The Use and Abuse of Power: Commercially Available Energy Drinks

Anand Sridhar, Ph. D.
Assistant Professor, Pharmaceutical Sciences
Pharmacy Society of Rochester, Rochester, NY
22.MAY.2016

Disclosures and Disclaimers
- The contents presented herein are the views of the presenter, and do not represent the official views or opinions of the Wegmans School of Pharmacy or St. John Fisher College
- The presenter does not have any existing or potential conflicts of interest with or financial interests in the companies and/or their products presented herein

Objectives
- List three reasons why people consume energy drinks
- Describe the FDA regulations and Senate recommendations of energy drinks
- Distinguish between energy drink and energy shot
- List any three positive effects of caffeine
- List any three adverse effects of caffeine
- List the main symptoms of caffeine overdose
- Discuss the metabolism of caffeine
- Describe the characteristics of non-caffeine components of energy drinks
- Describe some benefits of energy drinks
- Describe the problems that may arise from consumption of energy drinks
- Describe the role of the pharmacist

Introduction
- Red Bull: Austria, 1987; USA, 1997
  - Introduced as a niche product to X-treme sports enthusiast
- Energy drinks are multi-billion dollar industry
  - In 2010, sales were half the sale of Coke and Pepsi
  - In 2012, sales were > $8 billion
    - Soda consumption on the decline due to health reasons
      - Coke and Pepsi made lower sales
    - Advertising in 2012 was $282 million, up 71% since 2010
Top 5 Energy Drinks

- Red Bull®
  - 1997 in the US
  - 43% market share
- Monster®
  - 39% market share
- Rockstar®
  - 10% market share
- NOS®
  - 3% market share
- Amp®
  - 3% market share

Reasons for the popularity of Energy Drinks

- Provide extra boost in energy
- Increased endurance
- Reduced fatigue during workouts
- Increase strength and athletic ability
- Maintain Alertness
- Increase Wakefulness
- Improve concentration and cognition
  - Tasks required focus; studying
- Enhance mood, reduce anxiety
- Alcohol-related reasons
  - Reduce alcohol intoxication
  - Enhance the experience of alcohol intoxication

Sales

- No restriction on sale
- Easily available to all, including young teens
- Most sales occur in convenience stores
  - Impulse purchases
- Product positioning
  - Near alcohol, Near sugary drinks: “associative branding”
  - Targeted ads on TV
    - Channels watched by youth
      - MTV, Comedy Central
  - Social media branding
    - Facebook pages
    - Linked to main websites
  - Endorsements by celebrities

Definition of Dietary Supplements

- The Dietary Supplement Health and Education Act of 1994 defines a dietary supplement as a product (other than tobacco) that:
  - is intended to supplement the diet
  - contains one or more dietary ingredients (e.g., vitamins, minerals, herbs, amino acids)
  - taken by mouth as a pill, capsule, tablet, or liquid
  - is labeled on the front panel as being a dietary supplement.
Use of natural products in common culture

- Dramatic increase in the rise and widespread use of herbal products
- Significant percentage of people on conventional therapy
  - Elderly population on multiple drugs
  - Enhanced risk of therapeutic toxicity or ineffectiveness of medications
- Many do not disclose their use
  - Belief that they are safe
  - “The Dr. Oz” effect
- Energy drinks contain “natural” substances and supplements
  - Leading to incorrect perceptions of safety

Labeling of Dietary Supplements

- Label can only claim the following:
  - Description of the relationship between the product and the disease
    - Qualified Health Claims
  - Amount of nutrient or “active ingredient” in the product
    - Nutrient Content Claims
  - Description of how this may affect organs/systems
    - Structure/Function Claims
  - Statement: “This statement has not been evaluated by the FDA. This product is not intended to diagnose, treat, cure, or prevent any disease.”

Labeling Information

- Requirements established by the FDA
- Name; include the word “supplement”
- List of ingredients
  - Single ingredient
  - Proprietary blends
- Serving size and total quantity
- List of additives, colors, fillers, sweeteners, etc.
- Usage directions (oral, dissolve in water, etc.)
- Name of manufacturer or distributor

FDA Regulations

- Caffeine and other ingredients are GRAS
- Few adverse events have been reported
  - Only 145 between 2002 and 2012
  - FDA Center for Food Safety
  - Applied Nutrition Adverse Event Reporting System
    - 5-Hour Energy, Monster, and Rockstar
- Caveats
  - Small fraction of all events
  - Self-reporting
  - Manufacturer disputed conclusions
  - Lack of complete evidence for the FDA

http://www.fda.gov/Food/IngredientsPackagingLabeling/default.htm
FDA regulations

- FDA requirements for establishing the safety of ingredients used in dietary supplements (including energy shots and some energy drinks) differ somewhat from requirements for beverages
- Reporting the use of a new dietary ingredient is voluntary
  - 1997: Self-determination rule
  - Mfr. not required to notify the FDA, nor need to provide evidence of their safety
- Companies ensure the caffeine levels are within GRAS limits
  - Same for additional ingredients (ginseng, taurine)
- Code of Federal Regulations described caffeine as GRAS in concentrations up to 71mg/12 oz (0.02% concentration) in “cola-type beverages”
- FDA is tasked for ensuring safety “after” marketing
  - Low threshold for FDA to remove a product from the market

US Senate Hearings

- Senate Committee on Commerce, Science, and Transportation
  - 2013 hearing; investigation of energy drink marketing to youth
  - Industry representatives pledged that they would not market their products to young children* but refused to place limitations on marketing to children who were 12 and older
    - Red Bull is safe for teenagers and adults to consume
    - We believe our product [Monster Energy Drink] is safe for teenagers, and there is no reason why teenagers should not be part of being able to consume the brand.
  - *Analysis of their specific statements indicates that companies primarily pledged to limit advertising during children’s television programming
- FDA intends to evaluate the regulatory framework surrounding caffeinated foods and beverages

Policy Recommendations

- Senators Blumenthal, Durbin, Markey and Rockefeller called on energy drink manufacturers to voluntarily “take steps to improve transparency and representation of its products and ensure that children and teens are adequately protected from deceptive advertising practices”

- Recommendations made to manufacturers; Voluntary
- Role of the Federal Trade Commission and States Attorney General
  - NYS AG is investigating complaints of consumers being misled by product claims
- In 2013, Suffolk County New York was the first community to regulate marketing of energy drinks, prohibiting distribution of coupons and free samples to minors and sales in county parks and beaches

- Clearly label the caffeine content on product packaging, including caffeine in the entire container (in effect 1 serving) for nonresealable containers
- Include the following warning label on all products that contain caffeine in concentrations greater than the level affirmed as GRAS by the FDA (i.e., 71 mg/12 fl oz), “This product is not intended for individuals under 18 years of age, pregnant or nursing women or for those sensitive to caffeine. Consult with your doctor before use if you are taking medication and/or have a medical condition”
- Stop marketing energy drinks to youth under 18 years of age, including in traditional and social media, sponsorships, and other activities with a primarily youth audience; and
- Report all serious adverse events to the FDA, including for products labeled as beverages
### Caffeine

- CNS stimulant
- Most consumed “drug” as a part of our food
  - Coffee, tea, soda/cola
- Xanthine Alkaloids
  - obtained from *Coffee arabica* and *Camilla sinensis*
- Caffeine, theobromine, theophylline
- Binds to the G-protein coupled receptor, increased levels of cAMP, results in epinephrine-like actions
  - Elevated heart rate, lipolysis
- Binds to adenosine receptor and inhibits it
  - Wakefulness

### Main symptoms of Caffeine overdose

- **Central**
  - Irritability
  - Anxiety
  - Restlessness
  - Confusion
  - Delirium
  - Headache
  - Insomnia

- **Visual**
  - Seeing flashes

- **Ears**
  - Ringing

- **Skin**
  - Increased sensitivity to touch or pain

- **Muscular**
  - Seizures
  - Trembling
  - Twitching
  - Overextension

- **Respiratory**
  - Rapid breathing

- **Gastric**
  - Abdominal pain
  - Nausea
  - Vomiting (possibly with blood)

- **Systemic**
  - Dehydration
  - Fever

- **Urinary**
  - Frequent urination

---

### Health effects of caffeine

**Positive effects**
- Increased attention and alertness, decreased fatigue
- Lower risk of cardiovascular disease
- Lower risk of diabetes
- Increased metabolic rate

**Negative effects**
- Anxiety
- Increased vasoconstriction and blood pressure
- Reduced control of fine motor movements
- Stimulated urination

---

**References**


Energy Drinks

- Category of beverages that contain high levels of caffeine, and specialty ingredients, not usually contained in sodas or juices
- Features:
  - Usually carbonated
  - High levels of sucrose
  - Non-resealable containers
    - Usually 16 fl oz (473 mL)
- Energy Shot
  - Usually non-carbonated
  - “Shot” size of 2-2.5 fl oz (50-75 mL)
  - Single-serve “tonics”
  - Usually contains artificial sugars or sweeteners

Caffeine

- FDA Limit: 71 mg/12 oz
- Energy drink, 16 oz: 70-240 mg
- Energy shot, 2 oz: 113-200 mg
- Additional components
  - Non-caffeine stimulants
  - Cognitive enhancers
  - Added sugar and/or other sweeteners

Caffeine content

- Standard cup of coffee: 100 mg of caffeine
- Caffeine tablets: 200 mg of caffeine
- 12 oz serving size of these colas
  - Coca Cola® Classic: 29.5 g
  - Pepsi: 31.7 g
  - Dr. Pepper®: 36 mg
  - Mountain Dew®: 45.4 g
- Red Bull®: 8 oz, 66.7 g
- Amp™: 8 oz, 69.6 g
- Starbucks® Double Shot: 6.5 oz, 105.7 g

Common Components of Energy Drinks

- Caffeine
- Carbohydrates
  - Sugar
  - HFCS
  - Sugar-substitutes (Splenda®, Aspartame)
- Glucuronolactone
- Vitamins
  - B complex
- Taurine
- Ginseng
- Guarana
- Acai
- Bitter orange
Gingko

- Gingko biloba; leaves
- Extracts used to treat asthma, allergies, tinnitus
  - Over 40 phytochemicals: complex pharmacology
    - Flavonoids (quercetin, kaempferol) and
    - terpenoids (ginkgolides A and B, and bilobalide)
  - In the US, extracts have been standardized to 25% flavonoids and 6% terpenoids

---

Gingko: Validated Effects

- Shown to improving symptoms of Alzheimer’s, vascular, or mixed dementias
- Gingko extract stimulates receptor expression and neurotransmitter concentrations in the brain, particularly acetylcholine.
- Improving short-term visual memory and speed of mental processing in non-demented people with age-related memory loss.
- Improving thinking skills in healthy young to middle-aged people.

---

Nootropics

- Gingko
  - Rockstar®, Lightning Bolt®, Quick Boost®, Crunk™
- -racetams
  - Neurofuel®: Piracetam
- Acetylcholine substitutes
  - Citicholine: 5-hour Energy®

---

Weinmann, S. et al. BMC.Geriatr. 2010;10:14
Ginseng
- Amounts range from 8 – 400 mg in 16 oz
- Use: Boosts memory

Products:
- Rockstar Energy Drink, Rockstar Recovery Energy Drink
- Monster Original Energy Drink, Monster Hitman
- Crunk Sugar Energy Drink
- Jolt Endurance

Guarana
- *Paullinia cupana*
- Guarana, after the Guarini tribe; used widely in Brazil
- Uses
  - Increase stamina and energy
  - Suppress appetite
  - Stimulate the metabolism
  - Enhance memory
- Seeds are crushed
- 5% caffeine
  - *C. arabica* beans: 2-3%
  - Trace amounts of theophylline and theobromine

Quercetin
- Extracted from oak bark (*Quercus sp.*)
- Quercetin: Flavonoid
  - Found in many fruits (apples, blueberries)
  - Anti-oxidant properties
- Use: Antioxidant, energy boosting

Products
- FRS Energy Drinks
  - 325 mg per serving
- Claim: Provides sustained energy, increased endurance, and immune support

Taurine
- Physiological role
  - Taurine bile acid conjugates, for fat metabolism
  - Positive inotropic, chronotropic, and anti-dysrhythmic effects
- Double-blind placebo controlled study in healthy volunteers.
  - Drinks containing taurine and caffeine (1,000 mg and 80 mg/240 mL, respectively) were evaluated
  - Rapid visual information test, a verbal reasoning test, a set of mood measures, and a verbal and nonverbal memory test
  - Attention and verbal reasoning improved with the caffeinated taurine-containing drink compared to placebo
  - Not clear if it was taurine or caffeine causing the effects
- At doses > 2 g daily, adverse events such as diarrhea, itching, hyperkalemia were noted.
Bitter orange

- *Citrus aurantium*
- Ephedra substitute, contain synephrine and octopamine
- Same Adverse effects as ephedra
  - α-adrenergic activation
- Some role in weight loss but not without risk
- Reported AE include
  - Ischemic stroke
  - Exercise-induce syncope
  - QT prolongation
  - Possible MI
- Products: ABB adrenaline stack, Piranha, Extreme Ripped Force

Adverse Effects and Interactions

- Commonly seen with Energy drink ingredients

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Adverse Effect</th>
<th>Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bitter orange</td>
<td>Stroke, MI, Seizures, Hypertension, migraines</td>
<td>Ginseng, caffeine, guarana, yerba mate, ephedra</td>
</tr>
<tr>
<td>Ginseng</td>
<td>Insomnia, tachycardia, hypertension, vertigo, euphoria, mania</td>
<td>Bitter orange, caffeine, guarana, ginger, ephedra</td>
</tr>
<tr>
<td>Guarana</td>
<td>Insomnia, nervousness, irritability, tremors, dysrhythmia</td>
<td>Bitter orange, caffeine, kola nut, yerba mate, alcohol, ephedra</td>
</tr>
<tr>
<td>Taurine</td>
<td>Insufficient reliable evidence</td>
<td>None reported</td>
</tr>
</tbody>
</table>

Energy Drinks and Sleep

- Effects on sleepiness
  - Self-reporting study
- Consuming energy drinks
  - Reduced sleepiness
    - Reduced driving errors
    - Reduced lane swerving
- Energy drinks also contained other substances
  - Increased caffeine content from guarana
  - Increased energy from sucrose


Energy drinks and Mood

- Effects of energy drinks on cortisol levels, cognition, and mood
- A double-blind, mixed-measures study of 81 subjects involved in firefighter training
  - Glucose/Caffeine and placebo
    - 50 g/40 mg, 10.25 g/80 mg, placebo
- Individuals with 50g glucose/40mg caffeine beverage endorsed reduced anxiety and elevated mood following the stressor of firefighting training
Cognitive benefits of “energy drinks”

- Effects of caffeine and glucose were tested for cognitively demanding tasks
  - 38/68 mg, 46/68 mg, placebo; 33/60 mg, placebo
  - 380 mL or 330 mL drinks
- Double-blind, placebo-controlled cross-over studies
- Test
  - Overnight fasting, caffeine deprivation
  - 10 mins ‘cognitive demand battery’
    - Subtraction (3s) and Identification (serial 7)
  - Take the drink
  - Repeat the ‘cognitive demand battery’ 6x in succession
  - Rate fatigue after every test

Advantages

- Suitable combination of caffeine and glucose
- Reduced mental fatigue during repetitive tasks
  - Switchboard operator
  - Students taking long exams
- Reduced physical fatigue
- Mitigate deficits in cognitive performance
- Improved cognition
  - Useful in moderating cognitive decline in older patients
  - Cochrane review
- Addition of nootropics to commercially available energy drinks claim to do this

Energy Drinks and Alcohol

- AMED: Alcohol Mixed with Energy Drinks
  - Popular among college students, and adolescents
- Combination
  - Alcohol: sedation
  - Caffeine: stimulant
- Reduced sensation of intoxication
- Elevated risky behaviors
- Induces more drinking!
  - Poorer judgement

Kennedy DO, Scholey, AB; Appetite. 2004 Jun;42(3):331-3.
**Studies on AMED and College Students**

- Adjusted odds ratio for leaving the bar intoxicated
  - AMED v. Alcohol (without caffeine): 2.99: 1

- Adjusted odds ratio for leaving the bar intoxicated AND Intending to drive
  - AMED v. Alcohol (without caffeine): 4.29: 1

- 2X as likely to
  - more intoxicated
  - experience or commit sexual assault
  - ride with an intoxicated driver
  - be involved in an automobile crash
  - being physically hurt and requiring medical treatment

Howland, J.; Rohsenow, D. J.; (2013), JAMA, 309(3):245-246

---

**Additional Health Issues**

- Seizures
  - “Diet pill” with 24 oz Monster®

- Psychiatric effects
  - Initiate or exacerbate mania
  - Case reports of individuals on ginseng therapy-induced mania
  - Mania after ingesting 1 g caffeine daily; reversed on stopping
  - Mania after consuming three cans of Red Bull® in two days while on Lithium therapy

- Obesity
  - High levels of sugar

---

**Patients Beliefs**

- Patients lack awareness that energy drinks may interact, interrupt, and/or alter the efficacy of prescription or OTC pharmaceutical drugs

- Many believe that
  - Being “natural” they have no adverse effects
  - Don’t think of it, don’t disclose it
  - Believe that these products are not at odds with their healthcare provider’s treatment plan

---

**Additional Health Issues**

- Athletic performance
  - Red Bull recommends consuming the drink “prior to demanding athletic activities
  - Effects are due to caffeine

- Dental Health
  - Low pH products
  - Studies demonstrated erosion of dental enamel

- While energy drinks are safe for the majority of consumers when used in moderation (with caffeine intake of less than 300 mg/day), the high caffeine content poses serious health risks for certain populations.
Role of the pharmacist

- Key role in counseling patients on the adverse effects of
  - Excess caffeine consumption
  - Excess sugar consumption
- Pharmacists can help identify idiosyncratic adverse effects
  - Gather patient information
  - Discuss the use of natural, herbal, products
- Particularly,
  - Individuals sensitive to caffeine
  - Pregnant women and lactating women
  - Individuals with diabetes
  - Individuals with cardiovascular disease
  - Individuals with psychiatric disorder

Caffeine cleanse/detoxification

- *Evodia rutaecarpa*; Rutaecarpine
- Induces CYP1A2 and CYP2E1
- Increases the metabolic breakdown of caffeine and other xanthine alkaloids
- Just a faster detox
  - Does not help caffeine withdrawal

A more powerful breakfast ...

- **The Caffeinated Bacon Waffle Redefines Breakfast On The Go**
  - [http://www.huffingtonpost.com/2014/03/07/caffeinated-bacon-waffle-maple_n_4913635.html](http://www.huffingtonpost.com/2014/03/07/caffeinated-bacon-waffle-maple_n_4913635.html)

Conclusion

- Studies indicate more inimical effects of commercially available energy drinks than benefits
  - Controlled studies show some cognitive benefits
- Benefits of non-caffeine natural products are likely exaggerated
  - Levels of guarana, taurine, etc. are less-than-therapeutically-useful levels
  - Serious side-effects are also less
- Serious concerns exist
  - Levels of caffeine
  - Levels of sugar
- Public relies on the health-care professional, particularly the community pharmacist
  - Intervention
  - Education