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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** (eg, 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 vesiculosus*
- 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 p**
- **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

Agents in alphabetical order...

Garcinia cambogia

- 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...



Agents in alphabetical order...

Ephedra/ Ephedrine- 2

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

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**