Toxicants that Cause Skin Damage by Primary Photosensitization

V. Beasley

Department of Veterinary Biosciences, College of Veterinary Medicine, University of Illinois at Urbana-Champaign, Urbana, IL, USA.

Hypericum - St. Johnswort

Hypericum perforatum - St. Johnswort, klamath weed, goatweed, amber, goats beard, Tipton weed, Eolaweed, Pennyjohn, raisin rose, herb john, commock

H. punctatum

H. concinnum

Family - Hypericaceae (St Johnswort family)

Images

- St. John’s wort (Hypericum perforatum). Source: Cornell University, Poisonous Plants Informational Database (www.anisci.cornell.edu/plants/index.html). - To view this image in full size go to the IVIS website at www.ivis.org . -
- Dotted St. Johnswort (Hypericum punctatum) - U.S. G.S. Northern Prairie Wildlife Research Center. - To view this image in full size go to the IVIS website at www.ivis.org . -
- St. Johnswort, Hypericum perforatum - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org . -
- Dotted St. Johnswort, Hypericum punctatum - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org . -
- Gold wire, Hypericum concinnum - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org . -

Description

- Hypericum perforatum.
  - Plant - Perennial herb, erect, 1 - 2.5 feet high.
  - Stem - Main stems are usually clustered, woody below, many lateral, opposite branches, slender, produces runners from the base, glabrous, dark rings about the nodes, 2-edged.
  - Flowers - Numerous, deep yellow, leafy, flat-topped, petals, numerous with black dots on margins, stamens numerous, sepals, 5, lanceolate, acute, 5 - 7 mm long.
  - Fruit - 3-valved capsule with numerous seeds. Seeds are cylindrical, slightly pointed at ends, dark brown, mottled with rows of minute depressions, shiny and barely 1 mm long.
Rootstock - Underground rhizome.
Tiny translucent spots visible on leaf surfaces, when the leaf is held toward a light (thus the species name "perforatum").

Habitat

Europe, now naturalized in most of North America, especially troublesome in the western USA from Oregon to California and the plains states. Roadsides, overgrazed pastures, abandoned fields, open woods, sandy or infertile soils.

Toxic Principle

Hypericin, a fluorescent pigment which is a dianthrone derivative.

Susceptible Species

- Cattle, sheep, horses, goats, rabbits.
- Especially breeds with large areas of unpigmented skin.

Toxicity

- Sheep.
  - Consumption of approximately 5% of the body weight may produce toxicosis.
  - Readily grazed when succulent.
- Cattle.
  - Consumption of approximately 1% of the body weight may produce toxicosis. Partially detoxified by drying.

Absorption, Distribution, Metabolism and Excretion (ADME) and Mechanism of Action

- Hypericin remains intact upon ingestion, is absorbed and passes through the liver; the liver remains undamaged.
- The hypericin, therefore, reaches the general circulation and cutaneous structures.
- Molecular oxygen is required for reactions in the skin which cause the photosensitive reaction.
- There is no accumulation of phylloerythrin in St. Johnswort poisoning.
- Ordinarily glass or a layer of water will not protect against St. Johnswort photosensitization, which differentiates it from sunburn.

Signs

- Signs appear within 24 hours of ingestion.
- Increased respiration, heart rate and body temperature.
- Slight diarrhea, marked salivation.
- Mild dermatitis, pruritis, ulceration.
- Affected animals may immerse themselves in water.
- May be hyper-reactive to cold water.
- Convulsions and death may occur after ingestion of large quantities, but this rarely occurs on pasture.
- With the more common and chronic syndrome, the primary signs include: severe erythema of the conjunctiva and buccal mucous membranes, blindness, feed refusal and death due to starvation.

Diagnosis

Identification of Hypericum, evidence of consumption and accompanying (appropriate) clinical signs and lesions.

Treatment

- Keep in shade, pasture at night away from source of plant.
- Supportive care.

Comment

Black-skinned animals are rarely affected with photosensitization of any type. In St. Johnswort poisoning of Holstein cattle, the black pigmented areas were unaffected while the skin of white areas was inflamed and large sloughs occurred.
St. Johnswort, *Hypericum perforatum* L. - 1, plant in flower; 2, portion of stem with leaves; 3, flower and buds; 4, stamens and ovaries; 5, seed. Perennial, reproducing by seeds and rootstocks. **Root** system branched and extending to considerable depth. Shallow, short rootstocks extend out several inches from crown. **Stems** smooth, branched, erect, somewhat 2-edged, 1 to 2 feet (30 to 60 cm) tall, woody at base. **Leaves** opposite, elliptic to oblong, covered with small clear dots. **Flowers** about 3/4 inch (1.9 cm) in diameter, 5-petaled, orange-yellow with occasional black dots along edges of petals. **Seed pods** rounded, pointed, with 3 parts and many seeds. **Seeds** about 1/16 inch (1.5 mm) long, cylindrical, blackish, shiny with a rough, pitted, resinous surface. **Found** in pastures, meadows, rangelands and along roadsides. Not relished by grazing animals; may cause skin irritation and loss of condition in livestock, especially white animals. Also commonly known as Klamath weed.
Common St. John's-Wort (*Hypericum perforatum* L.)

**Family** - St. John's-wort (Hypericaceae).

**Growth Form** - Perennial herb from fibrous roots.

**Stems** - Upright, branched, smooth, sometimes slightly woody at the base, up to 2 feet tall.

**Leaves** - Opposite, simple, oblong, black-dotted, without teeth, smooth, up to 3/4 inch long.

**Flower Arrangement** - Flowers many, in terminal cymes.

**Flowers** - Yellow, up to 1 inch across.

**Sepals** - 5, green, pointed.

**Petals** - 5, yellow, black-dotted along the edges, free from each other.

**Stamens** - Usually 3 groups of five.

**Pistils** - Ovary superior; styles 3.

**Fruits** - Capsule ovoid, about 1/4 inch long, many-seeded.

**Habitat** - Fields, pastures, roadsides.

**Range** - Throughout the state.

**Time of Flowering** - June to September.

**Associated Plants** - Common milkweed (*Asclepias Syriaca*), Fleabane (*Erigeron Strigosus*), white prairie clover (*Melilotus alba*), and field goldenrod (*Solidago nemoralis*).

---

Spotted St. John's-Wort (*Hypericum punctatum* Lam.)

**Family** - St. John's-wort (Hypericaceae).

**Growth Form** - Perennial herb.

**Stems** - Upright, sometimes woody at the base, smooth, up to 7 feet tall.

**Leaves** - Opposite, simple, oblong to broadly lanceolate, rounded to pointed at the tip, rounded at the base, black-dotted, without teeth, smooth, up to 3 inches long, without a stalk.

**Flower Arrangement** - Many flowers in terminal cymes.

**Flowers** - Yellow, about 1/2 inch across, borne on short stalks.

**Sepals** - 5, green, free to the base, pointed at the tip.

**Petals** - 5, yellow. Black-dotted throughout, more or less rounded at the tip.

**Stamens** - Many, grouped together in sets of 5.

**Pistils** - Ovary superior; styles 3.

**Fruits** - Capsule ovoid, about 1/4 inch long.

**Habitat** - Roadsides, fields, and woods.

**Range** - Throughout the state.

**Time of Flowering** - July and August.

**Associated Plants** - Milfoil (*Achillea millefolium*), black-eyed Susan (*Rudbeckia hirta*), and tall goldenrod (*Solidago can? densis*).
**Fagopyrum - Buckwheat**

*Fagopyrum esculentum* - *F. sagittatum, Polygonum fagopyrum*, Buckwheat

<table>
<thead>
<tr>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herbivores</td>
<td>Within 24 hours to weeks</td>
<td>Days to weeks, rarely lethal</td>
</tr>
</tbody>
</table>

| **Family** - Polygonaceae (buckwheat family) |

**Images**

- Buckwheat (*Fagopyrum esculentum*). Source: Cornell University, Poisonous Plants Informational Database (www.ansci.cornell.edu/plants/index.html). - To view this image in full size go to the IVIS website at www.ivis.org . -
- Buckwheat, *Fagopyrum esculentum* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org . -

**Description**

- Plant - Small grain crop, annual.
- Leaves - Triangular, heart-shaped, with semicylindrical sheaths.
- Flowers - 8 honey-bearing yellow glands; calyx is petal-like and equally 5-parted; stamens - 8, styles - 3, racemes of white, greenish or rose- colored flowers.
- Fruit - Achene, acute and entire, smooth and shiny, 3-sided.

**Habitat**

- Europe; northeastern USA.
- Cultivated, seeds are used in human diet, and whole plant is fed to stock.
- Also planted as ground cover, for green manure and occasionally as a forage plant.
- Used in pancake flour for human use.

**Poisonous Principle**

- The poisonous principle is still the subject of some debate. It is most often asserted that toxicity is due to a fluorescent substance, the naphthodianthrone derivative fagopyrin. It has, however, also been suggested that a fungal metabolite may be involved.

**Susceptible Species**

All livestock with unpigmented skin. Humans are more often affected with allergy than photosensitization.

**Toxicity**

- All parts are capable of producing photosensitization in livestock.
- Moderate to large quantities of dry or green plant or seed may cause photosensitization.
- White Yorkshire pigs from 3 months of age to old brood sows developed signs in 24 hours after being placed on a flowering buckwheat field.

**Signs and Lesions**

- Signs may appear from 24 hours to several weeks after the first ingestion.
- In acute cases, nervous signs also may occur.
"Fagopyrism" is the name given to the photosensitivity caused by buckwheat.

- Inflammation and swelling, especially about the ears, face and eyelids.
- Itching, sloughing.
- In severe cases, inflammation may spread to unpigmented areas of the skin and vesicles may develop containing a yellowish fluid.
- Ruptured vesicles form a yellow or brown crusty scab.
- Erythema is followed by subdural edema and eventual necrosis.
- Nervous signs in acute cases include excitement, running about, grunting, squealing or bellowing, jumping, convulsions and prostration.
- *Fagopyrum* appears to be a primary photosensitizer. However, in a few instances liver damage has been mentioned.

Diagnosis

Identification of *Fagopyrum*, evidence of consumption, and appropriate signs and lesions.

Treatment

Prevent access and keep in shade.
**Cymopterus - Spring Parsley**  
*Family* - Rutaceae family (carrot family)

### Images

### Description
- Perennial grows 4 - 6 inches tall.
- Leaves - Finely divided, resemble parsley.
- Flowers - Small, white or cream-colored in umbrella-like clusters about 1 inch across.
- Root - Long taproot.

### Habitat
*C. watsonii* grows in an area extending from southeastern Oregon and southwestern Idaho throughout Nevada to southwestern Utah.

### Toxic Principle
- Believed to be due to one or more photoactive furocoumarins (psoralens) previously identified in genera of the carrot family.
- Parsley, carrots, parsnips and other members of the carrot family have produced photosensitivity in man.

### Susceptible Species
Sheep and cattle. Chicks have been affected experimentally by the feeding of seeds. Ducklings have also been experimentally affected.

### Toxicity
- The photoactive compound is in the leaves and seeds of the parsley but not in stems and roots. This is the case in other members of the carrot family.
- Photosensitivity has been produced both orally and topically with no major increases in liver enzymes and no liver changes on histologic examination in dosed chicks.
- Most poisonings in sheep are from March to May.

### Signs
- "Sunburn" varies from slight to severe.
- Blisters on sheep's bodies not covered by wool.
- Losses primarily occur in lambs (often high losses) because the udders and teats are so painful that ewe will not permit lambs to nurse.
- Surviving lambs often stunted from lack of milk.
- Cattle - Unpigmented area affected: possible blisters and rapid weight loss in adults.
- Cows also refuse to let calves nurse due to teat lesions, but calf losses are usually low.

<table>
<thead>
<tr>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep, cattle, birds</td>
<td>Within 24 hours to weeks</td>
<td>Days to weeks, rarely lethal</td>
</tr>
</tbody>
</table>
Recovery

Gradual recovery on withdrawal.

Treatment

- Shade, remove from source.
- Supplemental feeding, especially lambs and calves.
- Supportive care for skin lesions if animals are amenable to being handled.

Prevention

- Keep off range with spring parsley in early spring.
- Use of 2,4-D to control plant.

Phenothiazine (Thiodiphenylamine)

<table>
<thead>
<tr>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
<th>Full Table for Toxicants that Cause Skin Damage by Primary Photosensitization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calves, goats, sheep, fowl (horses are sensitive to phenothiazine but apparently do not develop photosensitization)</td>
<td>Days</td>
<td>Days to weeks; potentially lethal</td>
<td></td>
</tr>
</tbody>
</table>

Sources

- Phenothiazine is very insoluble in water and although stable when dry, is readily oxidized when wet. Due to the insolubility of phenothiazine in water, it is formulated in suspensions and if not shaken well prior to dosing, the drug will be unevenly distributed to the animals.
- Phenothiazine is also available in powdered form for addition to the feed or incorporation into salt, mineral or combined salt-mineral mixes, which are used either by addition to feed or as salt licks. The powdered phenothiazines are generally used for prophylaxis (depressed egg production by female worms in the intestine results from continuous low level medication) as an adjunct to regular deworming treatments.
- In earlier years, powdered phenothiazine was generally administered to horses in dry ground feed on a continuous, daily basis. There are reports of continuous dosing of individual horses for 5 - 10 years at up to 5 g/day without untoward effects and without development of resistance in the parasite. This procedure is still practiced in the UK. The primary reason for the widespread, continued use of phenothiazine in the horse is its efficacy against small strongyles.
- Chickens and turkeys are treated with phenothiazine to remove the cecal worm, *Heterakis gallinarum*. Fowl are most often treated monthly by addition of the drug to the feed.

Toxicity

- The toxicity of phenothiazine has limited its use in swine and altogether prevented its use in the dogs, cats and human beings. It is used in ruminants, horses and fowl. The problem in small animals is reportedly severe CNS depression.
- Deaths among sheep from phenothiazine toxicosis are rare. Sheep in good condition will tolerate single doses of 160 grams or continuous dosing with 10 g daily for 49 days without side effects. However, sheep in poor condition may succumb to doses as low as 5 grams.
- Although sometimes formulated with trichlorfon, generally phenothiazines should not be used with organophosphorus compounds due
to potentiation of the toxicity of the insecticide.

- Similarly, healthy cattle tolerate 250 g doses of phenothiazine or 3 successive daily doses of 100 g without illness. However, debilitated, anemic cattle are even more susceptible than similarly debilitated sheep. An important toxic effect of phenothiazine in animals in poor condition is hemolysis which compounds an existing anemia in some such animals resulting in death.
- Phenothiazine toxicosis and death has occurred more in horses than in other domestic animals. Most toxicoses have occurred in debilitated and anemic horses. Generally, a toxic dose is above 50 g for an adult horse and above 30 g for a young horse. However, 28 g has caused death in a debilitated adult horse, while 500 g has been tolerated by horses in good condition.
- Obviously, the use of phenothiazine in cachexic animals can be hazardous and other safer drugs should be used when possible, especially when the animals are anemic and emaciated.

Absorption, Distribution, Metabolism and Excretion (ADME)

- It is believed that phenothiazine is converted to phenothiazine sulfoxide by cellular enzymes of the intestinal epithelium. In sheep, some phenothiazine is absorbed intact. After absorption, phenothiazine is further oxidized in the liver, primarily to leucophenothiazine and leucothionol, 2 colorless substances which are excreted in the urine. Upon further oxidation in the atmosphere, these compounds form the brown-red dyes, phenothiazine and thionol. Urine and milk are, therefore, discolored for several days. The presence of these dyes is not, however, indicative of toxicosis.
- Constipation in the treated animals causes retention of phenothiazine and, thereby, increases absorption from the intestine, increasing the probability of toxicosis.

Signs

- Signs of phenothiazine toxicosis in the horse include dullness, weakness, anorexia, and possibly oliguria, colic, constipation, fever and rapid pulse. Hemolytic effects include icterus, anemia and hemoglobinuria.
- Photosensitization may accompany administration of phenothiazine when animals are subsequently exposed to bright sunlight. Photosensitization occurs especially in calves but may also occur in goats, sheep and fowl but not horses.
- When the dose of phenothiazine is sufficiently high, not all the phenothiazine sulfoxide is converted to leucophenothiazine and leucothionol by the liver. Calves are apparently less adept at this conversion than older cattle or sheep. A portion of the phenothiazine sulfoxide diffuses into the aqueous humor. On exposure to sunlight, photochemical reaction results in keratitis and often corneal ulceration within 36 hours. Bright sunlight reflected from snow cover has commonly resulted in phenothiazine associated corneal ulcers in calves.
- Non-pigmented areas of the skin may be reddened, especially commonly affected are the ears, muzzle and other parts of the face. Shaking of the head, rubbing of the ears and other signs of irritation may be seen.
- There was a slight increase in abortion in ewes given phenothiazine at 3 weeks before the end of gestation. Generally, phenothiazine is contraindicated only during the last month of gestation. Phenothiazine discolored milk can generally be regarded as safe for feeding other animals.
- Permanent staining of wool or haircoat may result from phenothiazine excreted in the urine or from spilling the drench on the animal.

Treatment

- Toxicosis can be reduced by the use of smaller doses in weakened animals, although these may be only partially effective in parasite removal.
- For acute overdose, a saline cathartic combined with activated charcoal is used to reduce absorption and hasten removal from the gut.
- Treatment of phenothiazine toxicosis in the horse is primarily intended to replenish lost red cells via blood transfusion. Fluids and bicarbonate may lessen the likelihood and severity of renal tubular damage due to hemoglobin released from red cells.

References

Hypercum - St. Johnswort


All rights reserved. This document is available on-line at www.ivis.org. Document No. A2631.0899.