Lecture 6: Supplements and Dieting

Critical Analysis of Popular Diets and Supplements

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Commercial Herbal Products and Weight Loss

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Magnitude of Use

- Potential audience: **24%** men, **38%** women are **trying to lose weight now**
- Use of herbal medicines in 1997: 5x 1990
- **<40%** of users tell their health care provider
- **$27 billion/yr** out-of-pocket cost (comparable to all traditional out-of-pocket expenditures)
- Minority, **~5-10%** is weight-loss related
Potential Risks of Herbal Supplements

- **Direct toxicity** (including allergic reactions)
- **Indirect toxicity** (e.g., heavy metal {Hg, As} contamination; bacterial contamination)
- **Inhibition of nutrient absorption** (competitively or via blockage of absorption)
- **Use in lieu of healthful dietary/behavior changes**
Indirect toxicity study (2002)

247 herbal products assayed

- 39 (16%) had high [heavy metals]
- 18 (7%) had significant bacterial contamination
Agents in alphabetical order…

Aromatherapy

- 2 published studies (Hirsch, 1992, 1994) show efficacy with 2-acetyl-pyridine,
  
  *but*...

  - same author
  - open, uncontrolled studies

- No plausible mechanism (save aversion therapy) for purported weight control effect
Agents in alphabetical order…

Bladderwrack

- *Fucus vesiculosis*
- No studies published
- May have thyroid-stimulating effect
Agents in alphabetical order…

Chitosan/Chitin

- **Chitin**: from shells of crabs, shrimp, lobster
- **Chitosan**: chitin-derived polymer of glucosamine
- **Binds fat in GIT, thus blocking fat absorption**
- **Studies:**
  - rodents lose weight
  - 5 studies in a single Italian J: mean 3.4kg loss vs placebo
  - 4 wk RCT (US): no weight loss/chol/TG change vs placebo
- **Mechanism is plausible, but probably ineffective at reasonable doses. May block fat-soluble vitamins.**
Agents in alphabetical order…

Chromium (picolinate)

- **Essential micronutrient**: CHO, lipid metabolism cofactor
- May enhance insulin sensitivity, decr plasma insulin
- **Deficiency of Cr**: raises glucose, insulin, cholesterol, TG
- **Studies**: most well-designed studies show no effect; a few do
- **FTC** recently concluded: insufficient evidence of any effect on weight, body composition, metabolic rate, appetite
- $100 million annual sales
Agents in alphabetical order…

Conjugated linoleic acid (CLA)

- Class of fatty acid found in meat and milk of ruminants
- Inhibits LPL (increases glycerol release, decreases fat deposition)
- Studies:
  - Animal: suggest anticancer and weight loss effects, esp. decreases weight gain with refeeding after loss
  - Human: 1 study- suggests a mild anabolic effect in body builders
  - No studies of safety, nor in obese individuals
Agents in alphabetical order…

**Dihydroepiandrosterone (DHEA)**

- Steroid hormone whose levels decline with aging
- Studies:
  - 10 non-obese males, 1 month RCT vs. placebo: decreased body fat, no decrease in weight (lean up)

*Safety concerns regarding androgenic effects*
Garcinia cambigia

- Rind of the brindell berry
- Contains a fruit acid, hydroxycitric acid (HCA)
- Found in many weight-loss products
- Found to increase hepatic glycogen synthesis, decrease food intake, decrease weight gain

- Studies:
  - 4/8 RCTs: significant weight loss, but 2/4 used multiple active agents concurrently
  - Lab study of adult males: no effect on metabolic rate or substrate oxidation

- Safety: no significant adverse effects reported yet
Agents in alphabetical order…

**Germander**

- Herb of the mint family used in Europe especially, in teas, mixtures
- No published efficacy data
- Known hepatic toxicity (hepatitis, jaundice)
- Banned in France
Agents in alphabetical order…

Ephedra/ Ephedrine- 1

- Can be derived from a plant whose name in Chinese is *Ma huang*
- Adrenergic stimulant found in many (most) OTC weight loss products
- Often combined with *caffeine/guarana*, another stimulant
- Studies: uncontrolled and RCTs suggest efficacy
- Safety: in doubt…
Efficacy data summary:

**Rand Report:**
Studies of up to 6 month duration show clinically significant weight loss of ~2 lbs/month over placebo.
Agents in alphabetical order…

Ephedra/ Ephedrine- 3

- **Safety:**
  - Many case reports of adverse effects, especially CV, CNS, likely related to elevation in BP, P
  - FDA proposed limiting use to low doses:
    - 8mg/serving
    - 24mg/day
    - 1 week recommended duration of use

Proposal withdrawn after objections
February 2000
Agents in alphabetical order…

Ephedra/ Ephedrine- 4

- **Safety- 2**
- **Case-control study (2003)**
  - Based on reports to the National Poison Control Center
  - Ephedra was associated with 64% of reported AEs for herbal OTC products
  - Ephedra accounts for 1% of sales of herbals
  - RR = 100- 770 c/w other herbs like ginko biloba and ginseng
  - Suggestive but not rigorous data: question of denominator and reporting bias, causation, dose
Agents in alphabetical order…

**B-OH-B-methyl butyrate (HMB)**

- metabolite of the essential AA leucine
- may supply a muscle cell repair precursor

**Studies:**
- Promotes slight increase in lean : fat
- Slight increase in strength in lean men, women, older adults
- Not tested yet in obese for weight loss

- No significant side effects yet reported
Agents in alphabetical order…

Psyllium

- Derived from leafy plantain seed (soluble fiber)
- Large literature on fiber and appetite
- Reduces energy density of the diet and thus promotes satiety
- Insoluble and soluble fiber, plant source as well as artificial

Studies:
- 17 lean women, Rx 20g 3hrs ac x 3d: increased fullness, decreased fat and calorie intake
- most studies in obese adults, including cross-over studies show superiority to diet-alone

Side effect: bloating; theoretical decrease absn
Agents in alphabetical order…

Teas

- **Source:** leaves of young shoots from tea plants
- **Epidemiology:** supports effect on cancer, CVD, lipids (tea users vs nonusers)
- **No described harm**
Agents in alphabetical order…

Teas

Processing tea leaves produces 3 kinds of teas:

- *Green*: produced by steaming (prevents oxidation)
- *Oolong*: produced by partial fermentation
- *Black*: produced by full fermentation
Tea’s Possible Active Ingredients

- Tannins/ polyphenols/ catechins (such as epigallocatechin gallate (EGCG)- inhibit lipid peroxidation, catchol-O-methyl-transferase, and fatty acid synthase)
- Caffeine- inhibits phosphodiesterases, thus may augment sympathetic (NE) thermogenesis
- Vitamin K (high levels in green tea only)
- Fluoride
- Theophyllines
Green Tea’s Effects

- **Antioxidant:** 200x the effect of Vitamin E mg/mg

- **Hypocholesterolemic effect:** inhibits intestinal cholesterol absorption and LPL oxidation

- **Anticancer effect:** inhibits urokinase, causes cancer cell apoptosis
Green Tea’s Weight Effects

Human Study*:

- Lean adults, weight maintenance diet, RC crossover (green tea, caffeine alone, placebo)
- Outcome measured- energy expenditure
- After 24 hours, green tea use raised 24 hr EE 3.5% vs placebo, 2.8% vs caffeine
- RQ significantly decreased on GT (fat ox up)
- 24 hr urinary NE up
- Heart rate unchanged

*Dullo et al Am J Clin Nutr 1999
Green Tea’s Weight Effects

- Animal studies:
  - Lean and obese rats- catechin EGCG caused 50-60% decrease in EI and acute weight loss
  - Effect only significant when given IP, not PO

- Mouse studies- 1. PO, 16 wk growth slowed (EI down, decreases in liver cholesterol, serum TG, FA)
  - 2. PO, 11 months: decreased EI 5.6%; beta oxidation of FAs in liver doubled
Green Tea’s Weight Effects

Summary:

Literature suggestive, but lack human weight loss studies

No known adverse effects

Contribution of caffeine to effect may be significant
Agents in alphabetical order…

**Oolong tea (Thea sinensis)**

- Traditional anti-obesity use
- Caffeine, theophylline contribute to effect
- Rats: inhibits pancreatic lipase and NE-induced lipolysis in adipose tissue
- No similar human studies
- No known harm
Recent and current studies:
1. Effect of ephedra on RMR and appetite

- 30 obese volunteers
- Ma huang-containing herbal supplement vs placebo
- Double-blind, cross-over design
- Results: RMR by IC up 50 kcal/d vs placebo (p=.05)
- Energy intake down by 250 kcal/d vs placebo (p<.05)
- Heart rate up 6 bpm vs placebo (p<.01)
Recent and current studies:
2. Efficacy and safety of long-term ephedra

- 52-week, parallel group RCT: ephedra-containing, ephedra-free, placebo supplements
- 50 volunteers per group
- Weight loss and weight maintenance phases
- Medically monitored
- Outcomes: safety, weight loss and maintenance, biochemical and other health parameters
- Ongoing blinded trial
Conclusions & Future Needs

- Arguably the only currently-available agents with proven efficacy, at least short-term, are ephedra, and fiber.
- Herbal agents must be recognized as drugs: natural products can be as toxic as synthetic.
- Unfortunately, it would be impractical and politically unlikely that all natural, orally-consumable ingredients could be subjected to the degree of scientific scrutiny now only pharmaceuticals undergo.
- Yet, increased power to regulate production, marketing and the post-marketing experience is clearly needed.