Caffeinds
The Cultural and Historical Uses of Caffeine-Containing Plants
Christopher Hobbs, Ph.D., Presenter

Some introductory slides modified with permission from UNM Biology (PJ Tolson and grad students)
• Caffeine is the world’s most popular psychoactive drug and is found in many different forms
• Used as a stimulant and psychoactive drink for at least 4,000 years.
• Can be addictive and cause withdrawal symptoms.
• Purine alkaloid
• Rarely-found in plants, only 8 genera/out of approximately 16,167 genera (0.05%) based on The Plant List (www.theplantlist.org)
Caffeine-Producing Plants

- *Coffea* coffee
- *Camellia* green and black tea, kucha
- *Theobroma* cacao, the source of chocolate
- *Herrania* closely-related to *Theobroma*
- *Cola* Kola nut, original ingredient in coca-cola
- *Ilex* yerba mate, yaopon
- *Paullinia* guarana
- *Citrus* found in the flowers of orange, ca. 10-times less than other sources (Kretschmar & Baumann, 1999)
American Caffeine Consumption

*Each year* Americans consume 45 millions pounds (120,000 tons) of pure caffeine

- On average each person consumes 2.6 cups of coffee a day or 363.5 mg of caffeine.

- In the US, more than 80% of adults consume caffeine on a daily basis.
  - Among individuals that do not drink caffeinated beverages the average intake is still ~91mg/day (from foods, medicines)

- Over 450,000,000 cups of coffee are consumed in the USA every day! Whoah
Caffeine—not just a stimulant --some of its many benefits

The consumption of moderate amounts of caffeine:

- increases energy availability and daily energy expenditure
- decreases mental and physical fatigue
- decreases the sense of effort associated with physical activity
- enhances physical performance
- enhances motor and cognitive performance
- increases alertness and wakefulness, feelings of "energy"
- quickens speed and accuracy of reactions
- increases the ability to concentrate and focus attention
- enhances short-term memory
- increases the ability to solve problems requiring reasoning
- increases the ability to make correct decisions
- enhances cognitive functioning capabilities and neuromuscular coordination

Review of the literature (Glade, 2010)
Potential Adverse Effects

- Tends to produce dependence
- Can cause drug withdrawal reactions
- Can cause or worsen psychiatric illnesses
- Impairs physical and mental performance
- Interferes with sleep
- May influence the risk of other illnesses that in turn exert frontal lobe effects through physical or mental stress
- May exert effects that impact on spiritual and social dimensions of our character
- Can cause toxicity, and even death
Risks of frequent caffeine use

• Risks
  – Reduced creativity
    • In one recent study, participants showed marked improvements on a task requiring creative thought—thinking of alternative uses for a common object, such as a newspaper—after they had engaged in a different, undemanding task that facilitated mind wandering
    • a break in intense concentration may increase unconscious associative processing
    • Caffeine prevents our focus from becoming too diffuse; it instead hones our attention in a hyper-vigilant fashion.
  
• Sleep
  – Consuming 200 mg of caffeine significantly increase the amount of time it takes to fall asleep (8 oz brewed coffee = 95-200 mg caffeine)
  – Quality of sleep is reduced in other ways
    • delta sleep and REM are diminished, shortened
    • Quality of sleep is directly related to immune functions, creativity, emotional stability and intelligence
Caffeine in Spiders

When Exposed:

- Webs varied in size, length of thread, organization, density and structure.

- Excess caffeine caused issues with proper techniques in construction of webs.
Realistic research-based view
most-supported benefits

– boosts energy and decreases fatigue
– enhances physical, cognitive, and motor performance
– aids short-term memory
– enhances problem solving, decision making
– results in better ability to concentrate
Ancient History of Caffeine

• Tea is likely the most ancient of all caffeine-containing plants
  – 2732 BCE, legend has it that Emperor Shen Nung discovered the flavor and uplifting effects of tea when leaves fell into his hot water
  – The ancient character for ch’a symbolizes wooden branches, grass, and a man between the two
  – Coffee use is documented first from the 15th century in Ethiopia (10th – 13th century CE) and 15th century CE in the Sufi monasteries of Yemen
History of Caffeine Consumption

• A factor in the modernization of European Society
• It became popular in Europe at the start of the industrial revolution
• Served as a substitution for beer, which was counter-productive
• Humans were forced to adapt as the job force switched from farming to industrial (indoor) jobs
  o Artificial light and caffeine became the way to adjust to new types of jobs; workdays were no longer regulated by just sunlight.
• Reasons for using caffeine are very similar to those of the past.
  • Increase in energy, drive
  • Alertness
  • Memory, mental performance
  • Endurance
  • The ability to work long hours, past what would normally be possible
  • Subvert the day/night cycle of rest and avoid (at least temporarily) the body’s need for sleep
• Particularly suited for the academic environment
• Long hours of focus in the lab and in front of the computer is required
Where is Caffeine found?

- Harvested from plants but can be synthetically made
- Not only found in coffee and energy drinks, but also in some unlikely places like:
  - chocolate, gum, and migraine medicine
- Concentration can vary depending on the source, where it comes from, and how it is made. (Table 1)
Table 1: Caffeine Content in a Variety of Sources.

<table>
<thead>
<tr>
<th>Item</th>
<th>Serving Size (fl. oz)</th>
<th>Caffeine content per Serving (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coffee (Brewed)</td>
<td>5</td>
<td>40-180</td>
</tr>
<tr>
<td>Decaf Coffee</td>
<td>5</td>
<td>2-5</td>
</tr>
<tr>
<td>Starbucks Coffee Grande</td>
<td>16</td>
<td>330</td>
</tr>
<tr>
<td>Espresso</td>
<td>1</td>
<td>64</td>
</tr>
<tr>
<td>Tea</td>
<td>5</td>
<td>24-50</td>
</tr>
<tr>
<td>Coca Cola Classic</td>
<td>12</td>
<td>35</td>
</tr>
<tr>
<td>Diet Coke</td>
<td>12</td>
<td>47</td>
</tr>
<tr>
<td>Mountain Dew</td>
<td>12</td>
<td>54</td>
</tr>
<tr>
<td>Pepsi</td>
<td>12</td>
<td>38</td>
</tr>
<tr>
<td>Diet Pepsi</td>
<td>12</td>
<td>35</td>
</tr>
<tr>
<td>Red Bull</td>
<td>8.3</td>
<td>80</td>
</tr>
<tr>
<td>Rockstar</td>
<td>8</td>
<td>80</td>
</tr>
<tr>
<td>Hershey's Chocolate Bar</td>
<td>1.55 oz</td>
<td>9</td>
</tr>
<tr>
<td>Excedrin, Extra Strength</td>
<td>2 tablets</td>
<td>130</td>
</tr>
<tr>
<td>NoDoz Maximum Strength</td>
<td>1 tablet</td>
<td>200</td>
</tr>
<tr>
<td>Jolt Caffeinated Gum</td>
<td>1 stick</td>
<td>35</td>
</tr>
</tbody>
</table>
Caffeine—Impact on the Environment

• Study on treated and untreated drinking water and streams (Stackelberg et al., 2004) showed that caffeine was detectible at 0.5 µg/L in untreated water, but not after traditional treatment.

• Caffeine potentiation of thiotepa*-induced chromosome damage was obtained in root tips of *Vicia faba* and *Allium proliferum* as well as in cell cultures of the Chinese hamster. No potentiation was obtained in the human cell line LU106 (Kihlman et al., 1974).

*Organophosphate alkylizing chemotherapeutic agent
Molecular Formula: C8H10N4O2

Molecular Weight: 194.19

Medically known as trimethylxanthine.

red = oxygen
Purple = nitrogen
grey = carbon
white = hydrogen

Figure 1: Caffeine Structure
Absorption

• Absorption from the GI tract takes approximately 45 minutes

• Plasma concentration peaks 15 to 120 min after consumption

• Caffeine can pass through many types of cell membranes because it is hydrophobic in nature

• Half life is about 2.5-5.7 hours, longer for those with liver impairment; during the first month of life it can be up to 100 hours, due to increased activity of cytochrome P-450

• There is no blood-brain or blood-placental barrier to caffeine
  o Associated with premature birth weight in infants
a = plasma caffeine
b = mean arterial pressure
c = heart rate

Closed square = mother
Open square = fetus

Source: Atik et al., 2014

- Humans: 2.5-5.7 hours.
  o individuals with a compromised liver have an extended half life.
  o during neonatal development half-life increases to 100 hours due to decreased activity of cytochrome P-450
Figure 1  Mean ± s.e. mean serum caffeine (○) and 1,7-dimethylxanthine (●) levels, following the oral ingestion of (a) 250 mg caffeine and (b) 500 mg caffeine in nine subjects.
Metabolism

• Takes place in the liver with help from Cytochrome P450, where it is metabolized into three separate substances

Figure 2: Caffeine derivatives
Metabolism of Caffeine

Caffeine
(1,3,7-trimethylxanthine)

CYP1A2 (4%)

- Theophylline
(1,3-dimethylxanthine)
  - 1,3-dimethylurate (50%)
  - 3-methylxanthine (30%)

CYP1A2 (12%)

- Theobromine
(3,7-dimethylxanthine)
  - 20%
  - 7-methylxanthine (50%)

CYP1A2 (84%)

- Paraxanthine
(1,7-dimethylxanthine)
  - 9%
  - 1,7-dimethylxanthine
  - 1-methylxanthine
    - NAT2 (16%)
    - AFMU
    - XO (39%)
      - 1-methylurate
Caffeine Metabolites

- **Paraxanthine**
  - Increases lipolysis, leading to elevated glycerol and free fatty acid levels in the blood plasma
  - Increases the amounts of Ca++ in the skeletal muscle

- **Theobromine** (significant amounts in cacao)
  - Dilates blood vessels and mildly increases urine production

- **Theophylline**
  - Relaxes smooth muscles of the bronchi, and is used to treat asthma

- Each of these metabolites is further metabolized and then excreted in the urine
Caffeine and Adenosine: a battle over receptor sites.

- Adenosine is the primary sleep mechanism and causes drowsiness because it slows neural cell activity.

- Caffeine increases alertness by binding to adenosine receptors in the brain, inhibiting the normal response.

- Scientists have learned that, largely as a consequence of its blockade of adenosine receptors, caffeine also has profound effects on most of the other major neurotransmitters, including dopamine, GABA, acetylcholine, serotonin, and, in high doses, on norepinephrine.
When caffeine is frequently present in the body and binds to adenosine receptor, the body can come to rely on caffeine to remain alert.
Some Effects of Adenosine

Heart
• Enhances blood flow to the heart muscle
• Decreases heart rate
• Prevents platelets from aggregation

Kidneys
• reduces blood flow, glomerular filtration rate, rennin secretion

Lungs
• constricts airways, reduces pulmonary artery pressure

Liver
• causes constriction of blood vessels and increases breakdown of glycogen to glucose

CNS
• depressant neurotransmitter

Adrenal glands
• steroid hormone production increases
How caffeine wakes you up

1. STOMACH: Stimulates acid production
2. BLOOD: Transports caffeine to organs
3. HEART: Higher pulse
4. BRAIN: Stimulates by replacing the brain’s own slow-down chemical
   - Effect: Alertness, concentration. Constrains blood vessels to the brain
   - Effect: Helps migraine headache
5. LUNGS: Relaxes involuntary muscles
   - Effect: Helps asthma
6. MUSCLES: Stimulates voluntary muscles for higher performance
7. KIDNEYS: Stimulates urine production
8. INTESTINES: Relaxes involuntary muscles — such as in colon

Peak effect: 15 to 45 minutes
Total effect: Two hours generally

Source: Home Health Handbook
Closer look at benefits, risks
Science-based
Main side effects of Caffeine

Eyes:
- Blurred vision

Sense of balance:
- Dizziness

Mouth:
- Dryness

Skin:
- Flushing
- Cold sweats
- Pallor

Heart:
- Fast heartbeat

Respiratory:
- Fruit-like breath odor
- Troubled breathing

Intestinal:
- Diarrhea

Central:
- Drowsiness
- Decreased or increased hunger
- Thirst
- Anxiety
- Confusion
- Irritability
- Insomnia

Systemic:
- Hyperglycemia

Muscular:
- Tremor

Gastric:
- Nausea
- Ache

Urinary:
- Increased urination
- Ketones in urine

Source,
Wikipedia,
fair use
Major Overdose Effects

- Mania
- Depression
- Lapses in judgment
- Disorientation
- Disinhibition
- Delusions
- Hallucinations and psychosis may occur
- Rhabdomyolysis (breakdown of skeletal muscle tissue) can be provoked.
- Lethal intoxication when blood concentration = 500 mM caffeine
Side Effects 1

Sleep
- Insomnia is common when taken before bed.

Disease risk
- Inhibits the absorption of iron and calcium from food, leading to an increased risk for development of osteoporosis. (Journal of AMA; JAMA, 26 Jan. 1994, p. 280-3.)
- Increased susceptibility to rheumatoid arthritis.
- Correlation between coffee consumption and a biochemical marker for rheumatism.
- Those who consume four cups daily are twice as likely to test positive for arthritis.
Dehydration
• Caffeine has a mild diuretic effect, increasing the possibility of dehydration during exercise.
• Reduced flow of blood to the brain from 10% to 20%
  Withdrawal symptoms can occur after regular consumption of just a single cup per day.

Reproduction
• Caffeine reduces rates of sperm motility.
• High levels of caffeine intake may delay conception among fertile women. *(Am J Epidemiol 1997; 145:324-34.)*
Overdose LD50

- X >300 milligrams per kilogram of body mass
  - Dependent on body weight/tolerance
  - a lethal overdose is hard to achieve; however with caffeine pills it becomes very easy
  - If consumed as little as 3-20 grams you can be hospitalized

- Death resulting from Ventricular Fibrillation, due to the effect of caffeine on the cardiovascular system
Toxicity during pregnancy

- **Pregnancy**
  - Consuming over 200mg per/day significantly increases the rate of miscarriage, can affect birth weight

- **Children**
  - Stunts Growth

- **Memory (Low Dose in mice)**
  - Slows development of hippocampus-dependent learning and impaired long-term memory in mice
    - Via inhibition of hippocampal neurogenesis.
Caffeine and Cancer
what is the risk?

• Caffeine consumption is hard to tease out in case-control studies, among many other factors (diet, exercise, obesity, stress, etc.)

• However, frequent coffee consumption has been associated with a reduced risk of colorectal cancer in a number of case–control studies.

• Data from the Nurses' Health Study (women) and the Health Professionals' Follow-up Study (men).
  • During almost 2 million person-years of follow-up, 1438 cases of colorectal cancer were observed.
  • Consumption of caffeinated coffee or tea with caffeine or caffeine intake was not associated with the incidence of colon or rectal cancer in either cohort.
  • Consumption of caffeinated coffee, tea with caffeine, or caffeine was not associated with incidence of colon of rectal cancer, whereas regular consumption of decaffeinated coffee was associated with a reduced incidence of rectal cancer.
Benefits of Caffeine

Parkinson's disease
• Researchers from the Harvard School of Public Health in Boston have concluded that regular caffeine consumption leads to a lower risk of developing Parkinson's by up to 80%.
  • Caffeine reduces the amount of neurotransmitters produced by the brain, which may cause damage to surrounding brain tissue.

Gallstones
• Those who drink two to three cups of regular coffee a day have about a 20 percent lower risk of gallstones than non-drinkers.
  o Caffeine may stimulate the gallbladder to contract, emptying stone-forming cholesterol and bile
Mental Performance
- Improves alertness and reaction time
- Stimulates the central system as it simultaneously lowers blood sugar and increases the brain's demand for sugar. Resulting in a temporary lift.

Mood
- Increase in positive mood including an increased state of well-being, happiness, energy, arousal, alertness, and sociability.

Physical Performance
- Caffeine helps the body burn fat instead of carbohydrates, and it lowers levels of perceived pain.
- Improvements in aerobic physical endurance and anaerobic performance.
More Benefits

Headache
· During a headache blood vessels dialate, but caffeine causes blood vessels to constrict relieving the pain.
· It is a mild analgesic.
· Helps the body absorb headache medications more quickly.
· Can makes pain relievers more effective by upregulating them.

Heart Health
· Coffee is full of antioxidants.
· Moderate coffee intake can help prevent some cardiovascular problems.
· Women who drink two to three cups of coffee a day have a 25% lower risk of heart disease and an 18% lower risk of developing diseases other than cancer than non-coffee drink
Caffeine is one of the most widely utilized drugs in the world.

Rewards include:
- Alertness
- Reduced Susceptibility to sleep
- Some Studies Show Increased performance

Side Effects Include:
- Anxiety
- Irritability
- Restlessness
- Sleep disruption (quality of sleep can be reduced)

May affect creativity, ability to slow down and savor life.
Summary and Conclusion

Tolerance
- Some people develop tolerances to caffeine
- Over time, a person can become acclimated to the initial increase in blood pressure associated with occasional caffeine use
- Opposite of desired effect can arise (tiredness)

Withdrawal effects
- Some characteristics of physical drug dependence with long term use
- Urge to re-administer not as strong as other addictive stimulants
- Does not appear to be a major issue
Possible Clinical Uses

• Parkinson’s
• Gallstones
• Poor mental performance, muddled thinking,
  – inability to concentrate
  – Lack of alertness
• Mild depression
• Poor physical performance, increase ability to do physical work
• Weight problems—burn calories and fat
• Headaches, pain
Clinical Uses—Herbalist
“get the benefit with the buzz”

- Green tea has greatest benefit/risk ratio
  - It usually has less caffeine than coffee or especially synthetic energy drinks
  - It’s antioxidant and protective effects well-studied
  - Sugar-free drinks widely available
  - Contains a variety of alkaloids, more balanced effect than synthetic caffeine
  - Contains L-theanine for a calmer overall effect
  - Standardized drinks are available from several manufacturers (standardized to caffeine, but then one wonders if synthetic caffeine is added)
Plants that synthesize caffeine
TEA (*Camelia sinensis*)

Franz Eugen Köhler, Medicinal Plants, 1887
Old Wild Tea Tree, Mountains of Yunan Province
Green Tea

• Second most widely-consumed beverage in the world (after water)
• 3 main varieties of tea, depending on processing
  – green, black, and oolong
  – green contains maximum amount of catechins
• Typical contraindications
  – blood thinners, anxiety, insomnia, arrhythmias.
History of Tea

- Complex history, likely known and used for thousands of years
  - Some writings suggest it was used as a medicinal drink during the Shang Dynasty (1600-1046 BCE)
  - Yellow River Valley, China
  - Morphological differences between the Assamese and Chinese varieties have led some to propose a dual origin for tea

- however, easy hybridization, chromosome numbers, molecular work and other work supports single origin in Yunnan (Yamamoto & Juneja, 1997)
Traditional Uses of Green Tea

• Traditional Chinese medicine (many uses)
• Bencao Gangmu (Materia Medica of Li Shizhen, 1578)
  – draining heat from the gall bladder
  – Emetic therapy (green tea on an empty stomach will induce vomiting—purges excess heat and damp)
  – Induces perspiration to relieve surface heat (rashes, skin infections, early stages of influenza)
  – Good for treating dysentery due to attack of pathogenic Heat and toxin
  – Treats asthma with excessive heat
  – “Treats somnolence in patient not able to wake up”
  – Painful urination (it’s a diuretic)
  – “Good for treating tea addiction!”
In Japan, micropowdered tea (matcha) (< 100 micron particle size) or sencha (leaf) is used in “the way of tea” ceremony

- Ritual social practice with prescribed steps, accoutrements, flower arrangement, performance
- Cultural activity for hospitality, demonstrate respect through grace and good etiquette, ceremonial preparation, presentation of matcha; can last for up to 4 hours
- First written record, 9th century CE

Chinese ceremony
- Often during weddings; couple serves tea to parents and thank them for parenting
① northeastern India (Arunchal Pradesh, Assam); ② northern Myanmar (Kachin and Shan states); ③ southern Yunnan (Xishuangbanna); ④ northern Lao PDR (Bokeo, Louang Namtha, Phongsali, Oudomxai) and ⑤ northern Vietnam (Lai Chau, Lao Cai, Ha Giang).

Source: www.teabox.com
Extraction, Brewing

Table 3. Changes in Composition of Leaf during the Manufacture of Black and Green Teas from the Same Fresh Assam (C. sinensis Var. assamica) Tea

<table>
<thead>
<tr>
<th>stage in the manufacturing process</th>
<th>% catechins</th>
<th>% TPP</th>
<th>% caffeine</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Black Tea Process</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>freshly plucked tea shoots (flush)</td>
<td>21.34</td>
<td>23.69</td>
<td>3.18</td>
</tr>
<tr>
<td>withered leaf</td>
<td>22.17</td>
<td>25.16</td>
<td>3.57</td>
</tr>
<tr>
<td>CTC rolled leaf</td>
<td>22.62</td>
<td>24.85</td>
<td>3.75</td>
</tr>
<tr>
<td>leaf after 60 min of fermentation</td>
<td>4.78</td>
<td>19.53</td>
<td>3.65</td>
</tr>
<tr>
<td>leaf after 120 min of fermentation</td>
<td>2.08</td>
<td>18.39</td>
<td>3.69</td>
</tr>
<tr>
<td>fired leaf (60 min of fermentation)</td>
<td>3.35</td>
<td>18.83</td>
<td>3.58</td>
</tr>
<tr>
<td>fired leaf (120 min of fermentation)</td>
<td>1.79</td>
<td>17.13</td>
<td>3.60</td>
</tr>
<tr>
<td>(b) Green Tea Process</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fresh flush</td>
<td>21.34</td>
<td>23.69</td>
<td>3.18</td>
</tr>
<tr>
<td>short withered leaf</td>
<td>24.20</td>
<td>24.90</td>
<td>3.82</td>
</tr>
<tr>
<td>pan-fried green leaf</td>
<td>22.00</td>
<td>24.82</td>
<td>3.77</td>
</tr>
<tr>
<td>shaped green leaf</td>
<td>21.63</td>
<td>25.05</td>
<td>3.74</td>
</tr>
<tr>
<td>fired green leaf</td>
<td>22.76</td>
<td>24.81</td>
<td>3.77</td>
</tr>
</tbody>
</table>

Table 2. Composition (70% Methanol Extract) of Green and Black Tea Products from Different Origins

<table>
<thead>
<tr>
<th>country of origin</th>
<th>green tea</th>
<th>black tea</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of samples</td>
<td>% catechins</td>
</tr>
<tr>
<td>Africa</td>
<td>1</td>
<td>13.8</td>
</tr>
<tr>
<td>Argentina</td>
<td>4</td>
<td>11.9</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>40</td>
<td>11.3</td>
</tr>
<tr>
<td>China</td>
<td>16</td>
<td>14.7</td>
</tr>
<tr>
<td>India (Assam)</td>
<td>5</td>
<td>6.30</td>
</tr>
<tr>
<td>India (Darjeeling)</td>
<td>2</td>
<td>1.25</td>
</tr>
<tr>
<td>India (south)</td>
<td>5</td>
<td>1.86</td>
</tr>
<tr>
<td>Indonesia</td>
<td>13</td>
<td>14.7</td>
</tr>
<tr>
<td>Japan</td>
<td>12</td>
<td>11.4</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>10</td>
<td>14.7</td>
</tr>
<tr>
<td>Vietnam</td>
<td>13</td>
<td>11.4</td>
</tr>
</tbody>
</table>
The results of these studies show that, although the product itself can have a significant effect, the preparation variables also greatly influence the composition of the infusion (Astill et al., 2001)
Composition, bioavailability

• Green tea contains purines (caffeine), polyphenols, flavonoids (antioxidants), amino acids such as L-theanine (calming), trace minerals

• Catechins (flavan-3-ols). The four major catechins are (-)-epigallocatechin-3-gallate (EGCG), that represents approximately 59% of the total of catechins; also chlorogenic acid, etc.

• Bioavailability of tea catechins is variable, depending on individual and specific compound
Science Summary

• Positive effect on blood sugar and insulin regulation (Zhong et al., 2006)

• Lower LDL levels as well as triglyceride levels, prevent LDL oxidation (precursor to cardiovascular disease)

• Likely the most-supported diet ingredient (increases metabolic rate, reduces appetite) -- (Hursel et al., 2009; Phung et al., 2010, meta-analyses)

• Reduced blood pressure (Khalesi et al., 2014)

• Systematic reviews and epidemiological studies support anticancer effect for various cancers, including endometrial (Zhao et al., 2015)

• Hepatoprotective effect; however idiosyncratic liver toxicity reported

• In large studies, green tea consumption (dose-dependent) was inversely related with mortality from heart disease in men and women; also up to 33% reduction in diabetes risk (Saito et al. 2015)
L-theanine is a unique amino acid in tea.

Green tea is proposed to be so popular and its use so widespread (2nd most popular beverage, worldwide) because it has a balanced stimulating effect due to theanine (Kimura et al., 2007); (Rogers et al., 2008); (Bryan, 2008); (Haskell et al., 2008); (Kelly et al., 2008).

Several studies have demonstrated anti-stress effects of theanine (Yoto et al., 2012a); (Unno et al., 2013); (Ritsner et al., 2011), increases in attention (Foxe et al., 2012), alertness (De Bruin et al., 2011), improvements in sleep quality (Lyon et al., 2011), and memory (Park et al., 2011).

Thought to bind to GABA receptors, reducing excitability, nervousness.
Wild Tea Tree, Mts. of Yunnan
Some Trees Dated at 1500 years

Source: Yunnan Longrun Tea Co. Group, Ltd.
Coffee (Coffea arabica)

- Origins—Ethiopia
- Dutch koffie from Turkish kahve and Arabic qahwah
- Qahway = Arabic quwwa (power, energy), but disputed
- Reached the U.S. in early 18th century
- Boston tea party—boycott British tea in favor of coffee
Coffea arabica  Rubiaceae

- Fruit is an indehiscent drupe
- Grown in the tropics, then a bush or small tree
- Grow at high elevations, but frost-intolerant
- One individual can produce for about 50-60 years
- Convergent evolution—different set of genes than tea, cacao
- Several species are sold as coffee
Historical Uses

- First introduced to Europe in the 16th century CE
- Through the capture of Turkish Muslim slaves
- Venice was an active trading port for coffee
- First coffee house in Venice, 1645; England a little later
- Many believed coffee to have medicinal benefits
- “…drying up the crudities of the stomach, expelling fumes from the head, giddiness”
- First plantations in Brazil in 1727—eventually turned coffee from an elite drink to a common drink for the masses
Social Impact

- Coffee as panacea medicine
- Coffee as the great soberer
- The replacement of alcohol
- Coffee houses as centers of intellectual meeting places; artists, musicians, writers
- Impact on business—how easy is it to sit in meetings for hours—why do you think they call it a “board” meeting?
- Echange, news, business etc.
Benefits Based on Research

- 3rd most commonly-consumed beverage
- $10 billion in trade
- Antioxidant effects from chlorogenic acid, caffeic acid, hydroxyhydroquinone, etc. (Butt & Sultan, 2011)
- Epidemiological and meta-analyses support benefits
  - Inverse association with diabetes
  - Parkinsonism
  - Alzheimer’s Disease
  - Benefits and drawbacks of caffeine
- Safety—pregnancy, excessive consumption of coffee can interfere with oral contraceptives or postmenopausal hormones
Kola Nut
(Cola acuminata, C. nitida)

- Malvaceae
- native to the rainforests of tropical Africa
- evergreen tree to 60 feet
- Seeds are bitter, then sweet and contain about 2-3.5% caffeine, theobromine (1-2.5%), theophylline, and kolanin
- Chewed in many cultures in ceremony, as a social drink
- History of use to restore vitality
The formula was created by a pharmacist, John Pemberton in 1886.
After the Civil War he wanted to create something successful for once (past efforts failed).
Soda fountain was rising in popularity.
He created the formula, and Frank Robinson businessman, registered the name, created the logo and slogan, “the pause that refreshes”.
Pemberton died before success; Asa Griggs Candler took over, great marketer; sold Coca-Cola as patent medicine—get rid of fatigue and headaches.
Coca-Cola, Original Formula

• Only one written copy survived—in a vault and only 2 people are allowed to know the formula at any one time; if one dies, a successor is chosen

• Original formula had coca leaf extract, kola nut

• Original recipe:
  – caffeine citrate, citric acid, vanilla extract, lime juice, sugar, fluid extract of coca leaf, water, caramel color + flavoring—orange, cinnamon, lemon, coriander, nutmeg, neroli oil; let stand 24 hours
Guarana (*Paullinia cupana*)

- Sapinaceae
- Liana, native to the Amazon, especially Brazil
- Twice the caffeine of coffee seeds (2-4.5%), theobromine, theophylline, timbonine
- Caffeine has been shown to act as a defensive toxin that repels herbivores
- Red fruits containing black seeds
- Guarana, from the indigenous name “warana” meaning “fruit like eyes of the people” due to seeds that look like eyeballs.
Cacao, source of Chocolate

*Theobroma cacao*  Malvaceae

- Cocoa is the partially fermented and dried bean obtained from the fruit of the cacao tree (*Theobroma cacao*)
- Native to Latin America and important to the Mayans and Aztec cultures
- *Theobroma*—”food of the gods”
- Mayans used cocoa to create a ritual beverage for betrothal and marriage ceremonies—first link between romance and chocolate!
- Chocolatl—Spanish learned of it in the early 1500’s during the conquest of the Maya, then became jealously-garded sole distributors of it for 100 years
- Jose de Acosta: “it is so much esteemed among the Indians that it is one of the richest and greatest traffickes of New Spain”
Left to right: *T. grandiflorum*, *T. bicolor*, *T. speciosum*, *T. cacao*

The aril is sweet and delicious

Source: Wikipedia, fair use
Benefits, Based on a Science Review

• Total polyphenol content in cocoa powder, as estimated by the Folin assay, is 5624 mg/100 g.
• Polyphenols, which have antioxidant, antiinflammatory properties
• Inhibition of LDL oxidation—prime etiological factor in the genesis of cardiovascular disease
• Suppression of platelet activation—similar to aspirin
• Lower systolic and diastolic bp (500 mg/d total polyphenols)
• Improved peripheral vasodilation (821 mg/d total polyphenols)

Source: Cooper et al., 2008
Yerba Mate (& *Ilex* spp.)

- Pre-Columbian Paraguay
  - Used culturally by indigenous Guarani as a medicine for energy and other purposes
  - Spanish became acquainted with the drink in early 1500s; widely consumed by Spanish in the late 1500s
  - 1596, Cbildo of Asuncion wrote: “the vice and bad habit of drinking yerba has spread so much among the Spaniards their women and children, that unlike the Indians that are content to drink it once a day they drink it continuously and those who do not drink it are very rare”
**Ilex vomitoria**

Only caffeine-containing plant in NA

- Range, from Maryland south to Florida and west to Oklahoma and Texas
- Native tribes brewed the leaves and stems to make a tea called “black drink” for male-only purification and unity rituals which included vomiting
- While excessive amounts cause vomiting, original use is in question
- Leaves and twigs contain caffeine and theobromine (up to about 1%)
References


http://www.erowid.org/chemicals/caffeine/caffeine_health.shtml
http://content.nejm.org/cgi/content/abstract/327/16/1109
