Reminder: Field trip Saturday or Sunday (9am-noon)

Meet in same parking lot as last time (just west of train bridge) at 9am

Drivers (please pick up keys from campus police on way to the vans): Hannah & Alex (Saturday); Mike & Joe (Sunday)

For Tuesday: Read articles for fiber and dyes
History of Medicinal plants

- Use of plants for medicines traces way to back to ancient times

- Western medicine traces back to Greek physician Hippocrates (Father of medicine), who used herbal remedies

- Dioscorides, Roman physician wrote account of over 600 species of plants with medicinal value

- Many of these plants incorporated into western medicine
History of Medicinal plants

One important plant that is not still used...

- Silphium (*Ferula* sp.; Apiaceae)

- Seeds used as contraceptive by Greek and Roman women for >1,000 years—extinct by 3rd or 4th century.

- Grown mainly in Cyrene (currently Libya, N. Africa); main component of economy, illustrated on Cyrenian coins
History of Medicinal plants

Doctrine of Signatures defined in 16th century in west; same idea used by various cultures.

Idea that the outer morphology of the plant or plant part corresponds to part of human body for which plant is effective.

- Lobed leaves of liverwort (*Hepatica*) to be used for liver problems
- Bloodroot (*Sanguinaria*), with its red sap, used for blood ailments
- Dutchman’s breeches (*Dicentra*) used for syphilis
History of Medicinal plants

19th century—purification of extracts from plants; led to formulation of synthetic drugs based on natural plant products

- 1806: Morphine extracted from opium poppy
- 1839: Salicylic acid identified as active ingredient in various plants that reduced pain
- 1853: Salicylic acid first synthesized
- 1898: Chemist at Bayer Company synthesized acetylsalicylic acid, more palatable, named Aspirin
• Salicylic acid, a common hormone in many plants, stimulates immune response, causing production/release of defense compounds

• Some converted to methyl salicylate (volatile compound—wintergreen) that allows for plant communication

• Aspirin (acetylsalicylic acid) inhibits enzyme cyclooxygenase (COX)

• Suppresses prostaglandins, hormones that mediate various physiological responses; overproduction can lead to headaches, cramps, inflammation

*Salix* sp. (Willow; Salicaceae)

*Filipendula* (Spirea) *ulmaria* (Meadowsweet; Rosaceae)
Currently 25-50% of prescription drugs in US include a plant product or contain a compound synthesized using a plant product as a model.

75-90% of rural population in other parts of the world use herbal medicine as only health care.

- **China**: Major user of herbal medicine, strong history of ancient Chinese medicine
- **India**: Ayurvedic medicine
- **Unani**: Islamic herbal tradition
<table>
<thead>
<tr>
<th>Class</th>
<th>Number of structures</th>
<th>Poisons</th>
<th>Psychoactive substances</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>With nitrogen</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alkaloids</td>
<td>20000</td>
<td>most</td>
<td>many</td>
</tr>
<tr>
<td>Non-protein amino acids (NPAAs)</td>
<td>700</td>
<td>some</td>
<td>few</td>
</tr>
<tr>
<td>Amines</td>
<td>100</td>
<td>some</td>
<td>some</td>
</tr>
<tr>
<td>Cyanogenic glucosides</td>
<td>60</td>
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<td>few</td>
</tr>
<tr>
<td>Glucosinolates</td>
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<td>some</td>
<td>none</td>
</tr>
<tr>
<td>Alkamides</td>
<td>150</td>
<td>most</td>
<td>none</td>
</tr>
<tr>
<td>Lectins, peptides, polypeptides</td>
<td>2000</td>
<td>most</td>
<td>none</td>
</tr>
<tr>
<td><strong>Without nitrogen</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monoterpenes (including iridoids)</td>
<td>2500</td>
<td>some</td>
<td>some</td>
</tr>
<tr>
<td>Sesquiterpenes</td>
<td>5000</td>
<td>many</td>
<td>few</td>
</tr>
<tr>
<td>Diterpenes</td>
<td>2500</td>
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<td>few</td>
</tr>
<tr>
<td>Triterpenes, steroids, saponins</td>
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<td>most</td>
<td>few</td>
</tr>
<tr>
<td>Tetraterpenes</td>
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<td>none</td>
</tr>
<tr>
<td>Phenylpropanoids, coumarins, lignans</td>
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<td>few</td>
</tr>
<tr>
<td>Flavonoids, tannins</td>
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<tr>
<td>Polycetylenes, fatty acids, waxes</td>
<td>1500</td>
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<td>few</td>
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<tr>
<td>Polyketides (anthraquinones)</td>
<td>750</td>
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<td>none</td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>200</td>
<td>few</td>
<td>none</td>
</tr>
</tbody>
</table>

Table reproduced from Wink & van Wyk, 2008. *Mind-altering and poisonous plants of the world.*
Figure from Van Wyk and Wink, 2004. *Medicinal plants of the world.*
Figure from Van Wyk and Wink, 2004. *Medicinal plants of the world.*
Two major categories of secondary compounds used as medicines

**Alkaloids**: Contain nitrogen; examples include caffeine, nicotine, quinine, atropine, morphine, ephedrine

- Found in 15% plants
- Some plant families especially alkaloid-rich including Rubiaceae, Solanaceae, and Apocynaceae
- Alkaloids stored in tissues that are important for survival and reproduction of plant
- Often in epidermal tissues as primary defense, also in latex
- Alkaloids may affect neurotransmitters or structures (especially microtubules) necessary for cell division (mitosis)
Alkaloids:

Quinine

- Quinine from bark; well known to Incas
- Historically important antimalarial drug
- Acts on *Plasmodium* parasite by inhibiting its metabolism
- Also works as prophylactic
- Gin and tonic to make quinine palatable

*Cinchona pubescens* (Fever bark tree; Rubiaceae)
• Recent development of **artemisinin**, terpenoid compound (as opposed to an alkaloid) to combat malaria--less side effects, effective against resistant strains, works very fast (24 hrs)

• From Chinese wormwood (*Artemisia annua*; Asteraceae); long used in China to reduce fevers
Alkaloids:

Ephedrine

\[
\begin{align*}
\text{OH} & \quad \text{H} \\
\text{CH}_3 & \quad \text{N} \\
\text{CH}_3 & \quad \text{CH}_3
\end{align*}
\]

Ephedra sp. (Mormon Tea; Ephedraceae)

- Dried stems as source of ephedrine, pseudoephedrine
- Stimulatory effects similar to adrenaline, also relieves nasal congestion by relaxing bronchial muscles
Alkaloids:

*Taxus brevifolia* (Pacific yew, Taxaceae)

- Bark and leaves contain drug
- Other *Taxus* species used too
- Inhibits cell division, important anti-cancer drug

![Chemical structure of Taxol](image)
Alkaloids:

Vinblastine

*Catharanthus roseus* (rosy periwinkle; Apocynaceae)

- Alkaloids in roots and leaves; leaves generally used today
- Traditionally used for diabetes (no evidence for this effect)
- Two alkaloids; vincristine and vinblastine block cell division, important anti-cancer drugs
Alkaloids:

Camptothecin

\[ \text{Camptotheca acuminata (Cornaceae)} \]

- Chinese happy tree
- Bark and wood, now use young leaves
- Used for centuries in China to treat cancer
- Inhibits DNA replication, cell division;
- Derivatives used in chemotherapy; some of most promising new anticancer drugs
Local plant used as anti-cancer drug (phenypropanoid class of compounds):

Podophyllum peltatum (May apple; Berberidaceae)

- Use dried rhizome
- Root extracts used by Native Americans as purgative, for skin disorders and growths
- Podophyllotoxin and peltatins
- Highly toxic, inhibit cell division
Two major categories of secondary compounds used as medicines

**Glycosides:**

Sugar molecule (*glyco-* ) attached to active molecule, usually glucose

Most common are cyanogenic glycosides, cardiac glycosides, and saponins
Cyanogenic glycosides:
Cyanogenic glycosides:

- Release cyanide (carbon atom triple-bonded to nitrogen) upon breakdown; occur in >2600 species, especially families Rosaceae, Fabaceae, Poaceae, Araceae
- Inhibits enzymes required for respiration (blocks production of ATP)
- Foods with cyanogens include cassava (*Manihot esculenta*) and sorghum (*Sorghum bicolor*); food processing important, plant breeding for lower levels of compounds
- Seeds of various Rosaceae also contain cyanogens, including almonds, apples, and cherries

Dhurrin: *Sorghum*  
Prunasin: Rosaceae
Glycosides

**Cardiac glycosides and saponins:** steroid molecule is active molecule

- Cardiac glycosides affect contraction of heart muscle

*Digitalis purpurea* and *D. lanata* (Foxglove; Scrophulariaceae)

- Digitoxin (and other cardiac glycosides) from leaves
- Slows heart rate while increasing the strength of each heartbeat
Glycosides

**Saponins** often affect membranes

Diosgenin in tubers of yams (*Dioscorea* sp.; Dioscoreaceae)

- Compound converted to progesterone for first birth control pills
- Precursor for cortisone synthesis (anti-inflammatory)
Why don’t we use more plant compounds in western medicine?
How do we identify useful new plants?

• Survey plants in the field—preferentially sample those without insect or pathogen damage, suggesting they are well defended

• Work with local healers to identify plants; importance of conserving *indigenous knowledge*, which may be disappearing even faster than tropical forests

• Ecological correlates: young/old leaves; shade/sun; phylogenetic relationships
Why would Coley et al. predict that young leaves would contain more bioactive compounds?
Why would Coley et al. predict that mature leaves of shade tolerant species would be more biologically active than leaves in high light (gap) areas?
Using ecological criteria to design plant collection strategies for drug discovery

Phylogeny does inform utility; some clades more bioactive than others