Dangerous Herbs: Poisons

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Virtue itself turns to vice, being misapplied,
And vice sometimes by action dignified.
Within the infant rind of this small flower,
Poison hath residence, and medicine power.

-William Shakespeare, Romeo and Juliet
Learning Objectives

• What is mankind’s history with poisonous plants?
• What are the main classes of poisonous plant compounds?
• What are the symptoms associated with the toxidromes discussed in lecture?
• What are some examples of poisonous gymnosperms and angiosperms?
Poisons in Human History

• Early humans likely experienced much poisoning in the search for new foods
• One function of early agriculture was to select for more palatable (less bitter, less poisonous) plant variants
• Food processing to remove poison also important

• Cassava *Manihot esculenta* (Euphorbiaceae)
  – Starchy tuber is the main source of carbohydrates in the tropics
  – Tuber is filled with poisonous cyanogenic glycosides and hydrogen cyanide (HCN)
    • A dose 40 mg of pure cassava cyanogenic glucoside is sufficient to kill a cow.
  – Tuber is processed to remove the poison (soaking, boiling, fermentation)
Manihot esculenta Crantz, Euphorbiaceae

Fermented cassava beverage (mashed with sugar cane juice & saliva)
Poisons and the criminal arts

• Agrippina (19-59 AD)
  – Empress and wife of Emperor Claudius and mother of Nero
  – used poisonous mushrooms to kill Lollia Paulina, Marcus Sianus, and her husband Claudius, among others

• Cleopatra (51-30 BC)
  – Tested poisons on her slaves
    • *Hyoscyamus niger* (henbane)
    • *Atropa belladonna* (belladonna)
    • *Strychnos nux-vomica* (source of strychnine)
Poisons and Drugs

• Most drugs are poisons:
  – Dose dependent curves (blood level vs. time)
  – Blood level is usually proportional to dose
  – Therapeutic dose vs. toxic dose
  – Variation in humans

• Pharmacological actions
  – Sub-therapeutic effects
  – Therapeutics effects
  – Super-therapeutic effects
    • Toxidromes (syndrome caused by a dangerous level of toxins in the body)
    Common symptoms include dizziness, disorientation, nausea and vomiting.
Poisons and Drugs

• Injurious plants
  – Internal poisons
  – Allergens
  – Cell-modifiers
    • Mutagens, teratogens and lectins (including mitogens)

• Human adaptations:
  – Liver enzymes
  – New niches:
    • Food plants
    • Psychoactive plants
    • Medicines
Allergens

Primary plant allergens
• Proteins found in any part of the plant.
  – Ex. Anacardiaceae (leaves, pollen, etc)
  – Ex. Poaceae (pollen)

Examples of plant allergen effects
• Dermatitis
• Allergic rhinitis
• Anaphylactic shock
Toxidromes

• Definitions:
  – clinical syndromes that are essential for the successful recognition of certain poisoning patterns
  – A constellation of signs and symptoms that suggest a specific class of poisoning
Toxidromes

• In a clinical setting, the most important toxidromes include:
  – Sympathomimetic
  – Sedative hypnotic
  – Opiate
  – Anti-cholinergic
  – Cholinergic
Stimulant Toxidrome

**Symptoms**
- Restless
- Excessive motor activity
- Insomnia
- Hallucinations
- Excessive speech
- Tremor
- Tachycardia
Sedative Hypnotic

Symptoms

• Sedation
• Confusion
• Delirium
• Hallucinations
• Coma
• Paresthesias
• Dysesthesias
• Diplopia
• Blurred vision
• Slurred speech
• Ataxia
• Nystagmus
Opiate

Symptoms

• Altered mental status
• Miosis
• Unresponsiveness
• Shallow respirations
• Slow respiratory rate
• Bradycardia
• Decreased bowel sounds
• Hypothermia

“The doctor gave me these zonko pain pills, but I promised him I’d only take them in case of extreme discomfort.”
Anticholinergic

Symptoms

• Fever
• Ileus
• Flushing
• Tachycardia
• Urinary retention
• Dry skin
• Blurred vision
• Mydriasis
• Decreased bowel sounds
• Myoclonus
• Choreaathetosis
• Psychosis
• Hallucinations
• Seizures
• Coma

*Hot as a hare, dry as a bone, red as a beet, mad as a hatter*
Cholinergic

Symptoms
- Salivation
- Lacrimation
- Urination
- Defecation
- GI distress (diarrhea)
- Emesis
- Bronchorrhea, Bradycardia
### What are toxins that cause:

<table>
<thead>
<tr>
<th>Coma</th>
<th>Hypotension</th>
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<tbody>
<tr>
<td>Alcohols</td>
<td>Arsenic Lithium</td>
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<tr>
<td>Beta Blockers</td>
<td>Carbon Monoxide</td>
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<tr>
<td>Lead</td>
<td>Phenothiazines</td>
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<tr>
<td>PCP</td>
<td>Sedative Hypnotics</td>
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<tr>
<td>Opiates</td>
<td>Sedative Hypnotics</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Pupil Changes</th>
<th>Temperature Changes</th>
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<tbody>
<tr>
<td>Miosis</td>
<td>Hyperthermia</td>
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<tr>
<td>Cholinergics</td>
<td>Anticholinergics</td>
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<tr>
<td>Clonidine</td>
<td>Glutethimide</td>
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<tr>
<td>Nicotine</td>
<td>Meperidine</td>
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<tr>
<td>Phenothiazines</td>
<td>Sympathomimetics</td>
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<tr>
<td>PCP</td>
<td>Withdrawal</td>
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<table>
<thead>
<tr>
<th>Respiratory Effort</th>
<th>Increased</th>
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<tbody>
<tr>
<td>Decreased</td>
<td>CO, CN</td>
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<tr>
<td>Alcohols</td>
<td>Drug induced metabolic acidosis</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>Drug induced hepatic failure</td>
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<tr>
<td>Benzodiazepines</td>
<td>Drug induced methemoglobinemia</td>
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<tr>
<td><strong>Opiates</strong></td>
<td>Salicylates</td>
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<table>
<thead>
<tr>
<th>Heart Rate Changes</th>
<th>Bradycardia</th>
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<tbody>
<tr>
<td>Tachycardia</td>
<td>Alpha blockers</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>Beta blockers</td>
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<tr>
<td>Antihistamines</td>
<td>Calcium channel blockers</td>
</tr>
<tr>
<td>Cyclic Antidepressants</td>
<td>Cardiac glycosides</td>
</tr>
<tr>
<td>PCP</td>
<td>Cholinergics</td>
</tr>
<tr>
<td>Sympathomimetics</td>
<td>Nicotine</td>
</tr>
<tr>
<td>(Cocaine, Amphetamine, Theophylline, etc.)</td>
<td>Parasympathomimetics</td>
</tr>
</tbody>
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Chemistry of Poisonous Plants

- **Alkaloids**
  - nitrogen containing compounds

- **Cardiac glycosides**
  - Act on cardiac muscle
  - >400 characterized

- **Cyanogenic glycosides**
  - Yield hydrogen cyanide (HCN)
  - Amygdalin is common in Rose family

- **Anthraquinone glycosides**
  - Purgative activity

- **Saponin glycosides**
  - Yield sapogenin (steroid or triterpene)
  - Irritate mucous membranes, destroy RBC, toxic especially to cold blooded animals like fish

- **Pyrrolizidine alkaloids**
  - hepatotoxins
Chemistry of Poisonous Plants

• **Resins**
  - Complex, chemical nature, insoluble in water, lack nitrogen
  - Toxic resins can be very poisonous (ex. Water hemlock)

• **Element & Nitrogen Absorption**
  - Plants may accumulate harmful elements such as mercury or selenium

• **Coumarin glycosides**
  - Not very common
  - Some prevent thyroid from accumulating inorganic iodine

• **Lectins**
  - High toxicity proteins found in small number of plants
  - Similar to bacterial toxins

• **Oxalates**
  - Oxalic acid is widespread in plants, can occur as soluble or insoluble (calcium oxalate)
  - Calcium oxalate is a skin and mucous membrane irritant
Cyanide

• Plant families that produce cyanogenic glycosides:
  – Rosaceae
  – Fabaceae
  – Poaceae
  – Euphorbiaceae

• Examples of genera:
  – Passiflora (passion flower)
  – Manihot (cassava)
  – Malus (apple)
  – Prunus (plums, cherries, peaches, apricots and almonds)
  – Pyrus (pears)
  – Cassia
Saponins

• Examples of plant families that produce saponins:
  – Fabaceae

• Examples of genera:
  – Glycyrrhiza (licorice)
  – Panax (ginseng)
  – Medicago (alfalfa)
Coumarins

- Examples of plant families that produce coumarin glycosides:
  - Fabaceae

- Examples of genera:
  - *Viburnum* (black haw)
  - *Trifolium* (sweetclover)
Oxalates

• Examples of plant families that produce oxalates:
  – Oxalidaceae

• Examples of genera:
  – *Oxalis* (sorrel)
Phytotoxins

• Examples of plant families that produce phytotoxins:
  – Euphorbiaceae

• Examples of genera:
  – *Ricinus* (castor, protein: ricin)
Other biological poisons

- **Bacteria**
  - *Staphylococcal* intoxication
  - Botulism (*Clostridium botulinum*)
  - *Escherichia coli* toxins
  - *Bacillus* toxins

- **Algae**
  - Blue-green algae
  - *Gonyaulax* spp.
  - Red tide
  - *Pfiesteria piscida*

- **Fungi (Mycotoxins)**
  - *Aspergillus* spp.
  - *Claviceps purpurea* (ergot)
  - *Amantia phalloides* (detah cap mushroom)

- **Ferns & fern allies**
  - *Pteridium aquilinum* (bracken)
  - *Equisetum* spp.
    (thiaminase could lead to toxicity after ingestion)
Hepatoprotective effects of Milk Thistle

- *Silybum marianum* (Asteraceae)
- Silymarin is a flavolignan mixture which can suppress toxic effects of death cap mushrooms (some of most potent liver toxins)
- Standardized silymarin extracts are used to treat liver damage and hepatic cirrhosis
- Milk thistle is also an important traditional medicine throughout the Mediterranean, where it grows in the wild

Silybinin (an active component of the silymarin mixture)
Gymnosperms

• All cycads and zamias have poisonous fleshy seeds
  – If the azoxy alkaloids are washed out, they can be eaten (or flour made from them)

*Cycas circinalis*, Cycadaceae (fern palm)  
*Dioon edule*, Zamiaceae (false sago palm)  
*Zamia integrifolia*, Zamiaceae (coontie)
Gymnosperms: Taxus, Taxaceae (yews)

- Taxanes: taxines and taxols (ester alkaloids)
- Taxols
  - Concentrations usually low
  - Most toxicity attributed to taxines
- Taxines are cardiotoxic
- Lethal dose: 4-20 mg/kg
- Rapid absorption from GI tract to circulatory system
- Affects sodium-potassium transport
- Sudden death occurs with trembling, labored breathing, and collapse
- Most deaths in animals that forage on leaves, human deaths rare

*Taxus baccata*
Gymnosperms: *Gingko biloba*, Ginkoaceae

- Seeds contain a neurotoxin:
  - 4-O-methyl pyridoxine
    - Interferes with amino acid metabolism
    - Results in convulsions and death (27% lethality)
Angiosperms: *Dieffenbachia seguine*, Araceae (Dumbcane)

- Common houseplant
- Active Compound:
  - Irritant juice and/or crystals of calcium oxalate
  - Burning sensation caused by enzyme or asparagine
- Symptoms:
  - Ingestion results in swelling of throat and mouth; possible asphyxiation
Angiosperms: *Ricinus communis*,
Euphorbiaceae (Castor bean; castor oil)

- Castor oil extracted from seeds is used medicinally as laxative – but eating the seeds can kill
- Active Compound:
  - Ricin: a highly poisonous phytotoxin
- Symptoms:
  - Nausea, muscle spasms, purgation, convulsions, and death
Angiosperms: *Abrus precatorius*, Fabaceae (rosary pea; jequirity bean)

- Toxic effect from chewing the seeds
- Active Compound:
  - Abrin (phytotoxin similar to ricin) & abric acid from thoroughly chewed seeds
- Symptoms:
  - Gastrointestinal distress
  - Fatal to humans and animals
Angiosperms: *Colchicum autumnale*, Colchicaceae (autumn crocus or meadow saffron)

- Colchicine derived from this plant used medicinally to treat gouty arthritis
- Active Compound:
  - Colchicine & other alkaloids
  - Highest concentration is in seeds and corm
    - Amount of colchicine in 2-3 seeds can kill
- Symptoms:
  - Burning of throat & stomach, vomiting, purging, weak-quick pulse, kidney failure, respiratory failure, often fatal, flowers have been fatal to children
Angiosperms: *Digitalis* spp., Plantaginaceae (Foxgloves)

- Controlled doses used to treat heart diseases like congestive heart failure
- **Active Compound:**
  - Cardiac glycosides (digoxin & digitoxin) in leaves, seeds, flowers
- **Symptoms:**
  - Poisoning from plant or overdose of medication
  - Vomiting, purging, severe headache, irregular heartbeat and pulse, convolution, sudden death
Angiosperms: *Nerium oleander*, Apocynaceae (oleander)

- Examples of poisoning events: ingestion after confusion with eucalyptus; ingestion by children; suicide attempts
- Active Compound:
  - Cardioactive glycosides; oleandrin is the main glycoside from leaves
- Symptoms:
  - Ingestion results severe vomiting, bloody diarrhea, irregular heartbeat, drowsiness, unconsciousness, respiratory paralysis, fatal
Angiosperms: *Senecio* spp., Asteraceae (groundsels or ragworts)

- Mistaken identity – confused with a *Gnaphalium* sp. & included in herbal remedy for colds
- Active Compound:
  - Hepatotoxic pyrrolizidine alkaloids
- Symptoms:
  - Ingestion results in acute illness and death in livestock and humans
Angiosperms: *Datura stramonium*, Solanaceae (jimsonweed)

- Used as recreational psychoactive drug – users often unaware of toxicity/poisonous nature of plant
- Active Compound:
  - Scopalamine, especially L-hyoscyamine; most found in leaves, unripe capsules, especially seeds
- Symptoms:
  - Even small amounts fatal; symptoms similar to *Atropa belladonna* (flushed skin, dilated pupils, dry mouth, delirium, death from respiratory failure)
Angiosperms: *Cicuta* spp., Apiaceae (water hemlock)

- European poison hemlock made famous by Socrates’ execution (contains toxic pyridine alkaloids)
- Active Compound:
  - Cicutoxin, in root and above-ground parts: is a violent convulsant that acts directly on the CNS
- Symptoms:
  - 2-3 cm section of root can kill an adult
Angiosperms: *Prunus armeniaca*, Rosaceae (apricot)

- Common edible plant (fruit)
- Active Compound:
  - Amygdalin and cyanide in seeds, leaves & bark
- Symptoms:
  - Ingestion results of parts with amygdalin results in cyanide poisoning, may be fatal
Angiosperms: *Strychnos nux-vomica*, Loganiaceae (nux-vomica)

- Tested by Cleopatra as possible suicide toxin
- Active Compound:
  - Indole alkaloids (strychnine and brucine) from dried ripe seeds; all parts contain strychnine
- Symptoms:
  - Agitation, muscle spasms, convulsions
  - Extremely toxic, strychnine is fatal to humans at doses of 60-90 mg
Summary

- The division between medicine and poison is often small – and all medicines have the potential to be toxic if used improperly.
- Humans have developed ways of limiting toxicity of certain plants by processing and selective agriculture.
- Some of the top reasons plant poisonings occur is because of:
  - Mistaken identity
    - individual collects and uses wrong species; or
    - wrong species is used in the preparation of an herbal product (example: tea; dietary supplement, topical cream) for sale
  - Ingestion by young children (particular problem with ornamental plants commonly found in homes and outdoor play areas)
  - Intentional use (suicide, murder, terrorism)