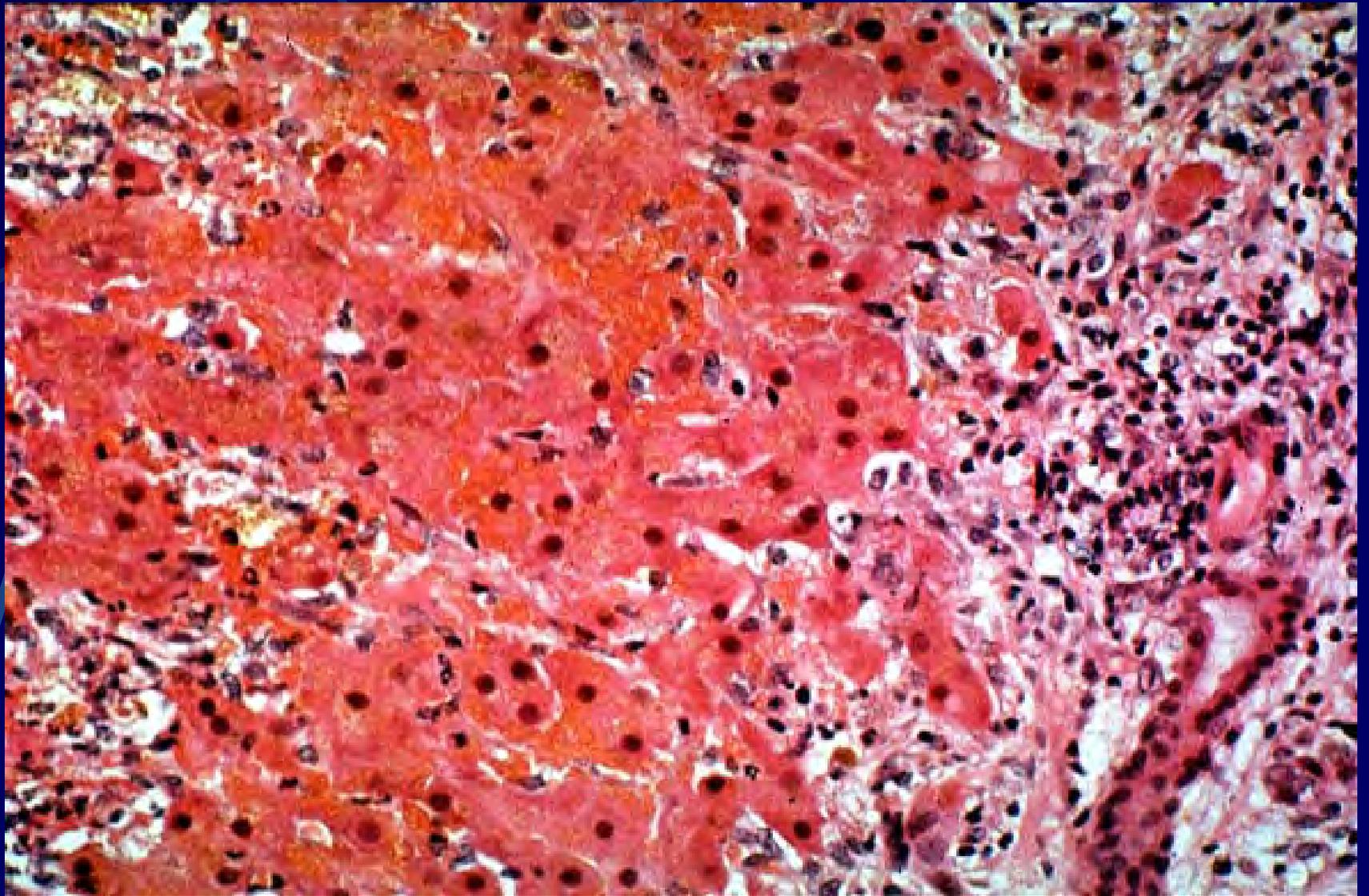
Drymaria arenarioides and *D. pachyphylla*

- Texas, New Mexico, Arizona
- Saponins? Glycoside of githagenin
- Mild periacinar necrosis

Alsike clover (*Triflorum hybridum*)

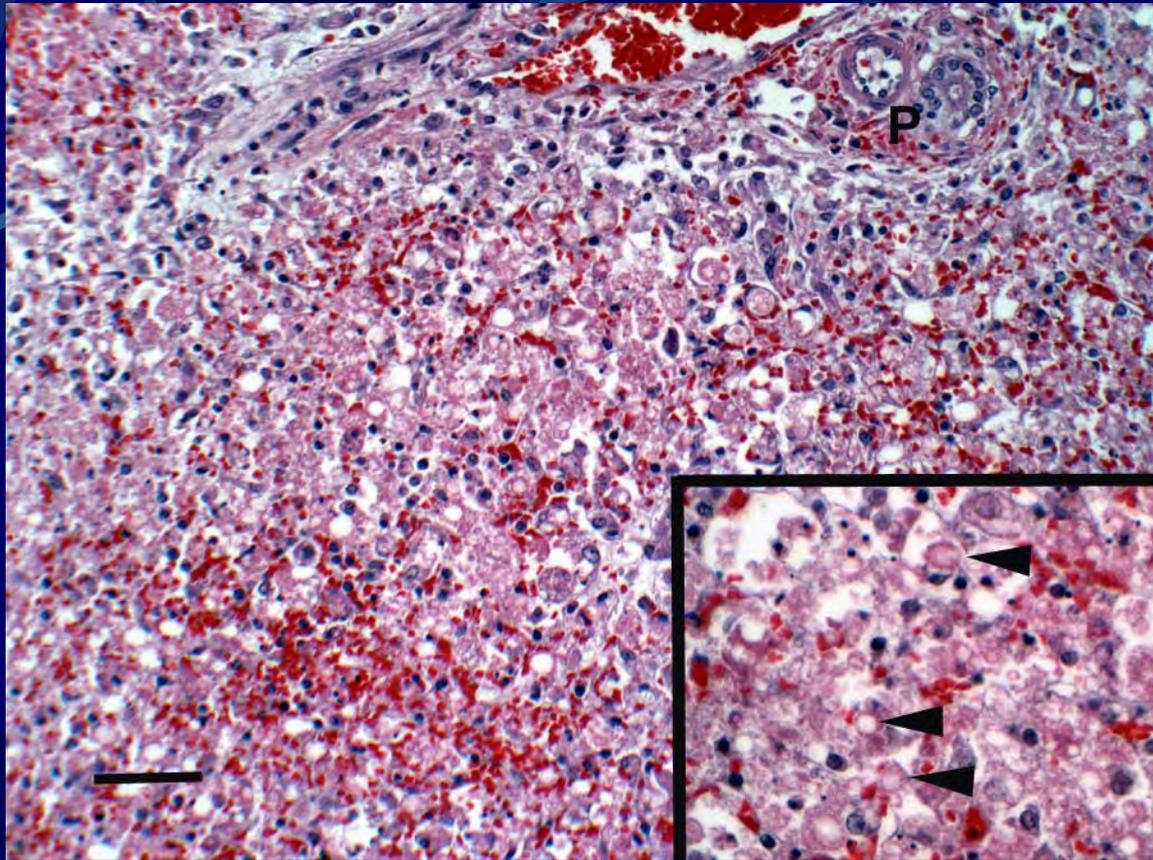
- Probably an aflatoxin
- Neurologic disease and hepatic failure
- Enlarged, fibrotic liver (bile duct proliferation and fibrosis)







Microcystis spp.



Microcystin microtubular collapse

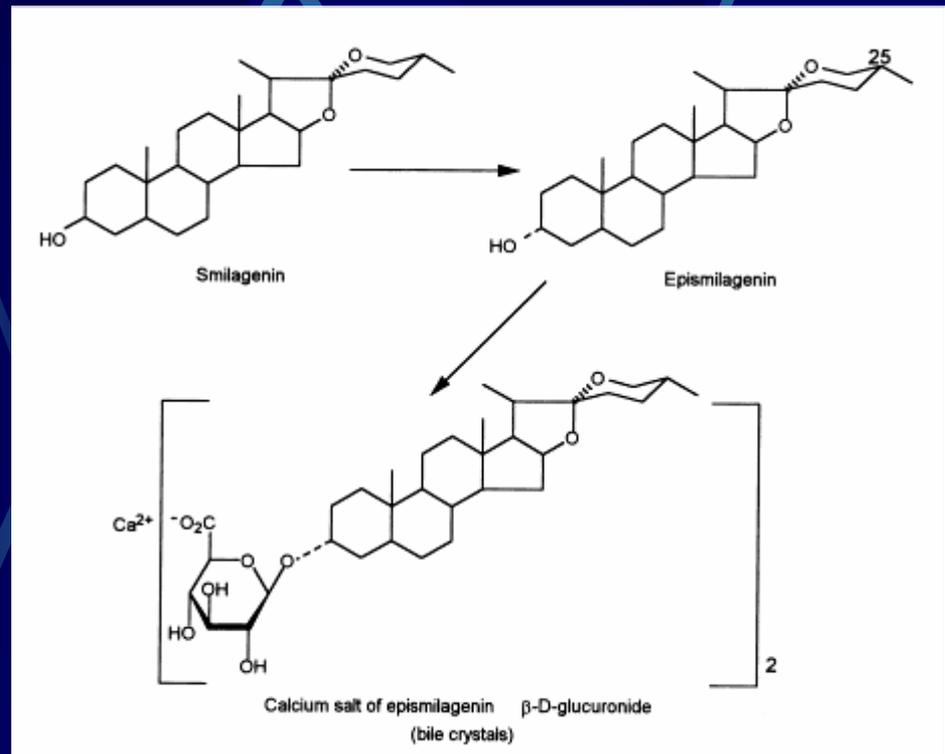
Panicum and *Brachiaria* spp.

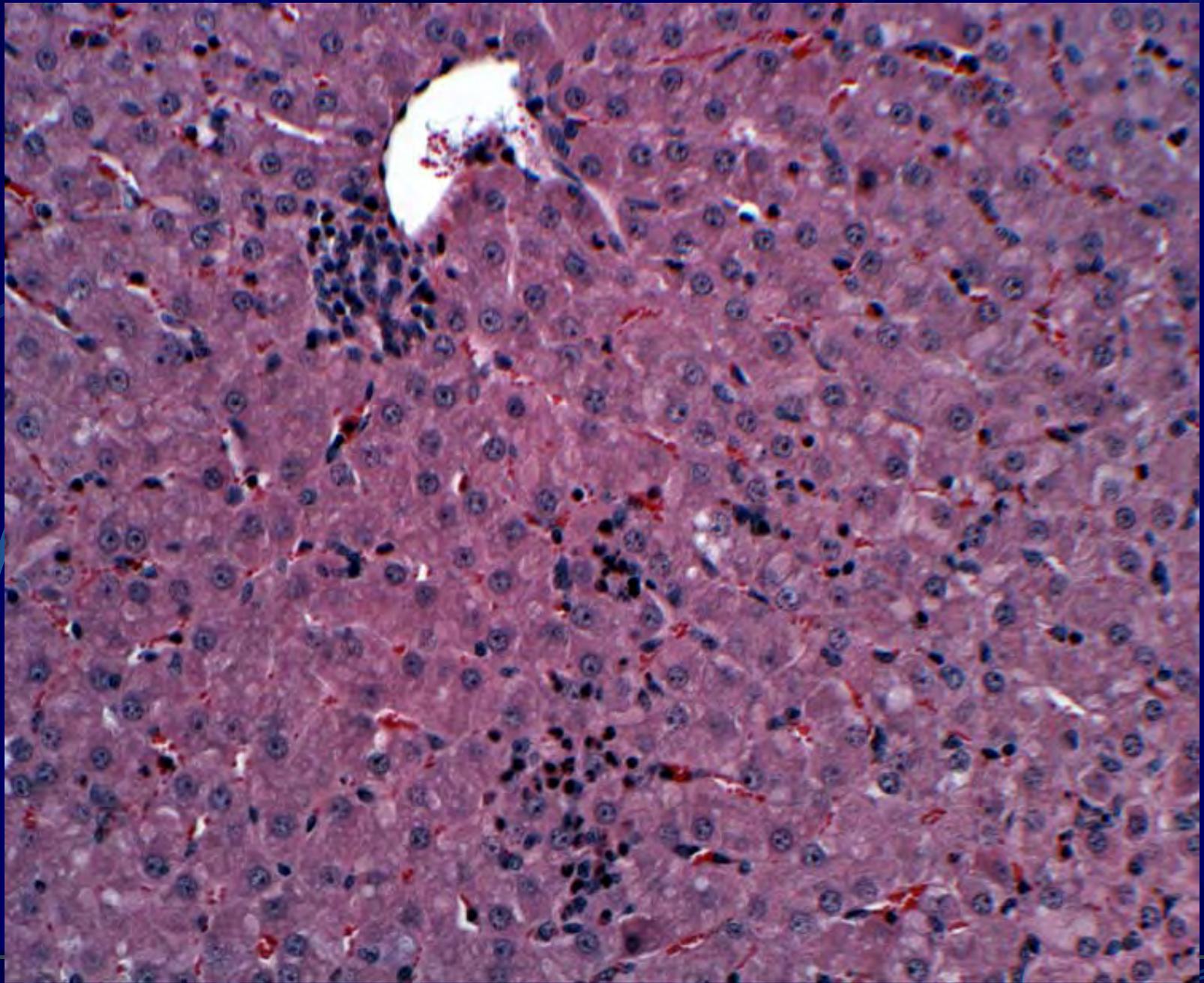
- Kleingrass (*Panicum coloratum*) common cause of photosensitization in sheep and horses in Texas.
- Switchgrass (*Panicum virgatum*) lambs in West Virginia
- Signalgrass (*Brachiaria decumbens*) cattle in tropics





- Liver damage caused by peribillary deposition of crystalline steroidal saponins glucuronides
- Saponins probably do not cause all the liver damage, but other mycotoxins such as sporidesmin probably contribute to toxicity





Geeldikkop (yellow head disease)

- Sheep and goats in South Africa
- *Tribulus* spp. causing lesions similar to *Panicum* spp. with insoluble calcium salts of saponin glucuronides.
- Puncture vine (*Tribulus terrestris*)



Other plants causing crystalline hepatopathy

Agavae lecheguilla (desert plant)
Nolina texana (beargrass, sacahuiste of the southwest),
Narthecium ossifragum (ALVELD (Elf Fire Bog asphodel



Lupinosis

- Ingestion of toxins produced by the fungus *Phomopsis leptostromiformis* that grows on lupin
- Toxins are phomopsins that inhibit cell mitosis by inhibiting microtubule polymerization
- Hepatic necrosis with subsequent jaundice and secondary photosensitization.



Other Potential Hepatotoxic Plants



- Kochia
- Tansymustard (*descurainia pinnata*) circumstancially linked with photosensitization in cattle and to wooden tongue
- Cicer milkvetch (*Astragalus cicer*)
- Birdsfoot trefoil (*Lotus corniculatus*)
- Moldy straw

- **Other causes of liver disease:**
- **Chemicals: carbon tetrachloride**
- **Infectious: Leptospirosis**
- **Immune mediated disease: Theiler's disease**

Reading Assignment

Natural Toxicants in Feeds, Forages and
Poisonous Plants. Peter Cheeke

Contact Dermatitis from plants pg 445

Photosensitization 451

Lantana Poisoning 353

Blue-Green Algae 354

Saponins 281

Alsike Clover Poisoning 293

Facial Eczema and Sporodesmin 257

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