University of Idaho

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 open 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 400 mg/day
- Causes tolerance and withdrawal – not considered drug abuse
- No regulation on sale or use

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Caffeine Content

Item	Average (mg)	
Home regular cup of Coffee (8oz)	65-175	
Starbucks (8oz)	180	
Starbucks (16oz)	330	
McDonalds (16oz)	145	
Latte or Mocha (16oz)	75	
Espresso (1.5oz)	64	Range 58 -185mg
Non - Caffeinated Coffee	2-4	
Tea (5oz)	50	
Amp Green Tea (16oz)	155	
Cocoa (5oz)	5	

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Others

Itemshttp://www.energyfiend.com/caffeine-source-reference

Item	mg
Coke Classic (12oz)	35
Coke Zero (12)	35
OTC analgesics (aspirin)	35-65
OTC cold remedies	30
No-Doz	100 per pill
No-Doz, Maximum Strength	200 per pill

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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

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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
  - http://www.energyfiend.com/death-by-caffeine

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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

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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

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Effects

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

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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

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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

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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

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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

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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

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Pharmacodynamics

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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 GABAa inhibitory neurons

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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 GABAa neurons

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Mechanism of Action

- Adenosine A_1 receptors
  - Inhibit the release of dopamine and glutamate
  - Inhibits the release of acetylcholine
- Blockade of A_1 receptors
  - Modest reward
  - Increased vigilance and mental acuity
  - Creates arousal effect

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Mechanism of Action

- Adenosine A_{2A} receptors
  - Stimulate $GABA_A$ neurons of inhibitory pathways
  - Inhibits dopamine activity
- Blockade of A_{2A} receptors
  - Increases the potency of endogenous dopamine

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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
  - Sill 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