CAM of Worms: Complementary and Alternative Medicine for Diabetes
Speakers

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Disclosures

Drs. Angelo and Patel declare no conflicts of interest, real or apparent, and no financial interests in any company, product, or service mentioned in this program, including grants, employment, gifts, stock holdings, and honoraria.
Learning Objectives

At the conclusion of this activity, pharmacists and pharmacy technicians should be able to:

- List examples of CAM used in the treatment of diabetes
- Discuss clinical benefits and risks of commonly used dietary and herbal supplements for diabetes
- Educate patients on appropriate use of herbal and dietary supplements
- Identify resources available to assess the safety and efficacy of herbal and dietary supplements
Of the following types of CAM practices, which one includes herbal and dietary supplements?

A. Biologically-based practices
B. Mind-body medicine
C. Manipulation
D. Energy medicine
E. Whole medical systems
Which of the following herbals and supplements is most likely to help with peripheral neuropathy associated with diabetes?

A. Gymnema sylvestre
B. Alpha lipoic acid
C. Bitter melon
D. Green tea extract
Which of the following resources provides safety and efficacy information about herbals and supplements and is sponsored by the National Institutes of Health?

A. Natural Medicines
B. Pharmacist’s Letter
C. Drug Information Handbook
D. National Center for Complementary and Integrative Health
Patients who wish to use dietary or herbal supplements to augment their diabetes treatment should be advised to monitor their blood glucose more frequently.

A. True
B. False
What is Complementary and Alternative Medicine (CAM)?

- A "group of diverse medical and health care systems, practices, and products that are not generally considered to be part of conventional medicine."

- Complementary medicine is used with conventional medicine, whereas alternative medicine is used instead of conventional medicine.


Examples of CAM

- Acupuncture
- Aromatherapy
- Biofeedback
- Chiropractic therapy
- Commercial diet programs
- Dietary supplements
- Energy healing
- Folk remedies
- Guided imagery
- Herbal remedies
- High-dose vitamin use
- Homeopathy
- Hypnosis
- Intercessory prayer
- Lifestyle diets
- Massage
- Naturopathy
- Osteopathy
- Relaxation/mediation
- Self-help groups
- Solitary prayer
- Spiritual healing by others
- Spiritual practices
- Yoga

Five Types of CAM

- Biologically-based practices
  - Herbal and dietary supplements

- Mind-body medicine
  - Yoga, tai chi, meditation

- Manipulation and body-based practices
  - Chiropractic therapy, osteopathic manipulation, massage

- Energy medicine
  - Reiki, external qi gong, therapeutic touch

- Whole medical systems
  - Homeopathy, naturopathy, Ayurveda, traditional Chinese medicine

Birdee GS, Yeh G. Clinical Diabetes. 2010;28(4).

- 1997 – 1998 survey of 2,055 people: 95 (4.6%) had diabetes
- Of those with diabetes, 57% used at least one CAM therapy in the past year and 35% used CAM specifically for diabetes

What CAM remedies have you encountered patients with diabetes using?
If you had a patient with diabetes taking dietary supplements, which organ would you be most concerned about?

National Center for Complementary and Alternative Medicine.
http://nccam.nih.gov/health/providers/digest/diabetes-science.htm
### Vitamins and Dietary Supplements
- Alpha-lipoic acid
- Chromium
- Fiber
- γ-linoleic acid
- Magnesium
- Omega-3 fatty acids
- Taurine
- Vanadium
- Vitamin E
- Zinc

### Herbal Products
- Aloe vera
- Berberine
- Cinnamon
- *Coccinia indica* (ivy gourd)
- *Emblica officinalis* (gooseberry)
- Fenugreek
- Garlic
- *Ginkgo biloba*
- Green tea
- *Gymnema sylvestre*
- *Momordica charantia* (bitter melon)
- *Opuntia streptacantha* (prickly pear cactus)
- *Panax quinquefolius* (American ginseng)
- *Panax ginseng* (Asian ginseng)

*Just because they are listed here, does not imply that they are safe and effective.*
Miguel is a 47 year-old patient with type 2 diabetes who has been to your ambulatory care clinic twice over the past year. He moved to the US from El Salvador 4 years ago. He was diagnosed with diabetes 5 years ago while in El Salvador. His A1C readings are:

- 10 months ago: A1C = 9.8%
- Today: A1C = 9.6%

The medications he was prescribed for diabetes are:

- Metformin 1000 mg twice daily
- Lantus 10 units qhs
Last week, you were reviewing the charts of patients who missed their last appointment. Miguel was one of those patients. You also noticed that he has not been back to refill his medications that were prescribed 10 months ago. Therefore, you called him and asked him to come back to the clinic and bring all of his diabetes medications with him.

Today he shows up with his glucometer (unopened), a bottle of metformin with 3 tablets gone, an unused bottle of Lantus, an unopened bag of insulin syringes, a bottle of Fenugreek, and a bottle of Diabetifin.
**Diabetifen**

**Supplement Facts**

- **Serving Size:** 2 capsule
- **Servings per Container:** 30 capsules
- **Quantity per container:** 60 capsules

**Amount per Serving**

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount (mg)</th>
<th>% DV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromium (AS Chromium Picolinate)</td>
<td>50 mcg</td>
<td>41%</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>100 mg</td>
<td>166%</td>
</tr>
<tr>
<td>Guar Gun</td>
<td>5 mg</td>
<td>*</td>
</tr>
<tr>
<td>Ginkgo Biloba Powder</td>
<td>50 mg</td>
<td>*</td>
</tr>
<tr>
<td>Fenugreek Seed</td>
<td>150 mg</td>
<td>*</td>
</tr>
<tr>
<td>Alfalfa</td>
<td>100 mg</td>
<td>*</td>
</tr>
</tbody>
</table>

% DV are values established in USA.
* Daily values not established in USA.

**Other Ingredients:** White Rice Flour, Magnesium Stearate, Gelatin from capsule.

**DIRECTIONS:** Adults- Take one (1) to three (3) capsules daily as a dietary supplement, or as directed.
What questions do you have?

Now what?
FDA NEWS RELEASE
For Immediate Release: July 23, 2013
Media Inquiries: Christopher Kelly, 301-796-4676, christopher.kelly@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA alerts companies to stop illegal sale of treatments for diabetes
Includes certain products containing undeclared active pharmaceutical ingredients

The U.S. Food and Drug Administration is taking action to remove from the market illegal products, including some labeled as dietary supplements, that claim to mitigate, treat, cure or prevent diabetes and related complications. The agency recently issued letters warning 15 companies that the sale of their illegally marketed diabetes products violates federal law. The letters were sent to foreign and domestic companies whose products were sold online and in retail stores.

www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm362012.htm

FTC Obtains $2.2 Million Judgment against Supplement Marketer that Made Phony Claims for Treating and Preventing Diabetes

FOR RELEASE
March 7, 2014

Vitamins and Dietary Supplements
Alpha-Lipoic Acid (ALA)

- An antioxidant made by the body and found in food
- Proposed uses in diabetes
  - Improves insulin sensitivity and fasting glucose
  - Lessens symptoms of peripheral neuropathy
- Doses used
  - 600 – 1800 mg per day (orally or intravenously)
- Adverse reactions
  - GI upset, nausea, vomiting, headache, skin rash

May be beneficial for peripheral neuropathy, may improve insulin sensitivity but effects on glycemic control unproven

Birdee GS, Yeh G. *Clinical Diabetes.* 2010;28(4).
Chromium

- Thought to increase insulin sensitivity, lower fasting glucose levels, and improve A1C
- If deficient, patient cannot use glucose properly
- Often used in parenteral nutrition and may be prescribed when large doses of insulin are needed
- May be more effective in patients with high insulin resistance
- Upper limit for safe and adequate dietary intake is 50 to 200 μg per day
- Doses studied ranged from 200 to 1400 μg per day
- Well-tolerated; cognitive and motor dysfunction reported at doses of 200 to 400 mcg/day; doses of 1.2 to 2.4 mg per day may lead to anemia, thrombocytopenia, hemolysis, hepatic dysfunction, and renal failure

**Effectiveness remains unproven; recommend if patient has chromium deficiency**

Birdee GS, Yeh G. *Clinical Diabetes.* 2010;28(4).
γ-linoleic acid (GLA)

- An omega-6 fatty acid
- Potential uses in diabetes
  - Diabetic neuropathy (360 mg – 480 mg per day)
- Adverse effects
  - Nausea, vomiting, diarrhea, soft stools, flatulence, belching
- Drug interactions
  - May have antiplatelet effects and increase the risk of bleeding

May be beneficial for diabetic neuropathy

Omega-3 Fatty Acids

- Favorable effect on triglycerides
- May *increase* blood glucose and LDL levels
- Concerns regarding inhibition of platelet aggregation and mercury toxicity

No beneficial effect on FBG, A1C, plasma insulin, or insulin resistance

Birdee GS, Yeh G. *Clinical Diabetes*. 2010;28(4).
Magnesium

- Magnesium is essential to processing glucose
- Deficiency has been associated with diabetes
  - Glycosuria → reduced magnesium reabsorption
- May help to reduce the risk of developing type 2 diabetes
- Tolerable upper intake level (UL) = 350 mg/day
- Drug interactions
  - Antibiotics, bisphosphonates
- Adverse effects
  - Diarrhea, abdominal cramping

Only beneficial if patient is deficient

Birdee GS, Yeh G. *Clinical Diabetes*. 2010;28(4).
National Center for Complementary and Alternative Medicine.
Vanadium

- May improve hepatic and peripheral insulin sensitivity
- Commonly found in food
  - Skim milk, lobster, oils, cereals, grains, vegetables
- Usual vanadium intake: 10 – 60 μg per day
- Upper intake level (UL): 1.8 mg per day
- Toxicity and death can occur with doses > 20 mg per day
- Adverse effects
  - Mutagenesis, carcinogenesis, GI upset, renal and neurologic symptoms

**Narrow therapeutic window and risks do not support its recommendation for use**

Birdee GS, Yeh G. *Clinical Diabetes.* 2010;28(4).
Vitamin E

- Purported uses in diabetes
  - Decreased A1C (600 mg per day)
  - Decreased urinary albumin excretion (680 IU per day, given with vitamin C)
- Tolerable upper intake level (UL): 1000 mg/day (1100 IU/day); limit to no more than 400 IU/day in non-healthy patients
- Safety concerns
  - May pose an increased risk of hemorrhagic stroke, heart failure, and prostate cancer

Negative data outweigh benefits – use is not supported

Fiber Challenge

- What is the role of fiber in diabetes management?
- What is the ADA recommendation for fiber per day?
- How can you help your patients meet this goal?
- What issues do we need to watch out for?


Herbal Products
Berberine

- Possible mechanism
  - Increases insulin receptors, AMPK activity, and GLP-1 activity
  - Inhibits gluconeogenesis in liver

- Purported uses in DM
  - May lower A1C, FBG, and post-prandial glucose

- Efficacy
  - 500 mg BID–TID
  - Some studies show equipotent effect to metformin 500 mg BID or rosiglitazone 4 mg daily

- Safely used for 3 months
  - Long-term use studies needed

**May be beneficial for glucose lowering for type 2 diabetes**

Cassia Cinnamon

- May lower blood glucose levels via a hypoglycemic effect
- Doses ranged from 120 mg to 6 grams daily
- Studies are conflicting, but evidence in favor of improved A1C and FBG
- No significant adverse effects reported; large amounts may result in hepatotoxicity due to coumarin content
  - Theoretical increased risk of bleeding
- Hypersensitivity reactions reported with topical products

May be beneficial for glucose lowering for type 2 diabetes

Deng R. *Recent Pat Food Nutr Agric* 2012;4(1).
Coccinia indica
(Ivy Gourd)

- High fiber content
- In a study to assess herbal remedy use in 220 patients with diabetes in Sri Lanka, ivy gourd was most commonly used (32%)
- Purported uses in diabetes
  - May act as an insulin mimetic
  - Shown to decrease FBG
- Suggested dose: 20 grams of ivy gourd leaves daily with breakfast
  - 1 gram and 6 grams per day have also been used
- Adverse reactions
  - Well-tolerated, may cause mild nausea, headache, and drowsiness
- Drug interactions
  - May cause hypoglycemia when taken with other glucose-lowering medications

Preliminary results are promising but further research is needed

Birdee GS, Yeh G. Clinical Diabetes. 2010;28(4).
Fenugreek

- Bulk laxative effect may decrease carbohydrate absorption
- May increase insulin secretion
- Doses ranging from 5 to 100 grams have been shown to be effective
- Adverse reactions
  - GI upset, hypoglycemia
- Drug interactions
  - May increase bleeding risk

Evidence is lacking but may be effective in reducing blood glucose levels

Birdee GS, Yeh G. Clinical Diabetes. 2010;28(4).
Deng R. Recent Pat Food Nutr Agric. 2012;4(1).
Ginkgo biloba

- Purported uses in diabetes
  - Peripheral neuropathy
  - Diabetic retinopathy
  - Erectile dysfunction

- No significant impact on blood glucose or A1C

- Drug interactions
  - Increased metabolism of insulin and oral hypoglycemic agents → hyperglycemia
  - Increased risk of bleeding, seizure medications

No compelling data to support use for diabetes

Epidemiologic studies in Japanese population with DM show benefit

Clinical studies in DM lack evidence

Green tea extract containing polyphenols (or catechins) shown to increase insulin sensitivity and reduce beta cell damage in vitro and in animal studies

Current evidence suggests no hypoglycemic effect

Deng R. Recent Pat Food Nutr Agric 2012;4(1).
Gymnema sylvestre

- Particular extract (GS4) may have additive effects when combined with other agents
- May act as an insulin secretagogue
- Doses of 200 mg, 400 mg, and 800 mg per day shown to reduce FBG and A1C
- No adverse effects reported
- Small, poorly designed studies

Insufficient evidence to support use, but preliminary findings are promising

Birdee GS, Yeh G. *Clinical Diabetes*. 2010;28(4).
Momordica charantia (Bitter Melon)

- Possible mechanism of action
  - Decreases hepatic glucose production
  - Increases hepatic glycogen synthesis
  - Insulin mimetic activity
- Doses ranged from 500 mg to 6000 mg
- Poorly designed studies with conflicting evidence

No strong evidence to support use

Birdee GS, Yeh G. Clinical Diabetes. 2010;28(4).
Deng R. Recent Pat Food Nutr Agric. 2012;4(1).
Opuntia streptacantha
(Prickly Pear Cactus)

- Possible mechanism
  - May increase insulin sensitivity
  - May decrease carbohydrate absorption
- Most evidence with single dose experiments
  - Dose studied: 100–600 mg/day
  - Data lacking for extended use
- Drug interaction
  - Use with antiplatelets and anticoagulants increase risk of bleeding

Insufficient evidence to support use for diabetes

**Panax ginseng**  
(Assian Ginseng)

- Different ginsenosides than American ginseng
- Limited and conflicting data regarding effects on glucose levels
- May cause insomnia and *increase* bleeding risk

No compelling data to support use for diabetes

University of Maryland Medical Center. Complementary and Alternative Medicine Guide.  
Panax quinquefolius
(American Ginseng)

- Purported uses in diabetes
  - Lower postprandial glycemia
  - A1C improvement
  - Reduced FBG
- Doses ranging from 200 mg to 3000 mg per day have been used
- May have estrogenic activity, may decrease effects of warfarin
- Data is conflicting, but stronger for American ginseng than Asian ginseng

No compelling data to support use for diabetes

Birdee GS, Yeh G. *Clinical Diabetes.* 2010;28(4).
Then There’s All This . . .
## Potential Interactions Between Herbals and Anti-hyperglycemic Agents

<table>
<thead>
<tr>
<th>Anti-hyperglycemics</th>
<th>Herbals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin</td>
<td>Chromium, ginseng</td>
</tr>
<tr>
<td>Oral anti-hyperglycemics</td>
<td>α-Lipoic acid, devil’s claw, Ephedra, fenugreek, feverfew, garlic, ginger, Gotu, Kola, guar gum, horse chestnut seed, licorice root, Panax ginseng, psyllium, Siberian ginseng, stinging nettle, karela, inositol, niacin</td>
</tr>
<tr>
<td>Statins</td>
<td>Red yeast rice, grapefruit juice, pectin, coenzyme Q10, vitamin C</td>
</tr>
<tr>
<td>Thiazides</td>
<td>Inositol, niacin</td>
</tr>
<tr>
<td>TZDs</td>
<td>Ginkgo biloba</td>
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</tbody>
</table>

Ineffective or Insufficient Evidence

<table>
<thead>
<tr>
<th>Vitamins and Dietary Supplements</th>
<th>Herbal Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-Q-10</td>
<td>Agaricus mushroom</td>
</tr>
<tr>
<td>Chia</td>
<td>Allium cepum (onion)</td>
</tr>
<tr>
<td>Glucomannan</td>
<td>Aloe vera</td>
</tr>
<tr>
<td>Selenium*</td>
<td>Arctium lappa (burdock)</td>
</tr>
<tr>
<td>Taurine</td>
<td>Banaba</td>
</tr>
<tr>
<td>Vitamin B6 (pyridoxine)</td>
<td>Emblica officinalis (gooseberry)</td>
</tr>
<tr>
<td>Zinc</td>
<td>Garlic</td>
</tr>
<tr>
<td></td>
<td>Phaseolus vulgaris</td>
</tr>
<tr>
<td></td>
<td>Stevia</td>
</tr>
<tr>
<td></td>
<td>Taraxacum officinale (dandelion)</td>
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</tbody>
</table>

*May cause type 2 diabetes

Time to Vote: Which of the following would you be comfortable with a patient with diabetes using?

<table>
<thead>
<tr>
<th>Vitamins and Dietary Supplement</th>
<th>Herbal Products</th>
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</thead>
<tbody>
<tr>
<td>Alpha-lipoic acid</td>
<td>Berberine</td>
</tr>
<tr>
<td>Chromium</td>
<td>Cinnamon</td>
</tr>
<tr>
<td>Fiber</td>
<td><em>Coccinia indica</em> (ivy gourd)</td>
</tr>
<tr>
<td>γ-linoleic acid</td>
<td>Fenugreek</td>
</tr>
<tr>
<td>Magnesium</td>
<td><em>Ginkgo biloba</em></td>
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<td>Omega-3 fatty acids</td>
<td>Green tea</td>
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<td>Vitamin E</td>
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</table>
Questions to Consider when Advising Patients

- Is it evidence-based?
  - Quality of the studies
  - Sample size and methodology
- Is it safe?
- Will it work?
- Is the patient using this in addition to or in place of FDA-approved medications?
Always let your health care providers know what you are using or trying
Not all remedies are safe
Few remedies are proven effective to treat or prevent diabetes
Approach the use of each independently to determine a cause and effect relationship
Monitor effectiveness (check BG and A1C at baseline and after beginning use)
Stop use if no improvement seen
These can be very expensive
Read the labels
Look for this Seal

[Image of the USP Dietary Supplement Verification Seal]
Fig. 1—Dietary Supplement Label Format From Kurzweil (1998)
Where Do You Go if You Don’t Know?  
Helpful Resources

- National Center for Complementary and Alternative Medicine (nccam.nih.gov)
- Office of Dietary Supplements (www.ods.od.nih.gov/index.aspx)
- Natural Medicines (https://naturalmedicines.therapeuticresearch.com/)
  - Merger of Natural Standard and Natural Medicines Comprehensive Database (www.naturaldatabase.com)
- University of Maryland Complementary and Alternative Medicine Guide (http://umm.edu/health/medical/altmed)
- Consumerlab.com (www.consumerlab.com)
- Cochrane Database Systematic Reviews (www.cochrane.org)
How will you help Miguel manage his diabetes?
Post-Assessment Question - 1

Of the following types of CAM practices, which one includes herbal and dietary supplements?

A. Biologically-based practices  
B. Mind-body medicine  
C. Manipulation  
D. Energy medicine  
E. Whole medical systems
Which of the following herbals and supplements is most likely to be help with peripheral neuropathy associated with diabetes?

A. *Gymnema sylvestre*
B. Alpha lipoic acid
C. Bitter melon
D. Green tea extract
Which of the following resources provides safety and efficacy information about herbals and supplements and is sponsored by the National Institutes of Health?

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B. Pharmacist’s Letter  
C. Drug Information Handbook  
D. National Center for Complementary and Integrative Health
Patients who wish to use dietary or herbal supplements to augment their diabetes treatment should be advised to monitor their blood glucose more frequently.

A. True
B. False
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