

## Herbal Medicine Update



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## Conflict of Interest Statement

- I have no conflicts of interest to disclose



## Objectives

- By the end of this presentation, participants will be able to:
  - Define complementary health, integrative health, complementary alternative medicine and herbal medicine.
  - Explain the scientific evidence for common herbal medicines.
  - List common drug-herb interactions.



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WHAT IS COMPLEMENTARY, ALTERNATIVE, INTEGRATIVE MEDICINE?



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## Use of Herbal Medicine in the U.S.

- More than **30% of adults** and **12% of children** use health care approaches outside of mainstream Western, or conventional medicine<sup>1</sup>
- **17.7%** use natural products<sup>2</sup>
- Over 50% of patients do not disclose use to their doctor<sup>3</sup>



1. National Center for Complementary and Integrative Health website. <https://nccih.nih.gov/health/integrative-health/ovs>. Accessed August 26, 2015.  
2. CHSRTC (U.S. THOR) to the use of complementary health approaches among adults: united states, 2002 - 2012. *National Health Statistics Report*. 2015(79).

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MPR > News > Pharmacists Encouraged To Learn More About Herbal Supplements

March 08, 2018

### Pharmacists Encouraged to Learn More About Herbal Supplements



HealthDay News — Pharmacists should be aware of the increasing use of **supplements**, and should learn about both the supplements and possible medication interactions to be able to answer patients' questions, according to an article published in *Drug Topics*.

The article states that a recent study in the *Journal of Nutrition* found that 70% of Americans age 60 years and older say that they use a vitamin, mineral, herb, or other supplement each day and 29% report using four or more per day. However, health care providers do not receive training needed to identify herb-drug interactions, herb-disease interactions, or other potential problems.



*70% of Americans age 60 years and older say that they use a vitamin, mineral, herb, or other supplement daily*



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### What are terms you have heard to describe complementary and integrative medicine?

Folkloric	Holistic	Irregular
Non-conventional	Non-western	Traditional
Unorthodox	Unproven	

**GMCCP**  
Reference: National Center for Complementary and Integrative Health website. <https://nccih.nih.gov/health/integrative-health/cvsa>. Accessed August 29, 2018.

### Complementary vs Alternative Medicine

Complementary	Alternative
if a non-mainstream practice is used <b>together with</b> conventional medicine	if a non-mainstream practice is <b>used in place of</b> conventional medicine

**GMCCP**  
Reference: National Center for Complementary and Integrative Health website. <https://nccih.nih.gov/health/integrative-health/cvsa>. Accessed August 29, 2018.

### Integrative Medicine

The diagram illustrates the concept of Integrative Medicine. On the left, a red circle labeled 'Conventional aka mainstream health care' and a green circle labeled 'Complementary approach' are connected by a red plus sign. A green arrow points from this combination to a large purple circle on the right labeled 'Integrative Medicine'.

**GMCCP**  
Reference: National Center for Complementary and Integrative Health website. <https://nccih.nih.gov/health/integrative-health/cvsa>. Accessed August 29, 2018.

### Complementary Health Approaches

Natural Products	Mind-Body Practices	Other Approaches
<ul style="list-style-type: none"> <li>Vitamins and minerals</li> <li>Botanicals</li> <li><b>Herbal Medicine</b></li> </ul>	<ul style="list-style-type: none"> <li>Chiropractic Manipulation</li> <li>Acupuncture</li> <li>Guided Imagery</li> <li>Hypnotherapy</li> <li>Qi gong</li> <li>Tai Chi yoga</li> <li>Massage</li> </ul>	<ul style="list-style-type: none"> <li>Traditional Healers</li> <li>Ayurveda</li> <li>Traditional Chinese Medicine</li> <li>Homeopathy</li> <li>Naturopathy</li> <li>Energy therapies</li> </ul>

**GMCCP**  
Reference: National Center for Complementary and Integrative Health website. <https://nccih.nih.gov/health/integrative-health/cvsa>. Accessed August 29, 2018.



**CASE**

**ML**

73 year old Hmong female referred by Dr. Johnson to the pharmacist for "New Start Insulin". Brought in some medications. Did not bring glucometer to the visit today. Rarely checks her blood sugar due to "pain" in her fingers. Taking metformin 1000 mg qPM with glipizide 5 mg qPM after dinner. Forgets morning dose of both medications as she takes care of her grandkids. States that she has been using an herbal tea over the last 6 months which is believed to cure diabetes. Last A1c 9.8% and BP 106/76 mm Hg (1 month ago). PMH: Type 2 diabetes, GERD, insomnia; SH: Denies alcohol use, non-smoker. Her prescription profile is as follows:

Drug	Dose	Frequency	Use
Metformin	1000 mg	1 tablet twice a day	Last filled 2 months ago
Glipizide	5 mg	1 tablet twice a day	Last filled 2 months ago
Lisinopril	10 mg	1 tablet once a day	Takes consistently
Vitamin B12	1000 mcg	1 tablet once a day	Takes consistently
Aspirin	81 mg	1 tablet once a day	Last filled 6 months ago

**CASE**

**ML**

She also takes the following:

**Ingredients**

Ingredients	Amount Per Serving
Aspirin (as Acetylsalicylic Acid)	20 mg
Vitamin B12 (as Cyanocobalamin)	5 mg
Vitamin B12 (as Cyanocobalamin)	250 mcg
L-Glutamine	150 mg
DIMAE (as Dimethylaminoethanol Bitartrate)	100 mg
Pyroglutamic Acid	100 mg
L-Tyrosine	100 mg
Gotu Kola (leaf) (standardized)	50 mg
100% Ginkgo (standardized)	5 mg
14% Ginkgo (standardized)	50 mg
24% Ginkgo (standardized)	7 mg
6% terpene lactones	40 mg
Choline (as Choline Bitartrate)	5 mg

**Question:** She is wondering if garlic will help lower blood pressure as she was told she is on a medication for high blood pressure?

**Think. Pair. Share.**

- What additional questions would you like to ask the patient?

**Top 15 Herbal Medicines in the U.S.**

Horehound	Cranberry	Echinacea	Garcinia
Green tea	Black Cohosh	Flaxseed	Ginger
Valerian	Turmeric	Fenugreek	Yohimbe
Aloe	Saw Palmetto	Milk thistle	

Smith T, Kawa K, Eckl V, Morton C, Surednyd, R. Sales of Herbal Dietary Supplements in US Increased 7.7% in 2016. *HerbalGram*. 2017; American Botanical Council.

**Red Yeast Rice**

- Product of rice fermented with a type of mold
- In foods, red yeast is used as a food coloring for Peking duck.
- Contains HMG-CoA reductase inhibitor similar to lovastatin called monocolin K
  - Monocolin K 5 – 10 mg/day equivalent to lovastatin 20 mg/day

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**Red Yeast Rice**

Common Use	Efficacy	Safety
High Cholesterol	Likely Effective (lowers TC, LDL, TG)	Possibly safe (taken by mouth for up to 4.5 years)
Heart disease	Possibly Effective	Elevated liver enzymes, myopathy
		Product quality concerns

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## Ginseng (Panax)



- Slow-growing deciduous plants that include 13 different species
- Grows in Korea, northeastern China and far-eastern Siberia
- The root is used to make medicine
- Referred to as a general well-being medication

© 2008 Panax Ginseng. In: Natural Medicines Comprehensive Database [database on the Internet]. Stockton (CA): Therapeutic Research Faculty; 1996-2008 [cited 28 August 2018]. Available from: <http://www.naturaldatabase.com>. subscription required to view.

Common Uses	Efficacy	Safety
Alzheimer's Disease (Taken daily x 12 weeks)	Possibly Effective	Likely safe when used orally for up to 6 months
COPD	Possibly Effective	Trouble sleeping (common)
Cognitive Function (mental arithmetic skills and reaction times) in healthy, middle-aged people	Possibly Effective	Menstrual problems, breast pain, increased HR, high or low BP, headache, loss of appetite, dizziness
Athletic Performance	Possibly Ineffective	Steven Johnson's Syndrome, liver damage (Rare)

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## Efficacy of Panax Ginseng

- Alzheimer's Disease:
  - Panax ginseng root 4.5 to 9 grams daily x 12 weeks can improve cognitive performance in patients with Alzheimer's Disease
- COPD:
  - Meta-analysis of clinical trials evaluating the use of Panax ginseng orally in patients with stable COPD shows significant improvement in pulmonary function tests and quality of life compared to placebo after 3 – 6 months of treatment.

© 2008 Panax Ginseng. In: Natural Medicines Comprehensive Database [database on the Internet]. Stockton (CA): Therapeutic Research Faculty; 1996-2008 [cited 28 August 2018]. Available from: <http://www.naturaldatabase.com>. subscription required to view.

## Efficacy of Panax Ginseng

- Cognitive Function:
  - Clinical evidence shows taking Panax ginseng orally can improve abstract thinking, attention, mental arithmetic skills, and reaction times in healthy, middle-aged people.
  - Some evidence exists that a combination of Panax ginseng + ginkgo leaf extract can improve memory in ages 38 to 66 years of age

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## Panax Ginseng Dosing

- **COPD:** 100 mg to 6 grams of Panax ginseng three times daily for up to 3 months has been used.
- **Cognitive function:** 200 to 400 mg of a specific Panax ginseng extract (G115, Pharmaton SA, Lugano, Switzerland) taken once daily or in two divided doses for up to 12 weeks, or 200 to 960 mg as a single dose, has been used.

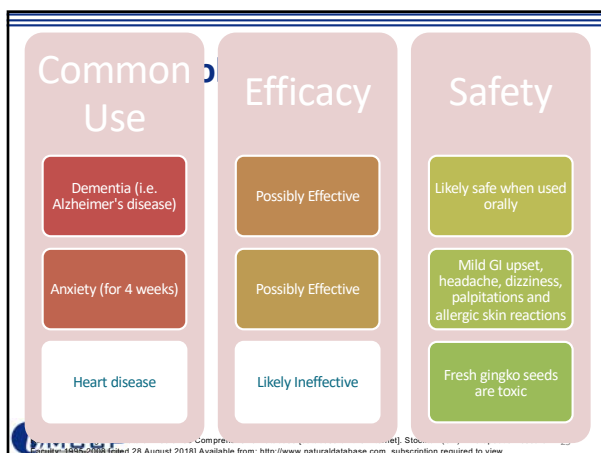
© 2008 Panax Ginseng. In: Natural Medicines Comprehensive Database [database on the Internet]. Stockton (CA): Therapeutic Research Faculty; 1996-2008 [cited 28 August 2018]. Available from: <http://www.naturaldatabase.com>. subscription required to view.

## Ginkgo Biloba



- Native to temperate Asia including China, Japan and Korea
- Cultivated in the US since 1784
- One of the oldest living trees
- In manufacturing, ginkgo leaf extract is used in cosmetics.
- Roasted ginkgo seed (with pulp removed) is an edible delicacy in Japan and China

© 2008 Ginkgo Biloba. In: Natural Medicines Comprehensive Database [database on the Internet]. Stockton (CA): Therapeutic Research Faculty; 1996-2008 [cited 28 August 2018]. Available from: <http://www.naturaldatabase.com>. subscription required to view.



## Efficacy of Ginkgo Biloba

- Taking ginkgo up to 1 year slightly improves symptoms
- Doses of 240 mg/day might work better than 120 mg/day
- There are conflicting findings which makes it hard to determine which people might benefit
- Ginkgo does not appear to prevent dementia from developing or prevent Alzheimer's related dementia from getting worse

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## Efficacy of Ginkgo Biloba

- Ginkgo vs prescription medications
- Early studies showed that Ginkgo daily was as effective as donepezil (Aricept) for treating mild to moderate Alzheimer's disease
- Other research suggested that ginkgo was less effective than donepezil and tacrine
- Ginkgo in combination with donepezil or rivastigmine was not better than monotherapy

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## Garlic

- Culinary herb
- Related to onion, leeks and chives
- Native to Siberia spread to other parts of the world over 5000 years ago

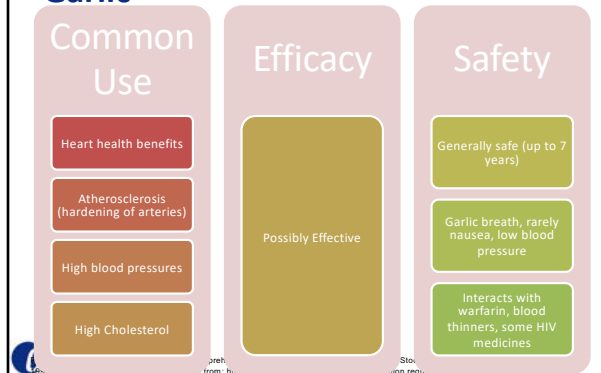


### Preparations:

- Garlic supplements
- Powder
- Oil
- Japanese method of preparing garlic involving kneading and pulverizing crushed garlic together with egg yolk

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## Garlic



## Efficacy of Garlic

- Animal studies suggest garlic has potential antilipidemic, antihypertensive, antiglycemic, antithrombotic and antiatherogenic properties
- Overall, clinical research suggests taking garlic supplements daily for more than 8 weeks may modestly reduce total cholesterol and LDL cholesterol levels in patients with hyperlipidemia.
- Garlic is unlikely to significantly increase HDL cholesterol or reduce triglyceride levels, long-term.
- Some clinical research shows taking garlic orally can modestly reduce blood pressure in hypertensive and normotensive patients

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## Garlic Evidence Summary

Author (Year)	Intervention	Outcome	Population of Focus	Study Design	Results	Limitations
McMahon FG, Vargas R (1993)	1.3% allicin (2400 mg)	Sitting blood pressure	N=9 Severe HTN (DBP > 115 mmHg)	Open-label	Sitting BP fell 7/16 mmHg approximately 5 hours after the dose, significant decrease in diastolic blood pressure ( $p < 0.05$ )	- Small sample size - Study not controlled - Severe HTN patients
Auer W, et al (1990)	Garlic powder vs placebo x 12 weeks	Blood Pressure Plasma Lipids at 4, 8 and 12 weeks	N=47 Mild HTN	Randomized, placebo-controlled, double-blind trial	DBP decreased from 102 to 91 mmHg ( $p < 0.05$ ) at 8 weeks and to 88 mmHg ( $p < 0.01$ ) at 12 weeks. Serum cholesterol and TG reduced at 8 weeks and 12 weeks.	- Randomized controlled trial which is strongest to infer causation - Unclear why DBP chosen

GMCCP - Global Medicines Comprehensive Database [database on the Internet]. Stockton (CA): Therapeutic Research Faculty; 1999-2008 [cited 26 August 2018]. Available from: <http://www.naturaldatabase.com>. subscription required to view.

## Increased Bleeding Risk

- 5 G's
- Willow bark is a salicylate



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## Liver Toxicity

**Black Cohosh** (used for menopausal symptoms)

**Kava** (used for stress/anxiety)

Caution with "tea blends" or mixtures



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## Cardiac Toxicity

- **Ma Huang aka ephedra**
  - In 2004, FDA banned ephedra
  - Stimulant effects
  - Linked to irregular heartbeats, heart attack, stroke, and sudden death.
- **Bitter Orange** - stimulant effects
- Watch out for products that contain stimulants e.g. "pre-workout" supplements



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## Herbs of Caution

- **Red Yeast Rice**
- **St. John's Wort**
- **Yohimbe**
  - Common uses: impotence, athletic performance enhancer
  - Taken in high dosages, yohimbe use may result in difficulty in breathing, paralysis, very low blood pressure, heart attack, seizures, and death.



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## Herb-Drug Interactions

- **St. John's Wort**
  - Inducer of CYP450 enzymes – CYP 3A4 and p-glycoprotein; CYP2C19 >> 2C9 > 1A2
  - Serotonergic effects
- **Goldenseal** – potent inhibitor of CYP3A4 and CYP2D6 enzymes
- **Ginseng** – inducer of CYP3A in liver and gastrointestinal tract



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Source: How Medications and Supplements Can Interact. <https://ncch.nih.gov/health/now-science/how-medications-supplements-interact>. Accessed on Aug 27 2018.

## Pharmacist Call to Action

- Ask patients about use of herbal products when taking medication histories
  - What prescription medications are you taking? Over-the-counter? Vitamins, Minerals, Supplements? Herbs? Eye Drops/Ear Drops? Creams/Ointments? Injections?
- Stock herbal products that meet Good Manufacturing Practice guidelines
- Detect and report potential adverse drug events, drug-herb interactions
- Provide unbiased evaluations and discuss benefits and toxicity of herbal medicines



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CASE  
MLCASE  
ML

73 year old Hmong female referred by Dr. Johnson to the pharmacist for "New Start Insulin". Brought in some medications. Did not bring glucometer to the visit today. Rarely checks her blood sugar due to "pain" in her fingers. Taking metformin 1000 mg qPM with glipizide 5 mg qPM after dinner. Forgets morning dose of both medications as she takes care of her grandkids. States that she has been using an herbal tea over the last 6 months which is believed to cure diabetes. Last A1c 9.8% and BP 106/76 mm Hg (1 month ago). PMH: Type 2 diabetes, GERD, insomnia; SH: Denies alcohol use, non-smoker. Her prescription profile is as follows:

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Aspirin	81 mg	1 tablet once a day	Last filled 6 months ago

CASE  
ML

She also takes the following:



Serving Size	1 Capsule(s)
Ingredients	Amount Per Serving
Garlic (as Aged Garlic Extract)	20 mg
Vitamin B6 (as Pyridoxine HCl)	5 mg
Vitamin B12 (as Cyanocobalamin)	250 mcg
L-Glutamine	150 mg
DMAE (as Dimethylaminoethanol Bitartrate)	100 mg
L-Pyrogutamic Acid	100 mg
L-Tyrosine	100 mg
Gotu Kola (leaf) (standardized)	50 mg
100% Ashwagandha	5 mg
Oriental Ginseng (root) (standardized)	50 mg
14% ginsenosides	7 mg
Ginkgo (leaf) (standardized)	40 mg
24% ginkgo flavonoid glycosides	9.6 mg
6% terpene lactones	2.4 mg
Choline (as Choline Bitartrate)	5 mg

Question: She is wondering if garlic will help lower blood pressure as she was told she is on a medication for high blood pressure?

gluten free

dairy free

soy free

nut free

actual size

### Supplement Facts

Serving Size 2 Capsules  
Servings Per Container: 120

	Amount Per Serving	% Daily Value
Red Yeast Rice Powder (Monascus purpureus)(seed)	1200 mg	*

\* Daily Value not established.

Other ingredients: Gelatin, rice flour.

Does not contain: Corn, Wheat, Gluten, Salt, Soy, Dairy, Citrus, Fish, Preservatives, Artificial Colors or Flavors.

† These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

Think. Pair. Share.

- What are potential drug-herb interactions?
- What is your unbiased evaluation of ML's herbal medicine use? Benefits vs risks?
  - Red Yeast Rice
  - Ginseng
  - Ginkgo Biloba
  - Garlic
- Would you recommend garlic in addition to lower ML's blood pressure?

## Summary

- Complementary health approaches include a broad range of practices, interventions and natural products which are not typically part of medical care
- Herbal medicine is the use of plant's seeds, berries, roots, leaves, bark or flowers for medicinal purposes
- Red yeast rice is likely effective for high cholesterol
- Ginseng and ginkgo biloba are possibly effective for memory loss
- Garlic is possibly effective for heart health
- Herbs may increase bleeding risk, liver toxicity and cardiac toxicity
- St. John's Wort, goldenseal and ginseng have a high potential of interacting with medications and should be used with caution



GMCCP - Evidence: How Medications and Supplements Can Interact. <https://nccih.nih.gov/health/known-science/how-medications-supplements-interact>. Accessed on Aug 27 2018.

## Resources

Textbooks include:

- The Complete German Commission E Monographs.
- Natural Medicines Comprehensive Database.
- Lexi-Comp's Natural Therapeutics Pocket Guide.
- Honest Herbal and Herbs of Choice.
- The Review of Natural Products (formerly The Lawrence Review of Natural Products).
- Natural Products: A Case-Based Approach for Health Care Professionals.



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## Resources

Journals include:

- Alternative and Complementary Therapies.
- Alternative Therapies in Health and Medicine.
- Complementary Therapies in Nursing and Midwifery.
- Journal of Alternative and Complementary Health
- Journal of Herbal Pharmacotherapy.
- Journal of Natural Products.



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## Resources

Internet-based resources include:

- [www.naturaldatabase.com](http://www.naturaldatabase.com).
- [www.naturalstandard.com](http://www.naturalstandard.com).
- [www.consumerlab.com](http://www.consumerlab.com).
- [www.usp-dsvp.org](http://www.usp-dsvp.org).
- [www.nsf.org/consumer/consumer\\_dietary.html](http://www.nsf.org/consumer/consumer_dietary.html).
- [www.fda.gov](http://www.fda.gov).
- [www.nih.gov](http://www.nih.gov).
- [www.altmedicine.com](http://www.altmedicine.com).
- [www.herbalgram.com](http://www.herbalgram.com).
- Dietary Supplement Label Database [www.dsld.nlm.nih.gov/dsld/index.jsp](http://www.dsld.nlm.nih.gov/dsld/index.jsp)



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## What questions do you have?

### Herbal Medicine Update



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## Primer on Essential Oils, Cleanses, and Weight-Loss Supplements

**Loren-Ashley Williams, Pharm.D.**  
Assistant Professor, Department of Pharmacy Practice  
Concordia University Wisconsin School of Pharmacy  
Area of Practice: Ambulatory Care





## Conflict of Interest

- I have no actual or potential conflict of interest in relation to this presentation or program



## Kahoot! Instructions

- Please open Kahoot! game at: [www.kahoot.it](http://www.kahoot.it)
- Please keep website open as I will be using it throughout the entire presentation



## Objectives

- Define aromatherapy/essential oils and discuss the history, use, administration, and safety regulations associated with aromatherapy
- Discuss common weight loss supplements and cleanses or detoxes and the safety of these products



Please open Kahoot! game at: [www.kahoot.it](http://www.kahoot.it)

## TIME FOR KAHOOT!: AROMATHERAPY/ESSENTIAL OILS



## What is aromatherapy?<sup>1,2,3</sup>

- Intentional clinical application of the plant essential
- Use of essential oils from plants to support and balance the mind, body, and spirit
- **Essential oils (volatile oils):** oils extracted by steam and/or water distillation from a botanical source
  - The fragrant (aromatic) part is released when the plant is crushed
- Essential oils are not typically oily, they may not have a pleasant odor
- Essential oils are very concentrated



## Common Uses<sup>1,2,3</sup>

- Cancer patients, primarily as supportive care
- Other uses:
  - Viral infections
  - GI upset: N/V/D
  - Anti-inflammatory
  - Antifungal
  - Analgesic



<https://ncch.nih.gov/health/aromatherapy>



## History of Aromatherapy<sup>1, 3</sup>

- Plants have been used in healing practices in ancient cultures for thousands of years
- Cultures such as Ancient Egypt, India, the Mesopotamian basin, Asia, and Australia and several Biblical references
- Current applications did not come until the early 20th century when the French chemist and perfumer Rene Gattefosse coined the term (aromatherapy) in 1937.
- Resurfaced in 1980s and 1990s in Western Countries as interest in Complementary and Alternative Medicine increased



## Administration of Aromatherapy<sup>1,2,3</sup>

- Absorption through the skin**
  - Compress, massage oils, bath, spray on skin
- Absorption through inhalation**
  - Diffuser, vaporizer, spray into the air
- Absorption through digestion (Not Recommended)**
  - Oral, suppositories, sublingual, cheek



<https://organicaromas.com/blogs/aromatherapy-and-essential-oils/the-differences-between-essential-oil-diffusers>



## Dosing<sup>1,3</sup>

- A couple drops of the essential oil should be enough as they are highly concentrated
- Oils should be diluted 2-5% in carrier substance
  - Carrier Substances: vegetable oils, lotions, bath gels, hair care products (shampoo, conditioners, etc.) petroleum, rubbing alcohol and other products



## Research and Evidence<sup>1,2</sup>

- Essential oils are not standardized
- It is difficult to conduct blinded studies with aromatic substances
- There is little published research on many essential oils
- Pharmaceutical companies have little motivation to fund these studies



## Research and Evidence Continued<sup>2,4</sup>

- Theorized that the chemical components of the essential oil bind to receptors in the olfactory bulb which impact the limbic system (emotional center)
- Animal studies show some sedative and stimulant effects depending on the oil
- Some studies in humans support the influence of odors to enhance mood
- Human clinical trials have investigated aromatherapy primarily in the treatment of stress and anxiety in cancer patients



## Safety of Aromatherapy<sup>1,2,3</sup>

- Very few bad side effects or risks when used correctly
- Most essential oils in food and fragrances are labeled generally recognized as safe (GRAS) by the FDA
- Allergic reactions and skin irritation may occur
- Phototoxicity when oils are applied before sun exposure
- Lavender and tea tree oils have been found to have some hormone-like effects



## Regulation & Licensure of Aromatherapy <sup>1,2</sup>

- Not FDA approved
- Not regulated by state law
- Room fragrance systems (deodorizers, odor control) are the responsibility of the Consumer Product Safety Commission
- Not governed by Good Manufacturing Practices (GMPs)
- No licensing required to practice aromatherapy in the U.S.
  - Licenses for the following: Massage therapy, acupuncture



## Quick links: Aromatherapy

- [www.naha.org](http://www.naha.org)
- <https://nccih.nih.gov/health/aromatherapy>



Please open Kahoot! game at: [www.kahoot.it](http://www.kahoot.it)

## BACK TO KAHOOT!: WEIGHT-LOSS SUPPLEMENTS



## Overview of Weight-Loss Supplements<sup>5</sup>

- One-third of Americans are overweight and/or obese
- Weight-Loss supplements are very profitable
  - Overall sales of 26.9 billion in 2009
- Consumers hold many misconceptions about safety and efficacy because they assume the products are “natural”
- Not all weight-loss supplements are dangerous but with the breadth of product availability, product quality, and heterogeneity amongst products, providers should be informed



## Top Weight-Loss Supplements 2018

- Garcinia Cambogia
- Hydroxycut
- Caffeine
- Orlistat (Alli)
- Raspberry Ketones
- Green Coffee Bean Extract
- Glucomannan (Lipozene)



## Categories of Weight-Loss Supplements<sup>5</sup>

- Supplements that **increase energy expenditure** (stimulants)
  - Raspberry Ketones
  - Hydroxycut
  - Green coffee bean extract
- Supplements that **modulate carbohydrate metabolism**
- Supplements that **increase fat oxidation or reduce fat synthesis**
  - Garcinia Cambogia
- Supplements that **increase satiety**
  - Glucomannan (Lipozene)
- Supplements that **block dietary fat absorption**
  - Glucomannan (Lipozene)





## Quick Links for Weight-Loss Supplements

- [http://www.medscape.com/viewarticle/845675?nlid=82194745&src=wnl\\_edit\\_medp\\_phar&uac=155237DK&spon=30](http://www.medscape.com/viewarticle/845675?nlid=82194745&src=wnl_edit_medp_phar&uac=155237DK&spon=30)
- <https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/MedicationHealthFraud/ucm234592.htm>



Please open Kahoot! game at: [www.kahoot.it](http://www.kahoot.it)

## BACK TO KAHOOT!: CLEANSSES



## Overview of Cleanses

- Common names: Cleanses, Flushes, Detoxification or “Detox”, Juicing
- Suggested to remove toxins from body or for losing weight



## Approaches to Cleanses<sup>11</sup>

- Fasting
- Consuming only juices or other liquids for several days
- Eating a very restricted food selection
- Using various dietary supplements or other commercial products
- Cleansing the colon (lower intestinal tract) with enemas, laxatives, or colon hydrotherapy (also called “colonic irrigation” or “colonics”)
- Combinations of the aforementioned



## Safety<sup>11</sup>

- Products may contain illegal or potentially harmful ingredients
- Juices that haven’t been pasteurized or treated in other ways to kill harmful bacteria may cause illness
- Drinking large quantities of juice may be risky for people with kidney disease
- Patients with diabetes should not fast and should follow a recommended diet
- Diets that severely restrict calories may not provide enough nutrients and are not effective long-term
- Colon cleansing procedures may have side effects
- Detoxification programs often include laxatives, which can cause diarrhea severe enough to lead to dehydration and electrolyte imbalances



## Case Study: Green Smoothie Cleanse<sup>12</sup>

- 65 y/o woman with a gastric bypass and recent prolonged antibiotic therapy started green smoothie cleanse
- Green smoothie cleanse is exclusive consumption of a beverage composed green leafy vegetables, fruits, and water for 10 days
- Kidney function deteriorated after cleanse
  - normal before cleanse → acute kidney injury → end stage renal disease
- Consumption of cleanse as well as predisposing risk factors lead to acute oxalate nephropathy
  - Oxalate found in a variety of plants
- Excessive oxalate in kidney binds to calcium → insoluble calcium oxalate crystals → acute/chronic kidney failure





## Effectiveness of Cleanses<sup>11, 13</sup>

- There isn't any convincing evidence that detox or cleansing programs actually remove toxins or improve a patient's health
- A handful of clinical studies have shown that commercial detox diets enhance liver detoxification and eliminate persistent organic pollutants from the body, but most these studies are hampered by flawed methodologies and small sample sizes
- Weight-loss with these products are likely attributed to calorie restriction



## SUMMARY



## Counseling Pearls

- Always ask specifically about supplements
- Realize that patients may not call them by the same name or consider them medicines
- Ask by several names and methods
  - Combine and separate from other OTC products
  - Call them herbals, supplements, anything to "improve their health", oils, shakes, etc...
- Whether or not they take weight-loss supplements and/or cleanses can change rapidly so ask at every encounter



## Counseling Pearls

- Instruct patients to read labels carefully
  - Plant names (genus and species) vs. common name
- Purchase products from reputable companies
- Use the same brand and formulation
- Always inform providers of supplements, cleanses, and use of oils
- Should be used for a limited amount of time
- Should not be used in children and in pregnancy
- Respect the patients beliefs, but be sure to counsel on safety and effectiveness



## Take Home Messages

- Aromatherapy has low risk but is not regulated for quality or efficacy
- Many weight-loss supplements and cleanses contain harmful ingredients and most are not safe or effective
- Research all products and product ingredients for safety and efficacy
- Patient safety is our first concern, ensure thorough patient history is taken



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## Drug-Induced Nutrient Depletion

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## Conflict of Interest

- I have no actual or potential conflict of interest in relation to this presentation or program



## Objectives

- Describe how five commonly used medications can inhibit nutrient absorption, synthesis, transport, storage, metabolism or excretion
- Explain tools and techniques that can be implemented to mitigate drug-induced nutrient depletion



## Match the Medication with Reported Nutrient Deficiency

Metformin	Vitamin B12
Bisphosphonates	Coenzyme Q10
Statins	Calcium
Oral Contraceptives	Magnesium
Proton Pump Inhibitors	Iron



## METFORMIN



## Metformin

- Nutrient depleted: Vitamin B12
- Prevalence of B12 deficiency with metformin use: 5.8-52%



Ahmed MA. BMC Pharmacol Toxicol. 2016;17:44.

## Mechanism – Metformin and B12

- Not fully elucidated
- Mechanisms include
  - Small intestine motility changes allowing for bacterial overgrowth and B12 deficiency
  - Competitive inhibition or inactivation of absorption
  - Altered intrinsic factor (IF) levels and interactions
  - Inhibition of calcium-dependent absorption of B12-intrinsic factor complex in ileum



Kibirige D. J Diabetes Metab Disord. 2013;12:17.  
Liu Q. PLOS ONE. 2014; e100379. doi:10.1371/journal.pone.0100379.

## Risk Factors

- Older age
- Higher metformin dose
- Longer duration of use (4 months or more)



Kibirige D. J Diabetes Metab Disord. 2013;12:17.

## Clinical Impact of B-12 Deficiency

- Biochemical
- Clinical Symptoms
  - Anemia
  - Peripheral neuropathy
  - Psychiatric changes
- Timeframe for Manifestation
  - 5-10 years



Chapman LE. Diabetes Metab. 2016;42:316.  
Kibirige D. J Diabetes Metab Disord. 2013;12:17.

## Screening Recommendations

- American Diabetes Association added a recommendation to consider periodic measurement of B12 levels with supplementation as needed
- Potential considerations
  - Prior to metformin initiation
  - Annually in elderly patients with metformin use for at least 3-4 years with metformin doses at least 2 g per day
  - Worsening peripheral neuropathy
- Homocysteine and methylmalonic acid?



Diabetes Care. 2017;40:S4.  
Kibirige D. J Diabetes Metab Disord. 2013;12:17.

## Treatment

- If deficiency present
  - Vitamin B12 supplementation (oral or intramuscular) 1000 mcg daily x1 week then weekly x4 weeks
  - Calcium supplementation?
- For patients with severe peripheral neuropathy: improvement in pain and paresthesias



Kancherla V. PLOS ONE. 2016;11:e0160802.  
doi:10.1371/journal.pone.0160802

## Prevention

- No sufficient evidence to support routine supplementation for prevention
- Evidence is conflicting
  - Multivitamin supplementation may lessen the decrease in B12 levels in diabetic patients
  - B12 supplementation at typical levels found in multivitamins in patients with diabetes did not change prevalence of deficiency



Kancherla V. PLOS ONE. 2016;11:e0160802.  
Reinstatler L. Diabetes Care. 2012;35:327.

## Key Points

- Deficiency likely due to decreased absorption
- Biochemical reaction
- Difficult to elucidate clinical impact in diabetic patients
- Treat documented deficiency with B12 supplementation



## PROTON PUMP INHIBITORS



## Proton Pump Inhibitors (PPIs)

- Nutrients depleted
  - Iron
  - Vitamin B12
  - Magnesium
  - Calcium



Eusebi LH. J Gastroenterol Hepatol. 2017;32:1295.

## Mechanism

- Iron
  - Gastric acid is needed to convert iron to soluble forms for absorption in duodenum
- Vitamin B12
  - Gastric acid and pepsin result in release from dietary sources
  - Alkaline environment prevents release and subsequent absorption does not occur



Eusebi LH. J Gastroenterol Hepatol. 2017;32:1295.

## Mechanism

- Magnesium
  - Undefined, possibly decreased absorption or renal wasting
- Calcium
  - Absorption decreased with achlorhydria



Eusebi LH. J Gastroenterol Hepatol. 2017;32:1295.

## Risk Factors

- Prolonged use of PPIs
- Advanced age
- Malnutrition



Freedberg DE. Gastroenterol. 2017;152:706.  
Eusebi LH. J Gastroenterol Hepatol. 2017;32:1295.

## Clinical Impact

- Anemia
  - Case reports and observational studies
- Vitamin B12 deficiency
  - Conflicting data
- Hypomagnesemia
  - Gastrointestinal symptoms, depression, tremor, seizures, tetany, ataxia



Eusebi LH. J Gastroenterol Hepatol. 2017;32:1295.

## Clinical Impact

- Hypocalcemia
- Bone fractures
  - Vitamin B12 deficiency may reduce osteoblastic activity
  - Hypergastrinemia



Eusebi LH. J Gastroenterol Hepatol. 2017;32:1295.

## Screening

- Anemia
  - Not routinely recommended
  - Consider if all other causes of anemia excluded
- Vitamin B12, magnesium, calcium
  - No routine monitoring recommended per best practice advice from the American Gastroenterological Association (AGA)
  - No routine monitoring of bone mineral density is recommended



Freedberg DE. Gastroenterol. 2017;152:706.  
Eusebi LH. J Gastroenterol Hepatol. 2017;32:1295.

## Treatment

- Supplementation may be of benefit in patients who are found to have anemia, hypomagnesemia, hypocalcemia or low vitamin B12 levels
- A recent meta-analysis suggests stopping the PPI with severe hypomagnesemia
  - Magnesium supplementation may not correct deficiency



Schoenfeld AJ. JAMA Int Med. 2016;176:172.

## Prevention

- Utilize PPIs only for the minimum necessary duration
- Vitamins or supplement use is associated with conflicting data
  - Best practice from the AGA states to not exceed the recommended daily allowance



Freedberg DE. Gastroenterol. 2017;152:706.

## Supplementation Tips

- Calcium
  - Take calcium with acidic meal
  - Utilize calcium citrate
- Iron
  - Consider pairing with vitamin C for increased absorption



Freedberg DE. Gastroenterol. 2017;152:706.  
Eusebi LH. J Gastroenterol Hepatol. 2017;32:1295.



## Key Points

- Gastric acid is important for absorption of vitamins and minerals
- PPIs may reduce absorption of vitamin B12, iron, calcium and magnesium
- No data supports routine screening or supplementation



## ORAL CONTRACEPTIVES



## Oral Contraceptives

- Nutrients depleted
  - Folate
  - Vitamin B12



Palmerly M. Eur Rev Med Pharmacol Sci. 2013;17:1804.

## Mechanism

- Folate
  - May be due to reduced absorption
  - May be due to increased excretion
  - May be due to increased metabolism
- Vitamin B12
  - May be due to decreased binding capacity of B12 in the serum
  - Independent of folate



Palmerly M. Eur Rev Med Pharmacol Sci. 2013;17:1804.

## Risk Factors

- Malnutrition



Palmerly M. Eur Rev Med Pharmacol Sci. 2013;17:1804.

## Clinical Impact

- Folate
  - Typically not clinically relevant due to attainment from dietary sources
- Vitamin B12
  - Anemia



Palmerly M. Eur Rev Med Pharmacol Sci. 2013;17:1804.

## Screening

- No recommendations for standard screening of vitamin deficiency in patients on oral contraceptives



## Treatment

- Multivitamin supplementation and/or B-complex vitamin supplementation may be considered
  - Especially for patients with poor dietary intake of these vitamins
- Folate – ensure supplementation in women recently on OCs who plan to become pregnant



Palmerly M. Eur Rev Med Pharmacol Sci. 2013;17:1804.

## Key Points

- Reduced folate and vitamin B12 are caused by unknown mechanisms
- Routine supplementation not routinely recommended if dietary intake is adequate
- Multivitamin or B complex vitamins are usually sufficient



## STATINS



## Statins

- Nutrient depleted – Coenzyme Q<sub>10</sub>
- Mechanism
  - Statins inhibit the development of mevalonate in the body
  - Mevalonate is used to synthesize Coenzyme Q<sub>10</sub>
  - Ultimate decrease in Coenzyme Q<sub>10</sub> synthesis



Barenholtz Levy H. Ann Pharmacother. 2006;40:290.

## Risk Factors

- Familial hypercholesterolemia
  - Small studies demonstrated a greater decrease of Coenzyme Q<sub>10</sub> in patients with familial hypercholesterolemia
- Heart Failure
  - May maintain diastolic function that statins may worsen
- Advanced age
  - Coenzyme Q<sub>10</sub> levels become saturated in younger adults



Barenholtz Levy H. Ann Pharmacother. 2006;40:290.

## Clinical Impact

- Statin-induced myopathy



Banach M. May Clin Proc. 2015;90:24.  
Barenholtz Levy H. Ann Pharmacother. 2006;40:290.

## Screening

- Routine screening not recommended



## Treatment

- Meta-analysis published in 2015 did not find myopathy improved with Coenzyme Q<sub>10</sub> supplementation
- Dosing: divided doses up to 1200 mg/day



Banach M. May Clin Proc. 2015;90:24.  
Barenholtz Levy H. Ann Pharmacother. 2006;40:290.  
Ubiquinone. Natural Medicines Database. Accessed Nov 2018.

## Prevention

- Conflicting results
- Consider Coenzyme Q<sub>10</sub> supplementation for at-risk populations
  - Familial hypercholesterolemia
  - Heart failure
  - Age greater than 65



Barenholtz Levy H. Ann Pharmacother. 2006;40:290.  
Taylor BA. Atherosclerosis. 2015;238:329.

## Risks with Coenzyme Q10

- Adverse effects: generally mild
  - Gastrointestinal: diarrhea, nausea, GI discomfort
  - Headache
  - Loss of appetite
- Drug Interactions
  - Warfarin?



Scott GN. Am J Health-Syst Pharm. 2002;59:339.  
Shalansky S. Pharmacotherapy. 2007;27:1237.  
Ubiquinone. Natural Medicines Database. Accessed Nov 2018.

## Key Points

- Statins decrease the synthesis of Coenzyme Q<sub>10</sub>
- Conflicting evidence to routinely recommend for statin-induced myopathy
- Benefit may exceed risk in at risk patients



## BISPHOSPHONATES



## Bisphosphonates

- Nutrient depleted: calcium
- Prevalence
  - 35-40% with IV bisphosphonate use



Ho JW. Medical Hypoth. 2012;78:377.

## Mechanism

- Bisphosphonates inhibit bone resorption by osteoclasts
- Bone resorption results in maintenance of physiologic serum calcium levels
- Inhibiting bone resorption may decrease serum calcium levels



Ho JW. Medical Hypoth. 2012;78:377.

## Risk Factors

- IV bisphosphonate use (zoledronate and denosumab)
- Renal failure
- Malnutrition or malabsorption
- States of high bone turnover (metastases)
- Other vitamin/mineral deficiencies
  - Vitamin D
  - Magnesium



Kreutle V. Swiss Med Wkly. 2014;144:w13979.

## Clinical Impact

Degree of Hypocalcemia Symptoms	Symptom Manifestation
Mild	Lethargy Low serum levels
Severe	Tetany Muscle spasm Seizures
Life-threatening	Laryngospasm Respiratory stridor Cardiac failure



Kreutle V. Swiss Med Wkly. 2014;144:w13979.

## Screening

- Calcium serum concentration
  - Hypocalcemia is defined as < 8.5 mg/dL if ionized calcium levels are < 4.4 mg/dL
- Vitamin D3 serum levels
- Magnesium serum concentration



Chennuru S. Int Med Journal. 2008;38:635.  
Kreutle V. Swiss Med Wkly. 2014;144:w13979.

## Treatment

Degree of Hypocalcemia Symptoms	Symptom Manifestation	Treatment
Mild	Lethargy Low serum levels	Oral calcium 1-3 g (elemental) per day
Severe	Tetany Muscle spasm Seizures	IV bolus supplementation calcium (elemental) 100-300 mg -calcium chloride 1g -calcium gluconate 2-3 g  Infusion at 0.5-2 mg/kg elemental calcium per hour
Life-threatening	Laryngospasm Respiratory stridor Cardiac failure	IV bolus supplementation -calcium chloride 1-2g followed by infusion  IV bolus magnesium sulfate 2g followed by 1g/hr infusion



Barton Pai A. Chapter 50 in DiPiro: A Pathophysiologic Approach, 10e.  
Kreutle V. Swiss Med Wkly. 2014;144:w13979.

## Prevention

- Not well studied
- Consider calcium and vitamin D supplementation in patients on IV bisphosphonates
  - Calcium (elemental) 1200 mg PO daily
  - Vitamin D 800 international units PO daily



Kreutle V. Swiss Med Wkly. 2014;144:w13979.  
Calcium and Vitamin D. LexiComp. Accessed Nov 2018.

## Risks

- Adverse effects: mainly gastrointestinal
- Precautions: history of kidney stones
- Drug interactions: typically require scheduling changes



Calcium and Vitamin D. LexiComp. Accessed Nov 2018.

## Key Points

- Bisphosphonates affect calcium homeostasis by inhibiting bone resorption
- Hypocalcemia most pronounced with use of IV bisphosphonates
- Prevention with calcium and vitamin D



## Drug-Induced Nutrient Depletion

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