Consumer Health Information:
Like it or Not, It Has a Big Impact on Practice

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Disclosure
I do not have a vested interest or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity, or affiliation with any organization whose philosophy could potentially bias my presentation.

Objectives

• Upon completion of this activity, the participant should be able to:
  – Evaluate the impact of consumer health informatics on self-care.
  – Discuss cases of reported adverse events associated with the use of products recently highlighted in the media.
  – Discuss the safety and efficacy of herbals recently publicized in the media.

Impact of Informatics on Self-Care

We are in an Electronic Media Age

• I-phones, other cell phones
• I-pads, other “pads”
• Laptop computers
• Desk computers
• Radio
• Cable television

The Age of Electronic Experts

• Dr. Mehmet Oz
• Dr. Marc Siegel
• Dr. Isadore Rosenfeld
• Dr. Nancy Snyderman
• Dr. Richard Besser
Herbal Supplement and Vitamin Use

- 50% of adults regularly take vitamin supplements
- 25% of adults take herbal supplements at least occasionally
- 2010 annual sales of supplements: $25 Billion
- 2011 annual sales of supplements $29 Billion
- Businesses: 1,455, Employment: 49,972

Drug Topics. 2010 Jul 14-16
www.ibisworld.com

Herbal Supplement and Vitamin Use

- Increased use of supplements driven by:
  - Obesity epidemic
  - Prevalence of chronic disorders
  - Pain syndromes
  - Anxiety
  - Depression
  - Desire for good health and wellness


Herbal Supplement and Vitamin Use

- Increased use of supplements driven by:
  - Disease prevention
  - Increasing cost of conventional medicines
  - Belief that Complementary & Alternative Medicine (CAM) is safe and more effective than prescription drugs that commonly have adverse effects
  - Belief that supplement use is “natural”


Food and Drug Administration (FDA)

- FDA regulates dietary supplements under a different set of regulations (foods) than those covering "conventional" drug products (prescription and over-the-counter)
- Regulations for foods are much less stringent than those for Rx and OTC products

www.fda.gov/biologics/NEWG2017/NEW51607.html

FDA Final Rule

- FDA Issues Dietary Supplements Final Rule:
  “Manufacturers are required to evaluate the identity, purity, strength, and composition of their dietary supplements.”
FDA Final Rule (cont.)

“If dietary supplements contain contaminants or do not contain the dietary ingredient they are represented to contain, FDA would consider those products to be adulterated or misbranded”

Herbals Products in General

• May have no activity at all due to:
  – No scientific evidence from reliable studies
  – Low therapeutic dose of active ingredients
  – Mislabeling (misbranding) of the product
  – Adulterated products

Herbals Products in General

• May have clinical activity due to natural properties of their chemical makeup
  – Sterols
  – Stanols
  – Red yeast rice
• May have activity due to adulterants or additives that do have therapeutic activity

Active Rx Medications in Herbal Products

Products Reported to MedWatch

• Claim to be “natural” dietary supplements
  – Contain undeclared drug ingredients
  – Considered unapproved new drugs
• Erectile dysfunction
  – X-ROCK for men
    • Contains sildenafil and hydroxythiohomosildenafil
  – RegenErect and ReganArouse
    • Contains tadalafil
  – Mojo Nights
    • Contains tadalafil and sildenafil

Products Reported to MedWatch

• Weight loss
  – Fruta Planta and Joyful Slim Herb Supplement
    • Contain sibutramine
  – Que She Herbal Supplement
    • Contains fenfluramine, propranolol, sibutramine, and ephedrine
  – Starcaps
    • Contains bumetanide
Products Reported to MedWatch

- Pain relief
  - Reumofan Plus and Reumofan Plus Premium
    - Contain methocarbamol and diclofenac
- Testosterone booster
  - Uprizing 2.0
    - Contains superdrol (synthetic steroid)
- Benign prostatic hyperplasia (BPH)
  - U-Prosta
    - Contains terazosin

Selected Herbals

- Raspberry Ketone
- Marijuana
- Green Coffee Bean Extract

Raspberry Ketone Gains Popularity

- In February 2012, TV personality Dr. Oz featured the product on his show calling it “the No. 1 miracle in a bottle to burn your fat”
- Dr. Oz explains how Raspberry Ketone may stimulate adiponectin, a hormone linked to lipolytic processes and adipocyte function
- He then explains how Raspberry Ketone can help people lose weight along with diet and exercise

Safety and Efficacy of Three Selected Media Reported Herbals

Raspberry Ketone (RK)

- Over several months, RK becomes a hot topic in the health section of most news outlets and consumer health resources
- Virtually every news organization has a story featuring consumer and expert interviews
- Health food stores and internet retailers report difficulty in keeping the products in stock
ABC News

• Reports on the consumer spike that occurred following endorsement by Dr. Oz
• Stresses that dietary and medical experts report no significant data proving efficacy or safety in human population
• One expert, a dietician at Boston University, reveals that some insurance companies may pay for a nutrition consultation to help begin a healthier lifestyle

Medscape News

• Article written by Gayle Scott, PharmD
• Explains the data available in simple terms
• Establishes the relationship between Raspberry Ketone and similar substances like Capsaicin, Synephrine, and Ephedra
• Cautions patients on use of Raspberry Ketone if they have pre-existing cardiovascular disease
• Advises patients to stick to plain old diet and exercise

Huffington Post

• A registered dietician corrects some common misconceptions in an informational blog post
• Discusses the short-comings of non-human trials as well as the insufficient data provided by in vitro study
• Explains how the supplements, as “natural products,” are not evaluated or even regulated by the Food and Drug Administration

What is Raspberry Ketone (RK)?

• AKA: RK, Red Raspberry Ketone
• IUPAC Name: 4-(4-hydroxyphenyl)butan-2-one
• A compound produced by red raspberries
• Gives the fruit its flavor and fragrance

What is it used for?

• Orally
  — Weight Loss
  — Obesity
  — Increasing lean body mass

• Topically
  — Alopecia

• Foods and Manufacturing
  — Fragrance
  — Flavoring Agent

Biological Properties

• Structurally similar to Capsaicin and Synephrine
• Capsaicin – reported to reduce adipose tissue weight and decrease triglyceride concentrations by improving energy metabolism
• Sympathetic – found to exert a lipolytic effect on fat cells
• Structural similarities and compelling pharmacologic activities have driven researchers to study Raspberry Ketone.
## Mechanism of Action

- Orally for weight-loss and fat management
  - Thought to be very similar to Capsaicin
  - Works by increasing sympathetic innervation of brown fat tissues
  - Results in increased lipolysis of brown fat stores
  - Also has an effect on white fat stores
  - Researchers also measured an increase in oxygen consumption by selected study participants

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## Adverse Effects

- Not enough clinical data to evaluate
- Some experts describe theoretical adverse effects based on similar pharmacologic agents
- Isolated case reports identify Synephrine as a possible cause of ischemic stroke, syncope, tachyarrhythmia, MI, and death

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## The “Skinny”

- Raspberry Ketone is thought to:
  - Improve fat metabolism and lean body mass if taken orally
  - Increase resting metabolic rate to promote fat burning mechanisms.
  - No apparent adverse effects or risks
  - Sounds great, right?

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## What Does the Data Really Say?

- Three studies featuring Raspberry Ketone:
  - Morimoto, et al. - weight loss
    - Oral Administration in mouse model
  - Park, KS – weight loss
    - *in vitro* study on human 3T3-L1 cell lines
  - Harada, et al. – hair growth
    - Topical Administration in rat and human models
- These three studies reveal the majority of the data regarding Raspberry Ketone

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## What Does the Data Really Say on Weight Loss?

- Weight loss studies featuring Raspberry Ketone:
  - Morimoto, et al.
    - Oral Administration in mouse model
  - Park, KS
    - *in vitro* study on human 3T3-L1 cell lines
Weight Loss: Morimoto Study

- 24 mice were fed one of five controlled diets
  - 4 diets w/ varying amounts of: Beef Tallow (40%), Casein (34-36%)*, Corn Starch (10%), Sugar (9%), vitamins and minerals (5%), and Raspberry Ketone (0-2%)*
  - Normal Laboratory-Controlled Diet
- Mice were fed this diet for 10 weeks, after which samples were taken from each site for histological study and weighing.

Morimoto Conclusion

- RK may:
  - Stimulate metabolism of white and brown adipose tissues
  - Inhibit pancreatic lipase activity
  - Increase norepinephrine-induced lipolysis in white adipose adipocytes
  - Increase thermogenesis in brown adipose tissue

Weight Loss: Park Study

- In vitro study examining effect of RK on 3T3-L1 adipocytes
- 3T3-L1 cells cultured and differentiated to adipocyte-like states
- Incubated with RK, isoproterenol, or control solution for a period of 12 days
- Level of lipolysis measured by glycerol levels, adiponectin secretion, and fatty acid oxidation
- Lipolysis examined alongside cytotoxicity as well, to verify such isn’t the mechanism for lipolysis

Weight Loss: Morimoto Study

- Results:
  - At week 6, HFD+2% RK showed significantly lower total body weights
  - At week 2, ND group showed significantly lower total body weights
  - Tissue weights were significantly reduced (p<0.01) in the HFD + 2% RK group and ND group

Morimoto Analysis

Strengths
- Well designed to isolate RK effect
- Low risk of confounding
- Objectively measures the potential effect(s) of RK
- Highly predictive of future results from future study
- No apparent adverse events (not really discussed in the study literature)

Weaknesses
- No randomization (subjects matched by weight)
- Sample size is quite small (n=24)
- Not a human study! (results not generalizable to human population)
- Study doesn’t address differences between mouse and human fat metabolism
- Mice fed lab controlled diets, not generalizable to mice living in the wild responsible for their own food.

Results
- RK treatment showed more than a 3-fold increase in lipolysis compared to control
- Adiponectin levels secreted by 3T3-L1 cells was significantly higher (~100%) than that of controls
- Fatty acid oxidation was shown to increase in 3T3-L1 cells treated with RK to almost 150% more than controls
- Biomarker for cytotoxicity (LDH level) was unchanged between RK and Control samples
• Objectively demonstrates the benefits of RK to adipocytes on the cellular level
• Measures lipolysis from three different mechanisms, to helps us see the whole picture

- Only an in vitro study. Not generalizable to life, including human life
- Unclear if the active site concentrations used in the study are compatible with life.
- Doesn’t address potential adverse effects from the required therapeutic dose

Raspberry Ketone is a new supplement marketed to help with weight management and hair loss
Consumer health resources have written and disseminated extensive information about it
Limited data shows that it may be a promising supplement in the future
Profound lack of human data regarding this herbal product

Marijuana

Marijuana illegality in the early 1900’s was enacted and enforced by states
Marijuana Tax Act of 1937
- All persons who deal with marijuana commercially, prescribe it, or possess it are taxed
- Criminalized all other use with penalties
- The Act was passed against the opinion of the American Medical Association

Marijuana in the News

- Reuters – “Two University of Colorado at Boulder students are accused of bringing marijuana-laced brownies to a college class, shocking their unsuspecting professor and five classmates, police said on Sunday.” – December 10, 2012
History of Marijuana Law

- Boggs Act of 1952
  - Set mandatory sentences for drug and marijuana offenses
- The Comprehensive Drug Abuse Prevention and Control Act of 1970
  - Separated marijuana from other narcotics
  - Eliminated mandatory sentences
- The Anti-Drug Abuse Act of 1986
  - Reinstated mandatory sentences for drug-related crime including marijuana

States with Laws for Medical Use

- Alaska
- Arizona
- California
- Colorado*
- Connecticut
- District of Columbia
- Delaware
- Hawaii
- Maine
- Massachusetts
- Michigan
- Montana
- Nevada
- New Jersey
- New Mexico
- Oregon
- Rhode Island
- Vermont
- Washington*
  - *Also legal for recreational use

Administration

- Smoke – marijuana alone or mixed with tobacco in an unfiltered joint
- Oral – by prescription form or marijuana in cookies, brownies, or other fatty substance (alfredo sauce, butter, etc.)
- Vapor – marijuana filtered through water such as a bong or water pipe
- Intravenous – by boiling marijuana leaves and injecting the broth
- Oromucosal spray – Sativex® prescription approved in other countries

Pharmacokinetics

- Cannabis contains at least 60 cannabinoids (the active compound) and numerous other compounds
  - Δ9-tetrahydrocannabinol (THC) causes psychoactive effects
- Mechanism of action – acts through cannabinoid receptors CB: found primarily in the CNS causing psychoactive effects and CB: found minimally in the brain and on immune cells, particularly leukotrienes
- There are different concentrations of the active compounds depending on production and preparations
- The concentration of THC is highest in the flowers and leaves of the plant and lowest in the stems, roots and seeds.

Pharmacokinetics

- T1/2 – 0.5 hr distribution phase, 30 hr terminal phase
  - Highly lipophilic
- Estimated bioavailability of THC
  - Smoke: 10-25%
  - Oral: 13-19%
- Metabolites appear in the urine 10 days or more after a single exposure and for several weeks after chronic exposure.
- THC accumulates in the brain and the CNS effects do not correlate with serum concentrations, unlike alcohol.
- Tolerance may develop within 4 days of daily use, but unlikely with intermittent use.
- Females with higher estrogen levels are more sensitive to medical cannabis effects on pain, behavior, and reward.

Indications

- Indications
  - Glaucma
  - HIV/AIDS-related weight loss
  - Multiple Sclerosis
  - Neuropathic pain
  - Appetite loss
  - Cancer pain
  - Nausea/vomiting

Other Possible Indications

- Alzheimer’s disease
- ALS
- Diabetes mellitus
- Dystonia
- Fibromyalgia
- GI disorders
- GLIoma/cancer
- Hepatitis C
- Huntington’s Disease
- Incontinence
- MSA
- Osteoporosis
- Parkinson’s
- Rheumatoid arthritis
- Sleep apnea
- Tourette’s Syndrome

Natural Medicines Comprehensive Database
Pharmacist Edition
PharmacistPoint
PharmacistPoint
PharmacistPoint
PharmacistPoint
PharmacistPoint
Approved Marijuana Derivatives

- Marinol® (dronabinol)
  - Indications:
    - Loss of appetite due to AIDS
    - Chemotherapy-induced nausea and vomiting
  - Off-label use:
    - Postoperative nausea and vomiting
    - Intractable pruritus secondary to cholestatic liver disease

- Cesamet® (nabilone)
  - Indication:
    - Chemotherapy-induced nausea and vomiting

Derivatives in the Pipeline

- Sativex® Oromucosal Spray (two extracts of Cannabis sativa)
  - Approved in many European countries, New Zealand, and Canada
  - Indications: Spasticity due to MS
  - Undergoing Phase III trials in the US for cancer pain

- Namisol® oral tablet
  - Pure, natural Δ9-tetrahydrocannabinol (THC) that leads to high, predictable bioavailability and has a long shelf-life at room temperatures
  - In Phase II clinical trials
  - Targeted indications for multiple sclerosis, Alzheimer's disease, and chronic pain

Safety and Efficacy

- Appetite Loss/Anorexia
- Chronic Pain
- Neuropathic Pain
- Multiple Sclerosis
- Nausea and Vomiting
- Glaucoma

Safety and Efficacy

- Appetite loss, anorexia, and HIV/AIDS related weight loss
  - Marijuana stimulates the appetite in patients who have AIDS.
  - Doses of 2.5-10 mg BID of dronabinol have been FDA approved for such use.

Safety and Efficacy

- Multiple Sclerosis
  - Smoking or orally consuming marijuana is effective for spasticity and tremor
  - It may also reduce urge incontinence and pain
  - Nabiximols (Sativex®) is approved in several countries for this use and is seeking FDA approval

Safety and Efficacy

- Chronic pain
  - May be moderately effective
  - Higher doses are more effective for pain relief
  - The moderate efficacy of cannabis for pain relief may be offset by the potential harm in adverse effects and the dangers of marijuana smoke
## Safety and Efficacy

### Neuropathic Pain
- One study showed that smoking marijuana three times a day (about 25 mg of 9.4% THC) might reduce the intensity of neuropathic pain.
- Another study found that vaporized low-dose 1.29% THC reduced neuropathic pain by at least 30%, similar to other neuropathic pain medications.
- More studies are needed to further delineate the effect.

### Nausea and Vomiting
- Relatively modest antiemetic
- Recommended as adjunct or second line agent by the National Comprehensive Cancer Network if other antiemetics are ineffective
- Dronabinol and nabilone are FDA-approved for this use

### Glaucoma
- Marijuana has been shown to lower intraocular pressure (IOP) in patients with normal IOP and with glaucoma.
- The duration of action is only 3-4 hours meaning to decrease IOP continuously, the patient would have to use marijuana every 3 hours.
- Given that marijuana decreases mental capacity and the number of doses per day needed, it is not recommended as a long-term treatment for glaucoma.

## Adverse effects

### Xerostomia (dry mouth)
- Nausea or vomiting
- Dry eyes
- Reddening of the eyes
- Headache
- Dizziness
- Numbness
- Cough
- Cardiovascular effects
- Tachycardia
- Hypotension or hypertension
- Syncope
- Palpitations
- Vasodilation
- Coordination problems
- Confusion
- Anxiety, amnesia

## Intoxication

### Impairment of reaction time, motor coordination, and visual perception
- Panic reactions
- Hallucination
- Flashbacks
- Depression
- Other emotional disturbances

## Adverse Events with Chronic Use

- Laryngitis
- Bronchitis
- Apathy
- Psychotic decline
- Sexual dysfunction
- Abnormal menstruation
- Increased risk of myocardial infarction
- Increased risk of psychosis
- Increased urinary tract infections
- Associated risk of stroke
- Associated risk of bullous emphysema
- Possibly link to testicular cancer
Patient Case #1

- Marijuana Associated Psychosis
  - 24-year-old man presented to the hospital for insomnia, irritability, and aggressiveness after using semi-daily cannabis use.
  - He was treated with quetiapine 100mg/day and discharged.
  - He later discontinued quetiapine.
  - Four months later, he presented to the marijuana dispensary complaining of chronic pain, insomnia, and anxiety from PTSD. He said that he wanted more potent marijuana and not get ripped off by drug dealers.
  - Later was readmitted to the hospital with new-onset hallucinations and delusions. He admitted to increasing marijuana use for pain, but it caused psychotic behavior.
  - He subsequently went to a drug treatment center, discontinued marijuana use, and psychiatric symptoms resolved.

Patient Case #2

- Marijuana Associated MI and Stroke
  - A 33-year-old man with a history of chronic cannabis use suffered from a myocardial infarction and stroke.
  - He reports smoking 6-10 cannabis cigarettes per day for the past 15 years.
  - 2 weeks before the event, he reports increasing his consumption to 20-25 cannabis cigarettes per day and no other drug use.
  - ECG showed negative T waves
  - MRI showed multi-focal acute infarctions
  - Possibly mechanisms include coagulopathy, hypotension or hypertension, vasospasm, reversible cerebral vasoconstriction syndrome, or cardioembolism

Patient Case #3

- Marijuana Associated with Stroke
  - A 36-year-old man who consumed heavy hashish with 3-4 alcoholic drinks developed an acute episode of isolated aphasia followed by a seizure.
  - MRI showed two acute ischemic infarcts
  - Treated with ticlopidine
  - A year later, he suffered another episode of aphasia after smoking hashish
  - MRI showed an acute left frontal cortical infarction
  - One and a half years later after heavy intake of hashish and 3-4 alcoholic drinks, he suffered auditory agnosia and an acute cerebral infarct.
  - After 2 years, he is stable on clopidogrel

Patient Case #4

- Smoking cannabis and lung cancer
  - 26-year-old man began smoking 1-2 joints daily at age 14
  - A joint is unfiltered cannabis wrapped with unfiltered tobacco
  - Began smoking up to 8 joints daily between the ages of 18-24.
  - He developed small cell lung cancer and was treated with chemotherapy
  - He survived 2 years and 16 days from diagnosis
  - Previous research has shown that smoking one joint per day is similar to smoking 20 cigarettes per day and increases the risk of cancer by 8%.
  - This patient more than likely developed cancer secondary to joint smoking

Summary

- Standardized marijuana derivatives have shown to be helpful in many medical conditions
- Are marijuana derivative more effective than other treatments?
- Marijuana continues to show signs of abuse and demonstrates many side effects
- The herbal form smoked, may vary in potency and since it has the capacity for abuse, this form may lead to more adverse drug reactions

Green Coffee Bean Extract
“Weight Loss Miracle in the Bottle?”

47th Annual Meeting  August 2-4, 2013  Orlando, FL

Background

• Active Ingredients:
  – Chlorogenic acid*
  – Quinides
  – Lignans

Supplement Facts

Other Ingredients: Vegetable cellulose, silicon dioxide.

GCA® is a registered trademark of Applied Food Sciences, LLC.
WARNING: This product contains 45 mg of naturally occurring caffeine per serving. Less than 1/2 cup of coffee.

Related Terms

• 2-Methoxy-3-(2-methylpropyl)pyrazine
• 5-chlorogenic acid (5-CGA)
• Coffea robusta
• Coffea canephora
• Coffea arabica
• Coffea canephora
• Green coffee bean extract (GCBE)
• N-methylpyridinium
• Phenyl ethyl alcohol
• Tannic acid
• Vanillic acid
• Unroasted coffee

Background

• “Green coffee” is raw or unroasted seeds (beans) of Coffea fruits.

http://www.officialgreencoffee.com/

• Coffee contains hundreds of components, each of which may have potential and independent pharmacological effects

http://www.officialgreencoffee.com/

Seen on TV

• The Dr. Oz show referred to it as “The green coffee bean that burns fat fast” and claims that “no exercise or diet is needed.”

THE OFFICIAL GREEN COFFEE BEAN EXTRACT - MADE IN THE U.S.

Seen on TV

• NBC news: “A small pilot study showed those who took doses of “extremely bitter” green coffee bean extract lost an average of 17.5 pounds in 22 weeks and reduced their overall body weight by 10.5 percent.”

THE OFFICIAL GREEN COFFEE BEAN EXTRACT - MADE IN THE U.S.
ABC news: “The effects, if real, are likely to be modest and we don’t know if they last over time.”

The Official Green Coffee Bean Extract Advertisement

- Active ingredient, GCA chlorogenic acid, featured on Dr. Oz, NBC, ABC, and CNN
- In a 22-week clinical trial, users lost an average of 17 pounds
- May slow the absorption of fat from food intake and help to activate metabolism

People use this for:
- Hypertension
- Diabetes
- Antiviral
- Cancer
- Cirrhosis
- Liver Disease
- Infections
- Obesity[1]

Standardization

- The major compounds in coffee is chlorogenic acid, an ester of caffeic acid, and quinic acid.
- Green coffee bean extract is sometimes standardized to more than 50% chlorogenic acid.
- Svetol® decaffeinated green coffee extract contains 45-50% total chlorogenic acids.
- The Original Coffee Bean Extract® claims to contain 50% chlorogenic acid.

Dosing for Weight Loss

Adult (age ≥18):
- Green coffee extract (Svetol®, Naturex®) 80-200 mg daily over period of 12 weeks.
- Green coffee extract (GCA, Applied Food Sciences) 700 mg daily or 1050 mg daily.

Children (age <18): Insufficient available evidence.

Mechanism of Action

- Inhibit the glucose-6-phosphatase (G6P) enzyme system in vitro.
- G6P catalyzes the formation of glucose from the liver and has a role in blood glucose regulation.
- Reduced risks of glycemic disorders with long-term coffee use.
- The hypoglycemic effects of chlorogenic acids may also underlie its purported antiobesity effects.
Safety Summary

- **Likely Safe**: When used by healthy individuals, in recommended doses, for up to four months.

- **Possibly Safe**: When used by obese or overweight individuals, in suggested doses, for up to 12 weeks.

- **Possibly Unsafe**: When used in individuals with cardiovascular disease, as large amounts of chlorogenic acid in coffee (2g daily). When used in patients with diabetes or those who are taking antidiabetic agents, as green coffee may interfere with blood glucose control.

- **Likely Unsafe**: When used in pregnant or lactating women, due to a lack of safety data.

Safety Summary:

- **Possibly Unsafe**: When used in individuals with cardiovascular disease, as large amounts of chlorogenic acid in coffee (2g daily). When used in patients with diabetes or those who are taking antidiabetic agents, as green coffee may interfere with blood glucose control.

- **Likely Unsafe**: When used in pregnant or lactating women, due to a lack of safety data.

Natural Standard Evidence-based Validated Grading Rationale

- **B** (Good Scientific Evidence)
  Statistically significant evidence of benefit from 1-2 properly randomized trials, OR evidence of benefit from >1 properly conducted meta-analysis OR evidence of benefit from >1 cohort/case-control/non-randomized trials AND with supporting evidence in basic science, animal studies, or theory....

Natural Standard Evidence-based Validated Grading Rationale

- **C** (Unclear or Conflicting Scientific Evidence)
  Evidence of benefit from >1 small RCT(s) without adequate size, power, statistical significance, or quality of design by objective criteria,* OR conflicting evidence from multiple RCTs without a clear majority of the properly conducted trials showing evidence of benefit or ineffectiveness, OR evidence of benefit from >1 cohort/case-control/non-randomized trials AND without supporting evidence in basic science, animal studies, or theory, OR evidence of efficacy only from basic science, animal studies, or theory.

Quality of Scientific Evidence

<table>
<thead>
<tr>
<th>Indication</th>
<th>Evidence Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>B</td>
</tr>
<tr>
<td>Cardiovascular disease risk</td>
<td>C</td>
</tr>
<tr>
<td>Impaired glucose tolerance</td>
<td>C</td>
</tr>
<tr>
<td>Obesity</td>
<td>C</td>
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</tbody>
</table>

Scientific Evidence: Vinson, et al.

- Vinson, et al. [2] conducted a randomized, double-blind, placebo-controlled, crossover study that evaluated efficacy and safety of a green coffee bean extract in overweight subjects:
  - 16 overweight adults
  - 22 week study
  - Primary measurement:
    - Body weight
    - Body mass index
    - Percent body fat
    - HR
    - Blood Pressure
Scientific Evidence

**Results:**

- Mean weight changes over time for all volunteer subjects.

<table>
<thead>
<tr>
<th>Weeks</th>
<th>0</th>
<th>6</th>
<th>12</th>
<th>18</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean weight (kg)</td>
<td>80</td>
<td>75</td>
<td>70</td>
<td>65</td>
<td>60</td>
</tr>
</tbody>
</table>

Abbreviations: HOH, high-dose; LOH, low-dose; PL, placebo.

- Treatment groups include:
  - Control group (n=20)
  - Treatment group (n=30)

- Adverse effects were not addressed
- Corresponding author of the study is affiliated with Berkem, the manufacturer of Svetol®

Scientific Evidence

**Study limitations:**

- The study was funded by a green coffee bean extract manufacturer
- Small sample size

Scientific Evidence: Dellalibera, et al.

- Dellalibera, et al. conducted a randomized controlled trial to examine the effect of Svetol® (decaffeinated green coffee) on body weight and composition in overweight volunteers:
  - 50 overweight men and women
    - Control group (n=20)
    - Treatment group (n=30)
  - BMI > 25
  - With a bland low-calorie diet
  - 60 days study
  - 200 mg Svetol® twice daily
- Primary outcomes:
  - Weight reduction
  - BMI decrease

Scientific Evidence

**Results:**

<table>
<thead>
<tr>
<th></th>
<th>Mean weight reduction</th>
<th>Body mass index</th>
<th>Muscle/Fat mass ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Svetol® group</td>
<td>4.97 ± 0.32 kg (5.7 ± 0.3%)</td>
<td>-1.9 ± 0.1 kg/m²</td>
<td>+4.1 ± 0.7%</td>
</tr>
<tr>
<td>Control group</td>
<td>2.45 ± 0.337 kg (-2.9 ± 0.4%)</td>
<td>-0.9 ± 0.1 kg/m²</td>
<td>+1.6 ± 0.6%</td>
</tr>
</tbody>
</table>

- Cardiovascular:
  - Caffeine can increase heart rate and affect cardiovascular function
  - The amount of caffeine found in some green coffee extracts is low (about 30mg per serving)
  - According to the manufacturer, Svetol® decaffeinated green coffee extract contains 0-2% caffeine

- Chlorogenic acid may adversely affect cardiovascular disease risk factors

Adverse Effects
**Adverse Effects**

- **Gastrointestinal:** Nausea
- **Genitourinary:** Urinary tract infection
- **Pulmonary/Respiratory:** Occupational exposure to green coffee had been documented to cause bronchial reactivity, asthma, and rhinitis

**Drug Interactions**

- **Antibiotics:** May interact with antibiotics
  - Fluconazole, quinolones → increase caffeine concentration
- **Antidiabetics:** Hypoglycemia
  - Chlorogenic acids are also major antidiabetic compounds in green coffee. Thus it may potentially interact with antidiabetic agents
- **Antihypertensives:** Green coffee may interact with antihypertensive agents, but the nature of this potential interaction is unclear, due to insufficient evidence

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**Drug Interactions**

- **Antiobesity agents:** Green coffee may interact with antiobesity agents, but the nature of this potential interaction is unclear, due to insufficient evidence
- **Anxiolytics:** Green coffee may interact with anxiolytic agents, but this potential interaction may depend on the caffeine content

**Summary**

- Green coffee extract may improve body composition and weight in overweight individuals, as supported by small clinical trials and a well-publicized animal study
- There are potential conflicts of interest, as the available studies were conducted by (or supported by) food or supplement manufacturers
- Conclusive results await larger independent clinical trials

**Conclusion**

- The media will continue to greatly influence how we practice pharmacy
- Supplements and alternatives to traditional medicine are popular and probably will remain so
- The growth of media influence and herbal supplementation expansion creates opportunities for pharmacists! Especially in the MTM areas of practice

**References**

- Webb JA. Drug Topics. 2010 Jul 154(7) p14-16
- www.Beaeworld.com