The Skinny Scoop on OTC Weight Loss Products

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Overview

- State of weight in the U.S.
- Non-prescription/herbal/supplement products for weight loss
Leanest State: Colorado
Fattest State: Mississippi

Percentage of Obese Adult Population
(3-year average from 2005–07 CDC Behavioral Risk Factor Surveillance System data)

United States of Obesity 2008

CalorieLab's
15.2% of adults (women 20.6%, men 9.7%) had used a weight-loss supplement

8.7% had used in past year (women 11.3%, men 6.0%)

Highest use was among women aged 18 to 34 years

1 in 10 (10.2%) reported ≥ 12 month use

Less frequent long-term use in women (7.7%) than men (15.0%)

73.8% used a supplement containing a stimulant including ephedra, caffeine, and/or bitter orange 

OTC Weight Loss Products

- Aggressively marketed - “Significant weight loss without adverse effects”
- Most have never been rigorously tested
- Possibly questionable content
What are Thermogenics?

- Thermogenesis - production of body heat through metabolism of fat
- May facilitate weight loss by increasing energy expenditure
- May occur centrally via stimulation of the sympathetic nervous system or peripherally by a mechanism without centrally mediated anorectic effects.
- Examples: ephedra, ephedrine, phenolpropanolamine, synephrine
Ephedrine/Ephedra

- Ephedra sinica (Ma Huang) and ephedra viridis (Mormon Tea, Brigham tea)
- Have been banned by FDA from dietary supplements for weight loss, muscle building, athletic performance since 2004
- Can still be bought on internet
- Sympathomimetic drug
  - Stimulates the release of norepinephrine to suppress appetite
  - Increases blood pressure and heart rate
Ephedrine/Ephedra - Efficacy

- Ma huang (90 mg/day ephedrine alkaloids) and kola nut (192 mg/day caffeine) vs placebo over 6 months in 167 subjects
  - > loss of weight & body fat, ↓ LDL, ↑ HDL
  - ↑ BP (3 mm Hg) and HR (4)

- Meta-analysis of trials
  - modest short-term weight loss
  - ~ 2 lbs/month more than placebo

Ephedrine/Ephedra - Adverse effects

- Tremor, dizziness, insomnia, nervousness, headache
- Tachycardia, increased blood pressure and heart rate, palpitations
- Anxiety, sweating
- Kidney stones
- Hemorrhagic stroke, myocardial infarction, and death
- Potential for dependence
Bitter Orange (Citrus aurantium)

- Also known as sour orange, Seville orange, zhi shi, and 6',7'-dihydroxybergamottin
- Marketed as a “safe” alternative to ephedra
- Example products: Solaray Bitter Orange extract, Thermosculpt, Ripped Fuel
- Contains synephrine with effects similar to ephedra
Bitter Orange

6-week study in 23 patients (BMI >25)

- Bitter orange 975 mg plus caffeine 528 mg plus St. John's Wort 900 mg daily; maltodextrin; and a control group that received no supplementation

- BO/caffeine/St John’s Wort group lost 3 lbs and 2.9% body fat

- No significant AE

Bitter Orange Adverse Effects

- Increase in blood pressure and heart rate
- Phototoxicity
- Case reports
  - Ischemic colitis
  - Angina
  - MI

Bitter Orange - Potential Interactions

- C. aurantium contains 6',7'-dihydroxybergamottin and bergapten inhibit cytochrome P450-3A (CYP3A), and would be expected to increase serum levels of many drugs.

- Examples: HIV protease inhibitors (ritonavir, indinavir, saquinavir, nelfinavir), nonsedating antihistamines, antidepressants (TCA, nefazodone, sertraline, venlafaxine), verapamil, glyburide
Contraindications

Heart disease, Hypertension, hyperthyroidism, prostatic hypertrophy, diabetes, pregnancy and lactation, anxiety disorders, and glaucoma
Bitter Bottom Line

- Synephrine has lipolytic effects in human fat cells only at high doses

- Little evidence that products containing C. aurantium are an effective aid to weight loss
Hoodia

- Succulent plant (13 species, including Hoodia gordonii)
- Rare, protected by national conservation laws in South Africa and Namibia - has to be grown/collected with a permit
- Proposed mechanism of action is suppression of the appetite center in the hypothalamus
  - oxypregnane steroidal glycoside (P57)
Hoodia

- 2 unpublished studies
  - 18 obese subjects given “high” doses ate 1,000 fewer calories/day
  - 7 subjects over 28-days ingested 1000 mg of hoodia capsules per day - lost mean 3.3% of body weight, median weight loss 10 lbs

- Pfizer and Unilever discontinued clinical development of P57 - “Unwanted effects on liver”

- Phytopharm appears to still be pursuing

www.phytopharm.com  NY Times 26 Apr 2005
Hoodia

- Dose: ???? 3,000-4000 mg/day
- Consumerlab.com - no standard for assessing hoodia as an ingredient
- Reported to be fake - SlimTron, Pure Hoodia, Inc., Hoodonii
- Weakly inhibits CYP3A activity
- Adverse effects - unknown

Hoodia Bottom Line

- Most popular natural nonprescription weight loss aid currently marketed

- Unfortunately, there is little evidence in the medical literature to support recommending this agent

- Most products out there are probably substandard
Hydroxycitric Acid

- Garcinia cambogia - a fruit native to India
- Example products - Citrimax, Super Diet Max
- Hypothetical action - Assist thermogenesis by stimulating the conversion of dietary carbohydrates to glycogen instead of fat to boost energy, suppress appetite, and promote weight loss
Hydroxycitric Acid

- 12 week randomized, double-blind, placebo-controlled trial
  - 66 overweight subjects received 1500 mg of hydroxycitric acid per day, 69 received placebo
  - No significant difference in weight lost

- There are clinical trials which show a LACK of effectiveness in humans when used alone

- When studied in combination products, some trials have shown efficacy (unclear if it is then a necessary part of the mixture)

*JAMA* 1998;280:1596-1600.
Hydroxycitric Acid

- **Dosage:** 50 – 200 mcg/day (current products)

- **Adverse effects/ Contraindications/ Interactions** -- None known

- **Inadequate scientific support for use in weight loss**
Chitosan

- Example products
  - Chitosan, All Natural Marine Fiber (500 mg), Chitosan Plus (500 mg, hydroxycitiric acid 200 mg, chromium 500 mcg),
  - A dietary fiber derived from shellfish

- Hypothetical action
  - Blocks fat absorption
  - Marketed as alternative to orlistat

- Maker of Fat Trapper and Fat Trapper Plus - banned from marketing by FTC
Chitosan - Efficacy

- 15 trials (1219 subjects) - ~3.7 lb weight loss, no significant change in fecal fat

- 23 healthy volunteers received either 120 mg orlistat or 750 mg chitosan during a standardized meal containing 30-35 grams of fat

  - Measured fecal fat from 36 hours before meal to 100 hours after meal
  - Orlistat inhibited the ingestion of $42 \pm 10\%$ of dietary fat versus $4.5 \pm 3.4\%$ for chitosan

Cochrane Database of Systematic Reviews 2008, Issue 3 Art. No. CD003892
Chitosan - Dose

- Fat Trapper – 1,200 – 2,000 mg with 8 ounces of water just before a high fat meal

- Chitosan Plus – 1,000 mg half hour before two meals daily with 8 ounces of water

- Chitosan, All Natural Marine Fiber – 1,000 mg half hour before lunch and dinner with 8 ounces of water
Chitosan

- **Adverse effects**
  - None reported
  - Constipation possible

- **Contraindications**: Avoid if allergic to shellfish

- **Interactions**
  - Unknown
  - One product suggests taking fat soluble vitamin supplements at least 2 hrs before or after product
Chitosan Bottom Line

- Not a fat blocker
- Maybe a 3-4 lb weight loss
Caffeine

- Examples: Guarana, Paullinia cupana, Brazilian cocoa, Kola nut, Yerbe Mate, green tea extract

- Action: Stimulating effect due to caffeine, theophylline and theobromine suppresses appetite

- Efficacy: Effective for short term mild weight loss in combination with ephedra in small studies
Caffeine

- **Dosage:** Quantities up to 400 mg caffeine per day (7 to 11 gm of guarana) spread throughout the day are toxicologically harmless to a healthy adult habituated to caffeine.

- **Adverse effects**
  - Nervousness, insomnia
  - Tachycardia
  - Increased blood pressure
  - Excessive diuresis
Caffeine

- **Contraindications:** Patients with sensitive cardiovascular systems, cardiovascular disease, renal disease, and hyperthyroidism should avoid use.

- **Examples:**
  - Ripped Fuel - “daily dose” contains equivalent of 14.5 cans of cola (~580 mg, + synephrine)
  - Xenadrine-EFX - 448 mg/day
  - Zantrex-3 - 1223 mg/day (30 cans of cola)
Green Tea Extract

- **Action**: Increases 24 hour energy expenditure by inhibiting the enzyme that causes the breakdown of norepinephrine, thus causing an increase in metabolic rate. Shown to increase the rate of brown fat metabolism.

- Antioxidant polyphenols, particularly epigallocatechin gallate, appear to be responsible for thermogenic effect.

- Also contains caffeine and theophylline (~8% methylxanthines).
Green Tea Extract

- **Efficacy**
  - Available human studies show a small increase in energy expenditure (~4%)
  - No weight loss in very small studies
  - Mild diuretic effect of caffeine

- No known harm from moderate intake

- Need to consider caffeine content
Green Tea Extract

- Dose: 90 mg tid

- Product that has best been studied is an alcohol extract of dried green tea leaves containing 8.35% caffeine and 24.7% catechins (epigallocatechin gallate, epicatechin gallate, epigallocatechin, epicatechin, gallocatechin, catechin)
Green Tea Extract

- In choosing a product, look for one which lists total catechin content

- Consumerlab.com testing
  - Nature’s Bounty, Life Extension Mega, and Puritan's Pride Green Tea extract
  - Significant lead content - Futurebiotics, Herbal Select
  - Less than labeled content - Food Science of Vermont
Chromium Picolinate or Nicotinate

- Example products
  - Ultra Chromium (800 mcg), GTF Chromium Polynicotinate (200 mcg)

- Chromium is a metallic element found in mushrooms, broccoli, potatoes, beer, brewer’s yeast, brown rice, and whole grains - Picolinate and nicotinate salts are used to improve the bioavailability of chromium
Chromium

Hypothetical action:

- Essential trace mineral that facilitates the cellular use of insulin and uptake of glucose and amino acids, enhances protein synthesis and the function of certain enzyme systems, and decreases levels of total cholesterol and triglycerides

- The underlying premise of chromium’s efficacy may be related to glucose tolerance factor (GTF).
Chromium

Efficacy

- Increases in body fat loss over 4 weeks when given in combination with inulin, capsicum, L-phenylalanine and other unnamed lipotropic nutrients (combined with diet and exercise)

- No effect of 200 mcg/day combined with 100 mg caffeine, 20 g soluble fiber and a low calorie diet over 16 months

- No effect from 400 mcg in addition to 30 minutes 3x/week of supervised physical exercise

- 1 study found modest weight loss

Chromium

- **Dosage**
  - No recommended dietary intake (RDI)
  - 50 – 200 mcg/day (National Research Council of the National Academy of Sciences)
  - Toxic dose - ≥ 600 mcg/day

- **Interactions** - Zinc may decrease chromium absorption
Chromium

- **Adverse Effects**
  - Hypoglycemia, rash, lightheadedness
  - Potential for chromium toxicity – nephrotoxicity, anemia, thrombocytopenia, hemolysis, hepatic dysfunction

- **Contraindications**
  - Avoid use in patients with renal dysfunction
Chromium Testing

- **Substandard products**
  - Trimspa X32 (42% more than labeled), EZ-Trim (25% less)
  - Trimspa X32 and Life Extension Chromium 200 mcg caps - high levels of hexavalent chromium

- **Passed products** - MegaFood GTF, New Chapter GTF, Nutrilite Chrompic Extra

www.consumerlab.com
Chromium Bottom Line

“Chromium is only a small part of the puzzle in the control of weight loss and body composition, and its effects, if present, will be small compared with those of exercise and a well-balanced diet”

Conjugated Linoleic Acid (CLA)

- Class of polyunsaturated fatty acids found in milk and red meat
- Example products: Tonalin CLA, Nature Made conjugated linoleic acid, CLA Fuel, Claranol

- Hypothetical action
  - Speculated it may help block fat cells from filling up with fat
  - Increases the ratio of muscle to fat
Conjugated Linoleic Acid

- One study of 71 obese individuals on reduced calorie diet and moderate exercise
  - 1 gm with each meal
  - Did not contribute to weight loss
  - Half-way through the study diet/exercise was discontinued in ½ of patients - patients taking CLA gained muscle and not fat when they began regaining weight
  - No adverse effects seen in study

- 1 yr of 3.4 g CLA/day
  - Did not prevent fat regain

Am J Clin Nutr 2006;83:606-12.
Conjugated Linoleic Acid

- Non-dieting obese patients
  - CLA 3.4 g or 6.8 g per day over 12 weeks
  - Subjects lost average of 3 lbs of body fat tissue

- 54 overweight subjects
  - CLA 1.8 g or 3.5 g/day vs placebo
  - CLA groups lost 6.9 ± 1.7% of body weight

*J Nutr* 2000;130:2943-2948.
Conjugated Linoleic Acid

118 obese subjects

- 3.4 g/day CLA vs placebo x 6 months
- Significantly reduced BMI and waist to hip ratio at 3 and 6 months
- Lean body mass increased in CLA group
- Most fat was lost from legs and in women

Conjugated Linoleic Acid

180 overweight/obese subjects

- CLA-triacylglcerol 4.5 g/day, CLA-free fatty acids 4.5 g/day, vs placebo x 1 year
- Decreased fat body mass (8.7 ± 9.1% & 6.9 ± 9.1%) compared to placebo
- CLA-TAG increased lean body mass
- ↑ LDL-C and Lpₐ, ↓ HDL-C
Conjugated Linoleic Acid

- Animal evidence - CLA isomer trans-10, cis-12 induces weight loss but may produce liver hypertrophy and insulin resistance via a redistribution of fat deposition that resembles lipodystrophy.

- Major dietary source (dairy products) - more than 90% cis-9,trans-11 CLA isomer.

- Commercial CLA preparations contain trans-10,cis-12 and cis-9,trans-11 CLA isomers in diverse proportions.
Conjugated Linoleic Acid

- **Dose** - ? 3 - 6 g/day

- **Adverse effects**
  - GI upset

- **Interactions/Contraindications**
  - Unknown at this time
CLA Testing

- Substandard - Allmax Nutrition CLA (75% of label)
- Passed - GNC Pro Performance, Metagenics Ultra, Natrol Tonalin, Tonalin, Natural Max Ultra Supertone, Nature’s Sunshine, Nutrilite, Ultimate Nutrition Patented CLA Pure, Vitamin World,

www.consumerlab.com
CLA Bottom Line

- May be beneficial but which isomer?
- Potential risks of liver hypertrophy & increased cholesterol
- Consume more low fat dairy products
Others

- Pyruvate - Small studies suggestive of efficacy in preventing weight gain
- Calcium - Increased intake of dairy products but not supplements is associated with greater weight loss when dieting
Nonprescription Combination Products

Laxatives

- Examples – cascara sagrada, senna, aloe
- Do not promote loss of body fat or lean tissue
- Adverse effects
  - Dehydration
  - Electrolyte disturbances
  - Laxative dependence
- Cannot be recommended for weight loss
Nonprescription Combination Products

**Diuretics**

- Examples – goldenseal, nettle leaf, buchu, uva ursi, cranberry juniper berries, couch grass, parsley, dandelion
- Result in water weight loss
- Do not promote loss of body fat or lean tissue

- Adverse effects
  - Dehydration
  - Hypokalemia
- Cannot be recommended for weight loss
Nonprescription Combination Products

Dietary fiber

- Guar gum, guar, guar flour, jaguar gum, glucomannan, psyllium
- Potential for esophageal or intestinal obstruction
- May help with feeling of fullness but studies of dietary fiber alone show no effect on weight loss
Orlistat OTC (Alli)
Orlistat - Mechanism of Action

Intestinal lumen

Orlistat

Pancreatic Lipase

TG

FA

Bile acids

Micelle

Mucosal cell

MG

FA

MG

Bile acids

Micelle
Orlistat 60 mg tid

16 wk trial, 391 overweight subjects

- Greater weight loss in orlistat group vs. placebo (6.7 lbs vs 4.2 lbs; p < 0.001, includes dropouts)
- Even more weight loss in those who stuck with orlistat for 16 wks (~ 4.8% of starting weight)
- Reduced blood pressure and lipids (TC & LDL-C)

Orlistat - Efficacy

- Majority of weight loss is in first year
- Patients who continue beyond 1 year regain some weight during 2nd year of treatment but not as much as placebo (3 lbs versus 5.5 lbs)
- OTC dose - ~5% weight loss in 16 weeks
Orlistat – Administration

- Dosage: 60 mg tid (Rx dose is 120 mg)
- Take with each main meal or up to 1 hour afterward
- If meal is missed or contains no fat, skip dose
- Combine with a reduced-calorie diet containing 30% fat or less
- No more than 15 g fat/meal
Advise patients to take a daily multivitamin containing fat soluble vitamins to avoid deficiencies

- A, D, K, and E
- ≥ 2 hours after orlistat or at bedtime
Orlistat Adverse Effects

- Oily stool, increased defecation, oily spotting, fecal urgency, and fecal incontinence

- Management
  - Adhere to < 30% fat in diet
  - Distribute fat intake throughout the day
  - Increase fiber intake - psyllium 6 gm/day, fiber bars, etc
Orlistat – Interactions

- Warfarin – potential for vitamin K levels to decline, monitor INR

- Cyclosporine – potential for decrease in cyclosporine level, avoid the combination

- Contraindicated in patients with chronic malabsorption syndrome or cholestasis
Recent FDA Warnings

72 weight loss products containing undeclared active pharmaceutical ingredients

- sibutramine, rimonabant, phenytoin, phenolphthalein, fluoxetine, furosemide, bumetanide

- Complete list is available at www.fda.gov/bbs/topics/news/2009/new01977.html
Hydroxycut Warnings

- 5-1-2009, FDA warned consumers to stop using all Hydroxycut products
- Cases of serious liver damage and rhabdomyolysis
- Unknown which ingredient is the problem
KEY POINTS

- Only effective OTC is Orlistat (Alli)
- CLA, green tea extract, chromium, and pyruvate - may be modestly effective but need more study
- Only modest weight loss with any
- Obesity treatment guidelines do not recommend herbals or supplements
- Issues with quality and content of some OTC weight loss products