Stimulants
Xanthenes and Caffeine

Psychology 472
Pharmacology of Psychoactive Drugs

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Many Types of Xanthenes

- Xanthenes
  - Theophylline (Tea)
  - Theobromine (Chocolate)
  - Caffeine (Coffee)

Theophylline

- Found in Tea
  - Has very little in it when made so it has minimal effects
- Primarily used for breathing problems in asthmatics
  - Relaxes and opens bronchial trees

Theobromine

- Found in Chocolate
- Has far less potency than caffeine

Caffeine

- Most commonly used psychoactive drug in the world
- Average intake per day in US 250mg/day
  - Sweden and Finland 400mg/day
- Causes tolerance and withdrawal – not considered drug abuse
- No regulation on sale or use

Caffeine Content

<table>
<thead>
<tr>
<th>Item</th>
<th>Average (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Home regular cup of Coffee (8oz)</td>
<td>65-175</td>
</tr>
<tr>
<td>Starbucks (8oz)</td>
<td>180</td>
</tr>
<tr>
<td>Starbucks (16oz)</td>
<td>330</td>
</tr>
<tr>
<td>McDonalds (16oz)</td>
<td>145</td>
</tr>
<tr>
<td>Latte or Mocha (16oz)</td>
<td>75</td>
</tr>
<tr>
<td>Espresso (1.5oz)</td>
<td>64</td>
</tr>
<tr>
<td>Non-Caffeinated Coffee</td>
<td>2.4</td>
</tr>
<tr>
<td>Tea (5oz)</td>
<td>50</td>
</tr>
<tr>
<td>Amp Green Tea (16oz)</td>
<td>155</td>
</tr>
<tr>
<td>Cocoa (5oz)</td>
<td>5</td>
</tr>
</tbody>
</table>

Range 58-185mg
### Others

<table>
<thead>
<tr>
<th>Item</th>
<th>mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coke Classic (12oz)</td>
<td>35</td>
</tr>
<tr>
<td>Coke Zero (12)</td>
<td>35</td>
</tr>
<tr>
<td>OTC analgesics (aspirin)</td>
<td>35-65</td>
</tr>
<tr>
<td>OTC cold remedies</td>
<td>30</td>
</tr>
<tr>
<td>No-Doz</td>
<td>100 per pill</td>
</tr>
<tr>
<td>No-Doz, Maximum Strength</td>
<td>200 per pill</td>
</tr>
</tbody>
</table>

### Energy Drinks

- Arizona Extreme Energy Shot®: 100 mg / 8 oz
- Beaver Buzz®: 110 mg / 8 oz
- BuzzWater®: 100 mg / 8 oz
- Daredevil®: 120 mg / 8 oz
- Hogan Energy®: 80 mg / 8 oz
- Sky Rocket® and Power Shot®: 100 mg / 1 oz
- Upshot™: 200 mg / 2.5 oz

### Positive Effects

- Enhanced mental alertness
  - Allows for sustained intellectual efforts - studying
  - No major disruption of coordinated intellectual thought or motor activity
- Provides increased energy
- Gives a sense of well-being
- Reduced fatigue
- Sleep onset is delayed

### Negative Effects

- Muscles
  - Decreases muscle coordination and timing
  - Causes muscle tremors and shaking
- Heavy doses - 1.5 grams
  - Agitation
  - Anxiety
  - Tremors
  - Rapid breathing
  - Insomnia
  - Diarrhea
- LD Approximately 10 grams
  - 100 cups of coffee
  - 100 OTC stimulant capsules

### Effects

- Caffeine causes stimulant action on the heart
  - Increases cardiac workload
    - Stronger contractility
    - Increases cardiac output
  - Dilates coronary arteries
    - Provides more oxygen to the heart

### More Effects

- Constricts cerebral blood vessels
  - Decreases blood flow by about 30%
  - Can relieve headaches
- Causes bronchial relaxation
- Causes increased secretion of gastric acid
  - Result, nausea, stomach aches
- Causes increased urine output
Effects

- Chronic use is associated with habituation and tolerance
- Quitting may cause withdrawal
  - Headaches
  - Drowsiness
  - Fatigue
  - Negative mood

Reproductive Effects

- Consumed by estimated 75% of pregnant women
- Breast milk contains equal or higher concentration levels than mothers' blood plasma
- Freely crosses the placental barrier
- Safety still unresolved
  - One study shows 300 mg relatively safe
  - Another study shows 160 mg may cause growth retardation
  - 300mg intake in the month before doubled the risk of spontaneous abortion
    - Moderate consumption does not increase the risk

Uses of Caffeine

- Asthma
  - Causes bronchial dilation
- Narcolepsy
  - Helps maintain daytime wakefulness and alertness
- Reduction of headache in conjunction with aspirin
- Migraines
  - Restricts blood flow in the cerebral cortex

Pharmacokinetics

- Intake is usually oral
- Is rapidly and completely absorbed
  - Significant blood levels reached in 30-45 minutes
  - Levels peak in about 2 hours
- Is distributed throughout total body water
  - Equal concentrations throughout body and brain

Continued

- 3.5 to 5 hours half life
  - Extended half life for
    - Elderly
    - Pregnant women
    - Up to ten hours
    - Infants
  - Decreased half life for smokers

Metabolized

- Metabolized by the CYP1A2 subgroup of liver enzymes into three metabolites
  - Theophylline
    - Bronchial relaxation
  - Paraxanthine
  - Theobromine
    - Theophylline and Paraxanthine act similar to caffeine
  - 10% is excreted unchanged
Pharmacodynamics

Adenosine

- Is created when the body uses ATP for energy
- Is a neuromodulator
  Impacts the rate at which neurons fire
  Uses a G-Protein system
  The greater the activity, the more adenosine that is produced
  - Causes sedative, depressant, and anticonvulsant actions
    - Works to slow down the system
    - Important to sleeping
  - Adenosinergic neurons form a diffuse system
    - No exclusively adenosinergic pathways
    - Adenosine stimulates GABAergic inhibitory neurons

Locations

- Throughout the body
  - Blood vessels
  - Fat cells
  - Heart
  - Kidneys
  - Smooth muscle
  - Others

Receptors

- Four types
  A1 inhibits excitatory neurons
    - Dopamine, glutamate, and ACh secreting neurons
    - Reduces production of cAMP
    - Slows the activity of the cAMP Protein Kinase
    - Reduces occurrence of the action potential
  - A2a Stimulates inhibitory neurons
    - Also inhibits Dopamine neurons
    - Stimulates GABAergic neurons

Mechanism of Action

- Adenosine A1 receptors
  - Inhibit the release of dopamine and glutamate
  - Inhibits the release of acetylcholine

- Blockade of A1 receptors
  - Modest reward
  - Increased vigilance and mental acuity
  - Creates arousal effect

Mechanism of Action

- Adenosine A2A receptors
  - Stimulate GABAergic neurons of inhibitory pathways
  - Inhibits dopamine activity

- Blockade of A2A receptors
  - Increases the potency of endogenous dopamine
Effects of Adenosine

- When occupied by adenosine they shut the system down
- Prevents the system from becoming over stimulated

Effects of Xanthenes

- Caffeine and others block Adenosine Receptors
- Results
  - Adenosine cannot bind to the receptor
  - Get stimulation
    - Does not stimulate dopamine release

Importance of Caffeine

- Creates additive and synergistic effects with other compounds
- Increases withdrawal symptoms of individuals coming off of alcohol and sedative hypnotics
  - Seizures
  - Agitation
  - Headaches
  - Nausea (also with Opiates)

Alcohol and Energy Drinks

- 6-12% alcohol with stimulants
- Allows you to drink longer
  - Get drunk faster
- Become a wide awake drunk
  - Still have the same alcohol effects on motor coordination
- Myth – Prevents hangovers
  - Alcohol causes dehydration
  - Energy drinks are diuretics – more dehydration
  - Greater headaches

Conclusions

- In moderation, are probably safe
- Do develop tolerance and withdrawal
- Can cause paranoia and other psychological disorders at high levels