Toxicological Investigations of Two Poisonous Plants, Tansy Ragwort (*Senecio jacobaea*) and Summer Dandelion (*Hypochoeris radicata*) with Potential Therapeutic Agents, Quillaja and Milk Thistle

Elyssa Trejo
Kip Panter, Bryan Stegelmeier, Kevin Welch, Peter Cheeke
Bioresource Research and the Department of Animal Sciences, Oregon State University, Corvallis, Oregon
USDA -ARS Poisonous Plant Research Laboratory, Logan, Utah
Investigation of a Chicken Model for Equine Stringhalt Caused by Summer Dandelion (*Hypochaeris radicata*)
Project 1: Stringhalt Model

- Stringhalt: disorder in horses characterized by high stepping with hyperflexion of the hind limb.

- Induced stringhalt in a horse
  - Consumed 490 kg *Hypochaeris radicata* in 50 days (Araujo et al., 2008)
Why try to find an animal model?
- Less expensive
- Further facilitate studies to identify the active principle in *Hypochnaeris radicata*

Why chicks?
- Bipedal
- Muscular degeneration of a limb should produce obvious signs of difficulty in locomotion
Materials and Methods

- **Summer dandelion**
  - AKA: false dandelion, cat’s ear
  - Collected from Corvallis, Oregon over a two year period
  - Dried and ground
Materials and Methods

- 18 chicks
- 3 dietary treatment groups
- Feed intake measured daily
- Weighed once a week
- 35 day experimental feeding period
- Euthanized and necropsied
- Liver, spleen, kidney, leg muscles, femoral & sciatic nerve, lower spinal cord, and brain

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>% Summer Dandelion in Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
</tr>
</tbody>
</table>
Results: Observations

- All chicks appeared healthy
- Similar feed consumption rates
- Walking normal
- No obvious problems
Results: Feed Intake

<table>
<thead>
<tr>
<th>Day of Feeding</th>
<th>Control</th>
<th>Treatment 1 (10%)</th>
<th>Treatment 2 (30%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>23</td>
<td>28</td>
</tr>
<tr>
<td>7</td>
<td>33</td>
<td>33</td>
<td>33</td>
</tr>
<tr>
<td>13</td>
<td>40</td>
<td>47</td>
<td>50</td>
</tr>
<tr>
<td>18</td>
<td>60</td>
<td>67</td>
<td>70</td>
</tr>
<tr>
<td>23</td>
<td>80</td>
<td>87</td>
<td>90</td>
</tr>
<tr>
<td>28</td>
<td>100</td>
<td>107</td>
<td>110</td>
</tr>
<tr>
<td>33</td>
<td>120</td>
<td>123</td>
<td>120</td>
</tr>
</tbody>
</table>
Results: Weights

<table>
<thead>
<tr>
<th>Weight of Chick (g)</th>
<th>Day of Feeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Treatment 1</td>
</tr>
<tr>
<td>Treatment 2</td>
<td></td>
</tr>
</tbody>
</table>

The graph shows the growth of chick weight over different treatments and days of feeding.
Results: Necropsy

10% summer dandelion

30% summer dandelion
Conclusion

- The summer dandelion did not induce stringhalt in the chicks
- More plant material would be required to extend the feeding period to conclude if chicks could be used as a model for stringhalt
Tansy ragwort: TOXIC
Introduction: Tansy Ragwort (*Senecio jacobaea*)

- Weedy biennial plant
- Infests pastures and hayfields
- Found throughout Europe, Africa, the United States, Canada, and Australia.
Contains highly toxic pyrrolizidine alkaloids (PA)

Consumed by cattle and horses

Bitter taste
It’s another big Tansy year

This season, many folks who have Tansy Ragwort (Senecio jacobaea) or want their neighbors to control it are calling us.

As we talk with people, we’ve come to realize that many of our callers don’t know tansy is poisonous to horses and livestock. The toxins in tansy accumulate in these animals, slowly poisoning them. While this used to be common knowledge in our community, it has become less well known.

This year, we will be focusing on the devastating nature of Tansy Ragwort at the County Fair. The simple flyer we’ll use is shown to the right.

Staff report seeing good populations of Cinnabar moth larvae on tansy plants in Clackamas County. Cinnabar moth larvae help control tansy. These “good” bugs are effective at reducing tansy populations, so if you see these caterpillars, please leave them alone to do their good work!


Toxicity in Horses and Cattle

- 6 months for symptoms to show
- Because of delayed response, incorrect cause of death
Tansy Ragwort: Economic Impacts

- Infestation in the 1960’s and 70’s
- Biological controls introduced
- Economic benefits of tansy ragwort control: $5 million
- Cost: Benefit = 13:1
- 2005 Outbreak
Pyrrolizidine Alkaloids from Tansy Ragwort

- Very toxic when converted to pyrroles in the liver
- Chronic liver disease, hepatic failure, cirrhosis, ascites, and death
- Irreversible
- Cumulative effects

Figure 2: Jacobine
Toxicological Interactions Between Quillaja Saponins and Pyrrolizidine (Senecio) Alkaloids in Rats
Why pair these two?

- **Saponins**
  - Triterpenoid nucleus and water soluble side chains
  - Natural detergents, foaming properties

- **3 possible effects**
  - No effect
  - Decreased toxicity
    - Binding bile acids reduces absorption of lipid soluble material
  - Increased toxicity
    - Increased absorption
What is Quillaja?

- Used as a feed additive in agriculture
  - Decreases environmental ammonia and odor
  - Lowers cholesterol (1)
  - Anti-inflammatory
  - Anti/protozoal activity
  - Increases permeability of mucous membrane (2)
  - Growth promotion and improved feed conversion efficiency

Quillaja saponaria
Question

- Does quillaja feed additive have an effect on pyrrolizidine alkaloid toxicity?
Materials and Methods

- Thirty-six rats
- Six dietary treatment groups

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Weight Percent TR</th>
<th>Quillaja (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>2.5</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>500</td>
</tr>
<tr>
<td>5</td>
<td>2.5</td>
<td>500</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>500</td>
</tr>
</tbody>
</table>
Materials and Methods

- **Food Preparation:**
  - Ground pellets
  - Cornstarch
  - Water
  - ‘x’ tansy ragwort
  - ‘x’ quillaja

- Food and water readily available

- Feed intake and body weights were measured twice a week
Materials and Methods

- 48 day experimental feeding period
- Euthanized and necropsied
- Liver, heart, and spleen organ weights measured
Results: Feed Intake

Average feed consumed per day (g)
Results: Body Weights

Average body weight (g)

<table>
<thead>
<tr>
<th>%TR</th>
<th>Without Q Powder</th>
<th>With Q Powder</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>300</td>
<td>320</td>
</tr>
<tr>
<td>2.5</td>
<td>275</td>
<td>290</td>
</tr>
<tr>
<td>5</td>
<td>250</td>
<td>265</td>
</tr>
</tbody>
</table>
Results: PA/kg Body Weight

- **T2**: 2.5%TR
- **T3**: 5%TR
- **T5**: 2.5%TR, 500ppm Q
- **T6**: 5%TR, 500ppm Q
Results: Observations

- Day 41: All is well
- Day 45- Death
- Lethargy
- Jaundice
- Ascites
- Decreased appetite
5% TR

5% TR, 500ppm Quillaja
Results: Organ Weights

Average spleen weights (as a % of BW)

%TR

Without Q Powder

With Q Powder
Results: Organ Weights

Average liver weights (as a % of BW)

- Without Q Powder
- With Q Powder

%TR

0 2.5 5
Conclusion

- No obvious difference in TR toxicity with and without the Quillaja
- No interaction between PA’s from TR and quillaja saponins
Effects of the Conclusion

- No effects can be good
- Desert King International
The Effects of the Administration of Milk Thistle on Pyrrolizidine (*Senecio*) Alkaloid Toxicity in Chicks
Project 3: Tansy Ragwort + Milk Thistle

- Milk thistle (*Silybum marianum*):
  - “Supports liver health”
    - Strengthening cell walls
    - Improved function
    - Promoting regeneration
  - Silymarin from the seeds

- Milk thistle capsules can be purchased at common vitamin stores and usually contain about 70-80% silymarin (3).
Milk Thistle

- 80% Silymarin & Silybin
- Taken by Recovering Alcoholics
- Promotes Liver Regeneration

Nature's Sunshine

- Powerful Antioxidant for Liver Protection

Milk Thistle PLUS

Support, detoxify and regenerate your liver with pure plant extracts

For improved liver function
Question

Does milk thistle lessen the effects of the pyrrolizidine alkaloid toxicity?

Tansy Ragwort + Milk Thistle
Materials and Methods

- Twenty-four chicks
- Four dietary treatment groups

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Weight Percent TR</th>
<th>Milk Thistle (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>160</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>160</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Materials and Methods

- Food and water readily available
  - TR mixed in with feed
  - Milk thistle gavaged
- Feed intake measured daily and body weights twice a week
Materials and Methods

- 47 day experimental feeding period
- Euthanized and necropsied
- Liver, heart, and spleen organ weights along with blood samples were collected during necropsy.
Results: Feed Intake

Average feed consumed per day (g)

%TR

Without MT

With MT

0

5
Results: Body Weights

- T1: 5%TR, 200mg MT
- T2: 200mg MT
- T3: 5% TR
- T4: Control
Results: Observations

- Day 43 and 45 deaths
- Lethargy
- Decreased appetite
- Ascites
- Weight loss
- Ended experiment early
5% Tansy

Healthy liver

5% Tansy + MT
Results: Organ Weights

Average spleen weight (as a % of BW)

%TR

Without MT

With Milk Thistle
Results: Organ Weights

Average liver weights (as a % of BW)

%TR

Without MT

With MT
Conclusion

- No obvious difference in TR toxicity with and without the milk thistle

- No evidence of protective effects of MT on hepatoxic TR PA’s
What to Change…

- Gavage the tansy ragwort and the milk thistle
- Dose the treatment groups not receiving the milk thistle with alfalfa.
- Lower tansy ragwort consumption
Thank you!!!

- Dr. Peter Cheeke;
- Everyone at the PPRL: Dr. Panter, Dr. Stegelmeier, Dr. Welch, Ed, Clint, Dr. Gardner, Scott, Joseph, Kermit, and Dr. Pfister
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- and to the USDA ARS PPRL
Figures:
- 1. http://oregonstate.edu/dept/nursery-weeds/

Text: