OTCs & Supplements in the Management of Metabolic Disease

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Learning Objectives

Become familiar with the most commonly used OTC products and supplements for treatment of different aspects of the metabolic syndrome

Identify those OTC products that have safety concerns when used in metabolic diseases

Recognize the potential for drug interactions and side effects with OTCs and supplements

Differentiate between those OTCs and supplements that have evidence in treating metabolic diseases vs those lacking solid evidence

Appraise the potential benefits that an OTC product may have in a patient with metabolic syndrome
**Dyslipidemia**

**Recommendation Chart for Natural Medicines Used for Hyperlipidemia**

<table>
<thead>
<tr>
<th>Product</th>
<th>Mechanism of Action</th>
<th>Efficacy</th>
<th>Adverse reactions</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benecol</td>
<td>Inhibits intestinal absorption of cholesterol</td>
<td>LDL-C down by 10-15%</td>
<td>Nausea, indigestion, diarrhea, constipation, &amp; gas</td>
<td>800 mg – 6 g qd with low fat meals</td>
</tr>
<tr>
<td>Plant Stanols</td>
<td>Inhibits dietary and biliary cholesterol</td>
<td>TC down by 3-11%</td>
<td>Diarrhea &amp; steatorrhea</td>
<td>800 mg – 4 g qd</td>
</tr>
</tbody>
</table>

**Plant Sterols & Stanols**

**Mechanism of action:**
- Inhibits about 50% intestinal absorption of cholesterol

**Efficacy:**
- ↓ TC, ↓ LDL-C, no effect on HDL

**Adverse reactions:**
- Nausea, indigestion, diarrhea, constipation & gas

**Dosage:**
- 800 mg – 6 g qd with low fat meals

**Plant Sterols**

- Inhibits dietary and biliary cholesterol

**Efficacy:**
- TC down by 3-11%

**Adverse reactions:**
- Diarrhea & steatorrhea

**Dosage:**
- 800 mg – 4 g qd
**Plant Sterols & Stanols**

**Interactions:**
- **Herbs:** Beta carotene and Vit. E.
- **Drugs:** Ezetimibe

**Clinical pearls:**
- Takes 2-3 weeks to be effective
- When discontinued, cholesterol levels rise back to baseline in 2-3 weeks
- Sterols and stanols appear to be equally effective

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**Red Yeast Rice** *(Monascus purpureus)*

[Image of Red Yeast Rice]


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**Red Yeast Rice**

**Mechanism of action:**
- Inhibit HMG-CoA reductase biosynthesis

**Efficacy:**
- Certain products contain about 6-10 mg of HMG-CoA reductase inhibitors

**Adverse reactions:**
- GI upset, heartburn, flatulence & dizziness
- ↑ liver enzymes & myopathy
- Kidney failure

**Dosage:**
- 600 mg – 1200 mg bid
Red Yeast Rice

**Interactions/Monitoring:**
- **Herbs:** Coenzyme Q-10, Niacin, Kava & St. John’s Wort
- **Food:** ETOH, grapefruit & food
- **Drugs:** CYP 3A4, cyclosporine & gemfibrozil
- **Labs:** creatine kinase, liver function test & serum cholesterol

**Clinical pearls:**
- Most red yeast rice products contain "statins"
- FDA role on adulterated product

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Garlic (*Allium sativum*)

[Image of garlic]

http://pages.intert.net/enyevonbye/garlic.htm

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Effect of Raw Garlic vs Commercial Garlic Supplements on Plasma Lipid Concentrations in Adults With Moderate Hypercholesterolemia

A Randomized Clinical Trial

Christopher S. Gardner, MD, Larry L. Young, MD, John Block, MD, Laura M. Chaitanya, MD, Elizabeth C. Goundal, MS, Raymond H. Talley, MD, William J. Jeffrey, MD

**Design:** RBPC, N = 220. Product: fresh garlic, dried powder, extract tablets, or placebo

**Outcome:**
- Primary: LDL-C at baseline, one month and post intervention
- Secondary: HDL-C, TG, BP and platelet aggregation

**Results:**
- Not statically significant to reduce LDL-C or secondary endpoints after 6 months

*Arch Intern Med 2007. 167(4) 346-53.*
Obesity

**Mechanism of action:**
- Alkaloid constituents of the plant: ephedrine, pseudoephedrine, and small amount of phenylpropanolamine
  - Ephedrine and pseudoephedrine are non-selective alpha and beta receptors agonist which stimulate nervous system

**Efficacy:**
- Weight loss of 0.9 kg/month up to 6 months with 50% of dietary fat intake with moderate exercise

**Adverse reactions:**
- Dizziness, anxiety, insomnia, HA, dry mouth, N/V, heartburn, tachycardia, palpitations, & MHP
  - Seizures, cardiomyopathy, MI, arrhythmias & sudden death
Ephedra

History:
- June 1997
- Proposed restriction and new warning labels
- 2002
- Health Canada ban all ephedra products
- December 30, 2003
- Announce the ban of ephedra products in US effective April 2004
- April 2005
- Federal judge in Utah challenged the ban
- Low does was not proven to be harmful
- August 2006
- Appeals court reversed the Utah judge's decision

Clinical pearls:
- Potential risk outweighs the benefit!

Calcium

Patients will low calcium intake often gain more weight and have a higher BMI

Efficacy:
- 800-1200 mg/qd dietary calcium had been shown to weight reduction & body fat loss
- 900-1000 mg/qd has been shown weight loss of 8-9 kg

Adverse reactions: belching & flatulence

Clinical pearl: supplement calcium alone low fat dietary intake

Obes Res. 2005 Jan; 13(1):191
J Clin Endocrinol Metab. 2000 Dec;85(12):4635-8
**Alli™ (Orlistat)**

**Mechanism of action:**
- Reversible inhibitor of pancreatic & gastric lipase

**Efficacy:**
- Drew B et al. 2007 meta-analysis review: patient with BMI 27 saw a significant reduction of weight loss ~ 5 % then diet alone
- FDA approve for long term weight loss (Rx)

**Adverse reactions:**
- HA, oily spotting, abdominal discomfort, gas, fecal urgency, steatorrhea & liver related events

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**Alli™ (Orlistat)**

**Dosage:**
- 60 mg tid with each meal that contains fat

**Drug Interactions:**
- Anticoagulants, amiodarone, levothyroxine, & vitamins

**Clinical pearls:**
- Take a MVI qd 2 hours before or after dose
- Due to risk of liver injury inform patient signs and symptoms
Diabetes

<table>
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<tr>
<th>Condition</th>
<th>Chromium</th>
<th>Oxygen</th>
<th>Iron</th>
<th>Magnesium</th>
</tr>
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<tbody>
<tr>
<td>Non-insulin dependent elderly patients in rehabilitation for stroke or hip fracture, N = 78</td>
<td>Chromium picolinate 200mg bid x 3 weeks</td>
<td></td>
<td></td>
<td></td>
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</table>

Results:
- Fasting blood glucose (190 mg/dL vs 150 mg/dL, p < 0.001)
- HbA1c (8.2% to 7.6%, p < 0.01)
- Total cholesterol (235 mg/dL to 213 mg/dL, p < 0.02)

**Chromium Picolinate Supplementation Attenuates Body Weight Gain and Increases Insulin Sensitivity in Subjects With Type 2 Diabetes**

**Design:** Type 2 DM patients, N=37
- At baseline: glipizide 5 mg/day with placebo for 3 months
- Randomized to either sulfonylurea plus placebo or sulfonylurea plus 1,000 mcg Cr for 6 months

**Results:**
- Fat-free mass (28.8, P < 0.05 vs. 15.9, P = 0.4)
- HbA1c (-1.16%, P < 0.005 vs. -0.4%, P = 0.3)
- Free fatty acids (-0.2 mmol/l, P < 0.001 vs. -0.12 mmol/l, P < 0.03)

_Chromium_  

**Mechanism of action:**
- Might reduce oxidative stress
- Low levels are associated with impaired glucose & insulin
- Chromium 0 has no activity
- Chromium III found in food and supplements
- Chromium VI used in welding industries & carcinogenic

**Adverse reactions:**
- HA, insomnia, irritability, mood changes & sleep disturbance
- Vomiting, diarrhea, & hemorrhage

**Dosage:**
- 200-1000 mcg divided doses
- About 0.4-2.5% is absorbed and rapidly excreted in the urine

**Chromium**

**Interactions:**
- **Herbs:** bilberry, brewer yeast, iron, Vit. C & zinc
- **Drugs:** insulin, levothyroxine, NSAIDs & corticosteroid
- **Disease:** diabetes

**Clinical pearls:**
- Several salt forms
  - Picolinate, nicotinate, polynicotinate and chloride
  - Chromium picolinate most often used in studies
- No reliable method to diagnose deficiency
Alpha-Lipoic Acid

Design: Modified frequently sampled intravenous glucose tolerance tests (FSIGTTs) before and after dose to evaluate insulin sensitivity and glucose effectiveness, N= 20

Dose: 600mg bid x 4 weeks

Results:
- Significant improvement in insulin resistance
- No lowering effects on HbA1c

Diabetes Care 22:280–287, 1999

Mechanism of action:
- Antioxidant activity that prevents oxidative damage
  - Endogenous form with pyrophosphatase produces ATP

Dosage: 600-1200 mg qd

Interactions:
- Herbs: garlic, ginseng & psyllium
- Drugs: antidiabetes & chemotherapy

Adverse reactions:
- Nausea and skin rash
- Thiamine deficiency
Vanadium

Mechanism of action: Activates insulin receptor proteins, stimulates glucose oxidation & transport
  - Liver: stimulates glycogen synthesis
  - Adipose: inhibits lipolysis
  - Skeletal muscle: promotes glucose uptake

Efficacy:
  - High doses of 100 mg qd may improve insulin sensitivity and possibly reduce blood glucose levels
  - Effective in Type 2 but not Type 1 diabetes

Adverse reactions:
  - GI upset, kidney toxicity, fatigue, lethargy & tongue discoloration

Dosage: 50 mg bid of the sulfate form

Interactions:
  - Herbs: garlic, ginger, ginkgo & ginseng
  - Drugs: anticoagulants & antiplatelets
  - Labs: blood glucose & serum creatinine
  - Disease: diabetes & renal dysfunction

Clinical pearls:
  - Average diet contains 6-18 mcg qd
  - Only 5% is absorbed
Coenzyme Q-10

Mechanism of action:
• Has antioxidant properties to stop damage and give energy to cells
• Cofactor in metabolic pathways

Efficacy:
• In combination with standard therapy might have some benefit in lowering BP

Adverse reactions: GI upset, heartburn, & appetite loss

Dosage:
• Isolated systolic HTN 60 mg bid
• HTN 60-100 mg bid
• Max daily dose of 300 mg daily
Coenzyme Q-10

**Interactions:**
- **Herbs:** Fish oil, stinging nettle, & red yeast rice
- **Drugs:** Antihypertensives & anticoagulants
- **Labs:** increase T4/T8 ratio in normal patients
- **Disease:** cigarette smoking may deplete body stores

**Clinical pearls:**
- Some medications can lower Co Q 10 levels
  
  E.g. statins, beta blockers, and diuretics

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**Pomegranate** *(Punica granatum)*

http://natureasmedicine.files.wordpress.com/2009/03/pomegranate400.jpg

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**Pomegranate Efficacy**

- **Juice 50 ml / qd x 1 year**
  - Systolic BP ↓ 5-21%
  - Diastolic BP no effects

- **Juice 240 ml / qd x 3 months**
  - No effects on either systolic or diastolic BP

*Am J Cardiol 2005;96:810-814*
Pomegranate

Mechanism of action: antioxidant activity
- Juice contains 0.2 - 1% polyphenols

Adverse reactions: rare
- Fruit has rarely caused angioedema

Interactions:
- Herbs: Coenzyme Q-10, fish oil & stinging nettle
- Drugs: Ace inhibitors

Dose: 50 mlqd

Conclusion

- Several OTC and supplement products have demonstrated possible efficacy in treatment of metabolic disease
- Evidence continues to evolve regarding legitimate CAM uses
- CAM therapies hold potential for drug/disease interactions
- Providers should include OTCs and supplements when obtaining a medication history and providing treatment recommendations
- Health professionals should learn where to find more information about OTCs and supplements
- "Do no harm" approach

References

References