Not so Sweet: Spices for Diabetes & other Metabolic Diseases

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Objectives
1. Discuss pathophysiology of DM type II/ metabolic syndrome
2. Cover spices:
   - Cinnamon
   - Fenugreek
   - Prickly pear
   - Bitter melon
   - Apple cider vinegar
   - Holy basil
   - Touchi
   - Gynostemma
   - Ginger
   - Ginseng
   - Berberine
   - Gymnema sylvestre
   - Others

Prevalence of Diabetes in the US
Source: Center for Disease Control
Pathophysiology of DM type II

- Normal cycle:
  - With carb intake glucose is produced and as it circulates in the blood triggers insulin release
  - Insulin facilitates intracellular glucose transport via the GLUT-4 transporter
  - Insulin release also inhibits gluconeogenesis in the liver
  - Key targets of insulin action: 75% skeletal muscle, followed by cardiac muscle, followed by adipose tissue and then liver

Pathophysiology of DM type II

- DM changes:
  - Excess glucose circulates flagging the pancreas to release insulin
  - At the cellular membrane level glucose transport becomes very inefficient
  - The cells at the intracellular are "daring" muscle this creates intracellular signaling to the liver to produce sugar production (gluconeogenesis) and fat breakdown
  - Over time the net physiological result is too much sugar and fat but relatively less insulin to rebalance the situation
  - Insulin inhibits of gluconeogenesis and lipolysis in the liver
  - The escalation of this cycle up regulates inflammatory cytokines

Diabetes and metabolic syndrome

- Cardiovascular disease
- Peripheral vascular disease
- Hyperlipidemia
- Hyper tension
- Stroke risk
- Neuropathy

Source: Rakel Integrative Medicine, 4th Ed 2018
Diabetes Risk by Ethnicity

People with Diabetes by Race and Ethnicity, 2004–2006

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Non-Hispanic Whites</td>
<td>6.6%</td>
</tr>
<tr>
<td>Asian Americans</td>
<td>7.5%</td>
</tr>
<tr>
<td>Hispanics</td>
<td>10.4%</td>
</tr>
<tr>
<td>Non-Hispanic Blacks</td>
<td>11.8%</td>
</tr>
<tr>
<td>*AIAN</td>
<td>16.5%</td>
</tr>
</tbody>
</table>

*Adjusted by age
*American Indian and Alaska Native

Spices: Cinnamon

• Several types of Cinnamon
  • Cinnamomum verum, C. Zeylanicum
  • Cinnamomum cassia
  • Cinnamomum Burmannii
  • Cinnamomum Loureiroi
  • Cinnamomum cassia used in trials
  • Clinical trials have mixed results
  • One systematic review showed favorable results

Ann Fam Med 2013;452-459

Cinnamon Use in Type 2 Diabetes: An Updated Systematic Review and Meta-Analysis

[Source: www.motherjones.com/wp-content/uploads/cinnamon-master.gif]
Meta analysis of 10 RCTs (n = 543 patients)

- Evaluated: HbA1c, fasting plasma glucose, total cholesterol, LDL-c, HDL-c, TG
- Cinnamon doses ranged from 120 mg/day to 6 g/day for 4 to 18 weeks
- Note: 1 tsp = 4.75 grams

Results: no effect on HbA1c, increases HDL avg (1.66 mg/dl), remainder of indices with heterogeneity, lower fasting glucose

Conclusion: significant decrease in fasting plasma glucose by an avg 24 mg/dl, CHO-t (avg 15 mg/dl), LDL-c (avg 9 mg/dl), and triglycerides (avg 12 mg/dl)

Spices: Cinnamon

- Parts used: bark
- Cinnamoldehyde is found in bark 7%-83% of the time and is antidiabetic
- Polyphenolic polymers of hydroxychalcone potentiate insulin via phosphorylation of the insulin receptor.
- This effect seen much more in Cassia cinnamomon than in C.

Coumarin content in Cinnamon

<table>
<thead>
<tr>
<th>Type of Cinnamon</th>
<th>Coumarin Content</th>
<th>Taste quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceylon Cinnamon</td>
<td>0.007 g/kg</td>
<td>sweet</td>
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<tr>
<td>True Cinnamon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mexican Cinnamon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indonesian Cinnamon</td>
<td>2.15 g/kg</td>
<td>cheap spicy flavor</td>
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<tr>
<td>Korintje Cinnamon</td>
<td></td>
<td></td>
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<tr>
<td>Padang Cassia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saigon cinnamon</td>
<td>6.97 g/kg</td>
<td>strong spicy flavor</td>
</tr>
<tr>
<td>Vietnamese Cassia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vietnamese Cinnamon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cassia Cinnamon</td>
<td></td>
<td>slight bitterness</td>
</tr>
<tr>
<td>Chinese Cinnamon</td>
<td></td>
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</tr>
</tbody>
</table>

Adverse reactions:
- Coumarin can cause hepatotoxicity in very high doses (50-7000 mg/d) and stops when discontinued

https://www.cinnamonvogue.com/Types_of_Cinnamon_1.html
Spices: Cinnamon

- Use Cassia cinnamon
- Dose 1-6 g daily (1 tsp = 4.75 g)

Spices: Fenugreek (Trigonella foenum-graecum)

- Fenugreek seeds are mainly found in Middle Eastern cooking and are a popular ingredient in curries and chutneys.
- The hard, dense seeds can be difficult to grind at home, so a fine powder is a handy way to include fenugreek in cooking.
- Seeds are rich in fiber.

Source: www.savoryspiceshop.com/fenugreek-seeds

3 yr randomized control study
N = 66
5 grams twice a day before meals
Monitored q 3 months

Results:
• Controls had 4.2 x increased chance of developing dm
• Fenugreek group showed a reduction in LDL
• Increased insulintropic response (increased serum insulin levels but lower serum glucose levels)
  Note: insulin levels were within normal range
Meta-analysis of 10 trials (N=278)
- Evaluated: fasting glucose, 2 hour post glucose load, HbA1c
- Dose range: 3 grams to 100 grams/day (mean 25 g)
- Duration: 10 to 84 days
- Results: decreased fasting blood glucose (avg 0.96 mmol/L), drop 2 hours post load glucose (2.19 mmol/L) and drop in HbA1c (0.85%)
- Note: no effects with doses less than 2 g/day, effective doses 5-25 g/day
- Conclusion: benefit from intake of moderate dose of fenugreek (>5 g/day)
- Problematic: low-quality methodology

Spices: Fenugreek (Trigonella foenum-graecum)
- Applicable part: seed
- Active constituents: trigonelline, 4-hydroxyisoleucine and sotolon
- Sotolon used in artificial maple syrup
- Mechanism: Seed has 50% fiber and may slow absorption of glucose, 4-hydroxyisoleucine stimulates insulin when glucose levels are elevated
- Warning: contains coumarins but negligible amount
- Dose: for DM 10-15 g/day single or divided doses for hyperlipidemia: 0.5-2.5 g twice a day

Prickly Pear Cactus (Opuntia ficus-indica)
- Many small clinical trials from the 1980s
- One small study in 2007
Prickly Pear Cactus (Opuntia ficus-indica)

- N=36
- BMI 24
- Subjects on oral dm meds
- Served a standardized meal (1 of 3 meal choices)
  - With or without nopales (cactus note it's cooked)
  - B-s measured 15, 30, 45, 60, 90, 120 min after consumption
  - The incremental area under blood glucose response curve (IAUC) was evaluated

Diabetes Care, 30 (5) May 2007

Addition of nopales adds ~3 g fiber

TABLE 3: IAUC and glycemic index of each breakfast beverage and mean difference between each breakfast drink and carbonated beverages

3 meal types

- 20% IAUC
- 30% IAUC
- 48% IAUC

Prickly pear cactus

- Parts: leaves, flowers, stems and fruit
- 500 g of cactus provides 14.3 g carbohydrates, 8.25 g protein, 1.05 g lipids, 18 grams cellulose, and ~99 kcal
- Dose: broiled stems 100-200 grams daily in divided doses
- Boiled stems more effective in lowering glucose than raw stems
**Bitter Melon (Momordica charantia)**

- Bitter melon fruit extract might also protect against hyperinsulinemia.
- Bitter melon contains an insulin-like polypeptide called polypeptide P, plant insulin, or p-insulin. P-insulin seems to have pharmacologic effects similar to bovine insulin with an onset of action between 30 and 60 minutes, and a peak effect at about four hours.
- Other components of bitter melon reported to have hypoglycemic activity are charantin, which is a mixture of two sterol glycosides, and vicine.

**The applicable parts of bitter melon are the fruit and seeds, and less commonly the leaves and roots.**

- The bitter melon fruit, seed, and leaf extracts seem to have hypoglycemic activity in humans and animal models of diabetes.
- Preliminary evidence suggests bitter melon decreases hepatic gluconeogenesis, increases hepatic glycogen synthesis, increases pancreatic insulin secretion, and increases peripheral glucose oxidation in erythrocytes and adipocytes.
- Dose: 1 gram three times daily.

**Apple Cider Vinegar**

- Acetic acid and citric acid in the vinegar acts similarly to acarbose (precose) and metformin by suppressing diacetylcarboxylase activity and increasing glucose phosphate concentrations in the muscle.
- Also delays gastric emptying.
- Dose: 20 g diluted in 40 g of water.
- Note: white vinegar 20-28 g in 8 g of olive oil can also lower blood sugar.
- NOTE: Another strategy increase endogenous acid production by removal of antacids.

Holy Basil (Ocimum sanctum)

- Holy basil is originally from India and is used in Ayurvedic medicine.
- It is considered a sacred plant by the Hindus and is often planted around Hindu shrines. The Hindu name for holy basil, Tulsi, means "the incomparable one."
- Holy basil is sometimes called "hot basil" due to its pungent taste. It is often added to stir-fry dishes and spicy soups.
- Preliminary evidence suggests that a holy basil leaf extract might decrease fasting and postprandial blood glucose by 17.6% and 7.3% respectively in patients with type 2 diabetes. More evidence is needed to rate holy basil for diabetes.
- Dose: For stress, a specific holy basil extract (M/s Natural Remedies Pvt. Ltd., India) 400 mg orally in the morning and 800 mg orally at night has been used.
  

Berberine

- A natural alkaloid found in a wide variety of traditional herbs, including goldenseal, barberry, goldthread, Oregon grape, tree tumeric and phellodendron.
- Within these plants, the berberine alkaloid can be found in the stem bark, roots and rhizomes (root like subteranean stems) of the plants.
- Yellow color

Berberine

J. Clin Endocrinol Met July 2008 93(7) 2559-2569

- N=116
- Duration: 3 months
- Intervention: Berberine 1.0 g daily vs placebo
- Outcomes: plasma glucose (fasting and post prandial), serum lipid, glucose disposal rate
- Berberine group: fasting glucose dropped from 7.0 to 5.6 mm/L, post prandial glucose dropped from 12.0 to 8.9 mm/L, HbA1c dropped from 7.5 to 6.6%, TG from 2.51 to 1.10 mm/L, total chol, LDL also dropped
Berberine

- Dose: 300-600 mg twice a day
- Adverse reactions
  - Use of berberine containing herbs during pregnancy, lactation or in newborn infants can cause hematochuria.

Gymnema sylvestre

- The applicable part of gymnema is the leaf.
- Active constituents: gymnemic acid, gymnemosides, gurmarin, conduritol, gymnemasins, and gymnemasaponins.
- Gymnemic: reduces intestinal absorption of glucose, stimulates pancreatic beta cell growth and may also have a direct effect on beta-cell function, increasing the release of insulin.
- In animal models of metabolic syndrome, gymnema seems to decrease weight gain and triglycerides but does not affect serum cholesterol.

Gymnema sylvestre

- Dose for DM: the gymnema extract GS4 400 mg/day
- Hindi name: gurmar means “destroyer of sugar” which is the basis for its name.
**Touchi (Soy)**

- Most evidence suggests soy has a hypoglycemic effect.
- On average, a whole soy diet (as opposed to isolated soy protein) can lower fasting glucose by 3.85 mg/dl.
- Fermented soy acts as an alpha-glucosidase inhibitor and lowers hemoglobin A1c.
- Dose: touchi extract 300 mg three times a day with meals or 30 g of soy protein daily.

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**Gynostemma Pentaphyllum**

- A Vietnamese herb used as a tea to treat DM.
- The applicable part of jiaogulan is the leaf.
- The leaves of jiaogulan contain a large number of triterpene saponins referred to as gypenosides. Many of the gypenosides are identical to the ginsenosides found in Panax ginseng.
- The amount of saponins in the leaves of jiaogulan is similar to the amount found in ginseng roots. Due to the similar chemical makeup between jiaogulan and ginseng, jiaogulan is often assumed to have the same effects as ginseng.
Most jiaogulan products are standardized by the amount of saponins they contain. However, jiaogulan contains a wide variation of gypenosides which makes standardizing according to specific gypenosides difficult.

For hypercholesterolemia, jiaogulan extract 10 mg three times daily has been used.

Taking American ginseng 3 grams orally, up to two hours before a meal, can significantly reduce postprandial glucose levels in patients with type 2 diabetes.

However, doses greater than 3 grams do not seem to offer any additional benefit.

Taking American ginseng 100-200 mg daily for 8 weeks also seems to reduce fasting blood glucose levels in patients with type 2 diabetes. The glucose lowering effect of American ginseng may vary among preparations due to variations in the concentration of ginsenosides.


Ginger (Zingiber officinale)

- Perennial that grows in India, Jamaica and China
- Cultivated for more than 3000 years in China
- Used for nausea, motion sickness, as an anti-inflammatory agent and anti-flatulent

- Volatile oils 1-3% of rhizome
- 400 compounds
- Can be oleoresins concentrated up to ~35% for extraction
- Phenolic compounds and sesquiterpenes
  - Gingerols
  - Shogaols
- Other volatile compounds
  - Zingerone

There is inconsistent evidence about the effects of ginger on glycemic control in patients with type 2 diabetes. Some clinical research suggests that taking ginger 2 grams/day in two divided doses for 8 weeks reduces plasma triglycerides by 13% and fasting insulin sensitivity by 14% compared to baseline, these changes are mild and not considered biologically significant. However, another study of patients with New Zealand dyspepsia did not find any significant change in HbA1c, fasting blood sugar or triglycerides.

However, other clinical research shows that taking ginger 3 grams/day in three divided doses for 8 weeks reduces fasting blood sugar by 18.17 mg/dL compared to baseline in patients with diabetes, this change was significant compared with placebo. However, other clinical research suggests that ginger does not affect HbA1c levels.

It is possible that the dose may have played a role in these inconsistent results. Also, the populations differed slightly, with patients having diabetes for at least 2 years or at least 10 years.
Ginger

- Anti-ulcer activity
- The gingerols have been shown to stimulate gastric muscular activity and may have anti-ulcer properties (animals)
- Anti-platelet aggregation may alter platelet aggregation (inhibit) by interfacing the thromboxane production
- Anti-inflammatory action via modification of interleukin-1, and inhibition of prostaglandin and leukotriene biosynthesis.

Dose: 2-4 caps a day for DM; 3 g/day in divided doses

Nausea: 250 mg QID

Anti-inflammatory: 250 mg BID (approx)

Keep doses under 4 grams

Interactions
- Theoretical: bleeding disorders (thromboxane synthetase)
- Gallbladder conditions: may exacerbate spasm

No toxicity reported

Anti diabetic botanicals

- Silymarin (Milk thistle)
- Citrullus colocynthis (Schrad fruit)
- Coccinia cordifolia (Ivy gourd)
- Banaba (Lagerstroemia speciosa)
- Omega 3 fatty acids (cardiovascular preventive)
Integrative management of DM

- Diet: low carbohydrate Mediterranean-type diet
- Reduction of red meat and fried foods
- Magnesium-rich foods (enhances insulin secretion)
- Activity: moderate physical activity
- Moderate stress
- Avoid excessive caffeine

DM: addressing functional domains

- Structural
- Mind-body
- Immune
- Gut
- Neurono-endocrine
- Oxidative
- Environment
Traditional Medical Systems

- Chinese medicine
- Ayurveda

To succeed in life, you need three things: a wishbone, a backbone and a funny bone.
- REBA MCENTIRE

Diabetes case
Case : DM

Jenna is a 40 year old mother of two sets of twins
She is a stay at home mom
She is busy busy busy ... all 4 children play soccer (ages 10 and 14)

In the last 4 years
She is not fitting into her close she’s gained 15#
Her diet is like her children’s food on the go (pizza, grilled chicken, burritos and sandwiches)
B: cereal and coffee  L: soda and burritos  Dinner: pizza
She doesn’t like fish
Sleep is poor

When she saw her primary care provider, her heahemoglobin indices showed :
Hb a 1c of 6.0
CHO-t 220  TG 175  HDL 38
TSH 3.8 T3 T4 nl range
Case : dm

- What kind of diet might help her?
- How would you assess her activity?
- What diet would help her?
- What spices could add to a low glycemic control?
- Does sleep matter?
- She feels busy and tired, some of this is a sense of overwhelm, what other things can bring peace?

Case : DM

- Motion: get pedometer, add interval training
- Sleep: magnesium, valerian, mind-body
- Perimenopausal: chasteberry, black cohosh
- Dm: cinnamon, more apple cider vinegar
- Diet: more greens, some omega 3 sources in diet, less carbs