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Dietary Supplements for Improving Body Composition and Reducing Body Weight: Where Is the Evidence?

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Weight-loss supplements typically fall into 1 of 4 categories depending on their hypothesized mechanism of action: products that block the absorption of fat or carbohydrate, stimulants that increase thermogenesis, products that change metabolism and improve body composition, and products that suppress appetite or give a sense of fullness. Each category is reviewed, and an overview of the current science related to their effectiveness is presented. While some weight-loss supplements produce modest effects (<2 kg weight loss), many have either no or few randomized clinical trials examining their effectiveness. A number of factors confound research results associated with the efficacy of weight-loss supplements, such as small sample sizes, short intervention periods, little or no follow-up, and whether the supplement is given in combination with an energy-restricted diet or increased exercise expenditure. There is no strong research evidence indicating that a specific supplement will produce significant weight loss (>2 kg), especially in the long term. Some foods or supplements such as green tea, fiber, and calcium supplements or dairy products may complement a healthy lifestyle to produce small weight losses or prevent weight gain over time. Weight-loss supplements containing metabolic stimulants (e.g., caffeine, ephedra, synephrine) are most likely to produce adverse side effects and should be avoided.

Keywords: stimulants, starch blockers, fat blockers, exercise, appetite suppressants

The growing obesity problem in the United States and other developed countries has dramatically increased the sales of supplements aimed at reducing weight and improving body composition. In 2008, ~34% of overweight or obese individuals in the United States reported using a dietary weight-loss supplement (Pillitteri et al., 2008); furthermore, in 2010 U.S. consumers spent over $2.4 billion on dietary supplements and meal replacements aimed at weight loss ("2011 Sport Nutrition," 2011). Consumers want a quick way to reach their weight goals, regardless of the scientific evidence concerning efficacy and safety. Currently, the U.S. Food and Drug Administration (FDA) does not evaluate the safety and efficacy of weight-loss supplements before they appear in the market (FDA, 2004). In addition, some over-the-counter weight-loss supplements contain pharmaceutically active ingredients, such as anabolic steroids or β-2 agonists, that are illegal without a prescription and prohibited in sports (Parr, Koehler, Geyer, Guddat, & Schänzer, 2008).

Weight-loss supplements typically fall into one of four categories depending on their hypothesized mechanism for reducing weight or changing body composition: products that block the absorption of fat or carbohydrate, thus decreasing the amount of energy absorbed from food; stimulants that increase metabolism; products hypothesized to alter nutrient partitioning, thus changing body composition by decreasing body fat while increasing lean tissue; and products that suppress appetite or increase satiety so that less energy is consumed. This review briefly covers each category, discussing mechanisms, efficacy, and safety issues. Many weight-loss supplements combine multiple ingredients from these categories into one product, which makes testing for efficacy and safety difficult.

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Absorption Blockers: Carbohydrate and Fat Blockers

One way to reduce energy intake and produce weight loss is to block the absorption of energy-containing macronutrients, especially carbohydrate or fat. Products intended to decrease macronutrient absorption use different mechanisms; however, the outcome is the same—the reduction of absorbed energy. Table 1 provides a summary of the supplements that are purported to achieve such results.

Carbohydrate or Starch Blockers

Carbohydrate or starch blockers are prevalent in the marketplace, with the most common product being an α-amylase inhibitor, *Phaseolus vulgaris,* extracted from white kidney beans. Only two randomized clinical trials (RCTs) report the acute use of *P. vulgaris* in humans. One 30-day study reported significant weight and fat loss in

Table 1 Weight-Loss Supplements With Hypothesized Mechanisms Involving Blocking Macronutrient Absorption

Supplement	Proposed mechanisms or use	Current level of evidence	Scientific findings	Potential side effects and safety issues	Current status
Phaseolus vulgaris	α-amylase inhibitor: reduces or prevents carbohydrate digestion and absorption.	Two 4-wk RCTs of efficacy in overweight subjects with equivocal results.	When added to an energy-controlled diet, 1 RCT reports increased fat loss (~2.5 kg) vs. placebo (Celleno et al., 2007). When added to a multicomponent weight-loss program, 1 RCT found no effect (~0.5 kg; Udani & Singh, 2007).	GI upset, bloating, and gas. No toxicity, based on animal studies (Chokshi, 2006).	Little research to support the efficacy of this product. More research is needed before a making a recommendation.
Chitosan	Fat binder: hypothesized to bind 4–6 g fat per gram of chitosan.	Extensively studied and subjected to meta-analyses (Cochrane reviews; Jull et al., 2008; Mhurchu et al., 2005b).	Cochrane review findings: Chitosan achieves a small but significantly great weight loss (~1.7 kg) vs. placebo; however, studies were suboptimal in design.	Generally regarded as safe. Can cause GI distress and flatulence. Symptoms depend on dose. Individuals allergic to shell fish should avoid chitosan.	Supportive evidence is minimal. Chitosan is unlikely to produce clinically significant weight loss.

Note. GI = gastrointestinal; RCT = randomized, double-blind, placebo-controlled clinical trial.

60 overweight men and women randomly assigned to the treatment (445 mg/day of Phase 2 starch neutralizer [Pharmachem Laboratories, Inc., Kearny, NJ] containing *P. vulgaris* extract) compared with the placebo group (Celleno, Tolaini, D'Amore, Perricone, & Preuss, 2007). The treatment group lost 2.93 kg (2.4 kg fat), while the placebo group lost 0.35 kg (0.16 kg fat). All subjects consumed 2,000–2,200 kcal/day under the supervision of a nutritionist and took the supplement before the high-carbohydrate main meal of the day. Conversely, a 30-day multicomponent weight-loss study found no differences in mean weight loss (treatment 2.7 kg vs. placebo 2.1 kg) or reductions in waist circumference (treatment 5.6 cm vs. placebo 5.3 cm) in overweight individuals randomly assigned to either *P. vulgaris* extract (1,000 mg/day, twice a day) or a placebo (Udani & Singh, 2007). No negative side effects were reported in these studies or in animal toxicity reports (Chokshi, 2006). Starch blockers are also being marketed for glycemic control; however, the data on them are still preliminary (Barrett & Udani, 2011).

Fat Blockers

Fat blockers are hypothesized to decrease the amount of fat absorbed. Chitosan, the major ingredient in most fat blockers, is a cellulose-type polysaccharide extracted from the exoskeletons of marine crustaceans (Ormrod, Holmes, & Miller, 1998) and hypothesized to bind 4–6 g of dietary fat per gram. One study measured the fat-trapping ability of chitosan (2.5 g/day) in an 8-day controlled-feed study (4-day control, 4-day treatment) in college-age men and women (Gades & Stern, 2005). They found that chitosan supplementation produced little increase in fat excretion: 1.8 g/day (16 kcal/day) in men and 0.0 g/day in women.

Unlike starch blockers, chitosan has been extensively studied as a weight-loss aid. Three recent meta-analyses reviewed its efficacy for weight loss from double-blind RCTs. They concluded that there is limited evidence that chitosan produces a clinically significant reduction in body weight in humans (Jull, Ni Mhurchu, Bennett, Dunshea-Mooij, & Rodgers, 2008; Mhurchu, Dunshea-Mooij, Bennett, & Rodgers, 2005a; Mhurchu, Dunshea-Mooij, Bennett, & Rodgers, 2005b). The Cochrane review by Mhurchu et al. (2005b) summarizes the results from 14 RCTs (n = 1,131; mean = 8.6 weeks) that provided 0.24–15 g/day (mean 3.7 g/day) of chitosan. They found that chitosan supplementation produced a greater average weight loss (1.7 kg) than in the placebo group. When the analysis was limited to trials that used chitosan alone (n = 7), however, the weight loss was reduced to 0.88 kg. The Cochrane group repeated this meta-analysis in 2008 (Jull et al., 2008), when they identified 15 RCTs (n = 1,219, ≥4 weeks) examining the effect of chitosan to decrease body weight in overweight or obese adults. As with the earlier review, they found that chitosan resulted in a significantly greater weight loss (1.7 kg) than in the placebo group but concluded that most studies were suboptimal because of short duration and small sample sizes. When they examined studies lasting longer than 4 weeks (n = 7), the additional weight loss attributed to chitosan averaged 0.8 kg. Thus, the evidence that chitosan will result in clinically significant weight loss is minimal. Finally, research suggests that chitosan may reduce weight gain over time. Kaats, Michalek, and Preuss (2006) found that chitosan (3 g/day) fed to overweight, free-living adults (n = 134) resulted in 2.8 kg of weight lost over 60 days

compared with a placebo group that gained weight (0.8 kg). In summary, chitosan has limited ability to block fat, produce the weight loss desired by most overweight individuals, and may help prevent weight gain. Table 1 lists the side effects of chitosan.

Stimulants: Increase Metabolism

Stimulants are the most popular ingredient added to weight-loss and performance-enhancing products (Dhar et al., 2005; Sharpe, Granner, Conway, Ainsworth, & Dobre, 2006). Substances that generally fit into this category are shown in Table 2. Theoretically, stimulants bring about weight loss by increasing metabolism to increase the total amount of energy expended or by decreasing appetite (Hursel & Westerterp-Plantenga, 2010). Stimulants may also help maintain weight loss by keeping metabolic rate elevated.

The most common stimulants used in weight-loss supplements are ephedra (ma huang), caffeine, green tea, guarana, and bitter orange (Sharpe et al., 2006). Recognizing the stimulant in a weight-loss product can be difficult, because there are over 40 different species of ephedra alone and hundreds of other plants that contain stimulants (Mayo Clinic, 2008). Weight-loss products frequently contain one or more of these stimulants or are combined with other weight-loss substances such as diuretics. Combining multiple stimulants in one product can lead to dangerous side effects, depending on the amount and combination used (Andraws, Chawla, & Brown, 2005; Dhar et al., 2005; FDA, 2004). Finally, many stimulants are banned in sport. Athletes who compete under antidoping codes should check the information provided by their relevant governing bodies on prohibited substances, including information provided by the World Anti-Doping Agency (http://www.wada-ama.org). Of course it must be recognized that some supplements contain prohibited stimulants as contaminants or undeclared ingredients, meaning that athletes may not be able to identify these ingredients. Therefore, athletes may not be aware that they cannot prevent ingesting a prohibited substance simply from reading supplement labels. In fact, weight-loss products have been identified as supplements that are at high risk of being contaminated and a source of inadvertent doping outcomes in sport (Geyer et al., 2008).

Caffeine

Caffeine can potentially contribute to weight loss or prevent weight gain through increasing thermogenesis by inhibiting the breakdown of cAMP (Diepvens, Westerterp, & Westerterp-Plantenga, 2007) or increasing fat oxidation through sympathetic activation of the central nervous system (Diepvens et al., 2007; Hursel & Westerterp-Plantenga, 2010). The metabolic effects of caffeine depend on the dose and can act synergistically with ephedrine/ephedra or nicotine. For example, 100 mg of caffeine increases resting metabolic rate (RMR) by 3–4% over 150 min (Dulloo, Geissler, Horton, Collins, & Miller, 1989), and 200 mg increases RMR by 5–8% over 3 hr (Collins, Cornelius, Vogel, Walker, & Stamford, 1994). When caffeine (100 mg) is combined with nicotine (1 mg), RMR increases by 8.5% over a 3-hr period (Jessen, Toubro, & Astrup, 2003). It should be noted that these doses can easily be found in everyday use: One cigarette contains ~1.9 mg of nicotine (Connolly, Alpert, Wayne, & Koh, 2007), while one cup of Starbucks Americano coffee (8 fl oz, 0.25 L) contains ~112 mg of caffeine (Pennington & Spungen, 2010). RMR increased to 9.8% over a 3-hr period when 2 mg of nicotine were combined with 100 mg of caffeine.

Although caffeine increases thermogenesis acutely, there are limited data supporting caffeine for long-term weight maintenance. Only one study reports that caffeine alone significantly reduced weight gain in individuals who increased their caffeine consumption compared with individuals who decreased caffeine intake over a 12-year period (Lopez-Garcia et al., 2006). Lack of research supporting the effectiveness of caffeine for long-term weight regulation is most likely a result of the development of caffeine tolerance (Diepvens, Kovacs, Nijs, Vogels, & Westerterp-Plantenga, 2005; Hursel & Westerterp-Plantenga, 2010).

Ephedra

Ephedra, a central nervous system stimulant, is a generic term for several species of plants containing ephedrine and similar alkaloid compounds (Andraws et al., 2005; MayoClinic, 2008). Ephedra increases the release of norepinephrine and epinephrine and stimulates α- and β-adrenergic receptors (Diepvens et al., 2005). These metabolic changes provide a quick energy boost by increasing thermogenesis, heart rate, blood pressure, and alertness. For weight loss, ephedra is marketed to increase metabolism and suppress appetite, while for athletic performance, it is marketed to increase mental sharpness and performance (Dhar et al., 2005).

Between the years 1993 and 2002, researchers reported a 10-fold increase in the number of ephedra reports to poison centers and calculated the hazard rate (total moderate and major outcomes + deaths/total number of exposures) to be ~2.5 times higher than other nonephedra botanicals (Woolf, Watson, Smolinske, & Litovitz, 2005; see Table 2). These adverse events led the FDA to ban ephedrine alkaloids in 2004 (FDA, 2006), which prompted supplement manufacturers to substitute botanical extracts of the ephedra plant (*Ephedra sinica* or ma huang), which were not banned. Although ephedrine alkaloids are banned by some countries and sport-governing organizations, consumers can buy ephedra on the Internet from countries where the products are legal. There are no standards or laws regulating supplement manufacturers, so illegal substances such as ephedra or other drugs only intended for prescription use can be added to supplements without consumers' knowledge. In-depth reviews of ephedra, including health risks, have been published by others (Abourashed, El-Alfy, Khan,

Table 2 Weight-Loss Supplements With Hypothesized Mechanisms Involving Stimulating Metabolism

Supplement	Proposed mechanisms or use	Current level of evidence	Scientific findings	Potential side effects and safety issues	Current status
Caffeine	Increases thermogenesis by inhibiting degradation of cAMP (Diepvens et al., 2007). Effects can be potentiated with ephedra or nicotine.	Extensively studied and reviewed in combination with ephedra and GT (Diepvens et al., 2007; Westerterp-Plantenga, 2010).	Caffeine increases metabolic rate in the short term. Chronic use produces tolerance. Small effect when combined with ephedra.	High intakes (≥300 mg/day) can result in insomnia, irritability, heart palpitations, and anxiety.	Little research to support the efficacy of this product for long-term weight loss or maintenance.
Ephedra or ephedrine alkaloids	CNS stimulant that increases release of NE and epinephrine and stimulates the α- and β-adrenergic receptors. May aid in weight loss through increased metabolism and appetite suppression.	Extensively reviewed (Coffey et al., 2004; Diepvens et al., 2007) and subjected to meta-analyses (Shekelle et al., 2003).	Effective when combined with caffeine, but effect is only a small increase in weight loss (~1 kg/month; Shekelle et al., 2003).	HTN, stroke, serious heart problems. In 2004, the FDA banned ephedrine alkaloids because of adverse effects.	Still available in the market. Many manufacturers have replaced ephedra with other stimulants such as bitter orange.
GT or GT extract	Active ingredients are caffeine and catechins, especially EGCG. May increase thermogenesis, reduce lipogenesis, and decrease fat absorption or increase fat oxidation.	Extensively studied, reviewed (Cabrera et al., 2006; Diepvens et al., 2007; Westerterp-Plantenga, 2010), and subjected to meta-analyses (Hursel et al., 2009; Phung et al., 2010).	EGCG-caffeine mixture results in ~1.3–1.4 kg more weight loss vs. controls, but habitual caffeine use decreased effect (~0.27 kg). Whites show less of an effect than Asians (Hursel et al., 2009; Phung et al., 2010). Mixture of EGCG + caffeine appears to be necessary to see an effect.	Generally regarded as safe if taken as tea. GT extracts have been associated with liver damage, especially if ingested on an empty stomach (Sarma et al., 2008).	May have small effect on weight loss (<2 kg).
Guarana	Caffeine content twice that of coffee beans. See caffeine.	None.	None.	Increased HTN, HR, anxiety, and irritability.	No documented effectiveness for weight loss.
Yerba mate	See caffeine.	None.	None.	Adverse effects because of caffeine. Hot mate drinks may increase esophageal cancer risk.	No documented effectiveness for weight loss. Consumed in South America similar to coffee.
Seville, or citrus aurantium (bitter orange)	Contains synephrine alkaloids, which are structurally similar to epinephrine, and may increase metabolism and have lipolytic properties.	One RCT documenting effectiveness (~2.6 kg more than placebo, 12 weeks; Dallas et al., 2008).	Few well-designed studies examining weight loss that used only bitter orange. Most weight-loss supplements combine bitter orange with other compounds.	Increased HR, HTN, angina, ischemic colitis, and seizures.	Evidence does not support bitter orange as an effective weight-loss supplement. Well-designed studies are needed.
Yohimbe, extracted from yohimbe bark	Antagonist of the central α-2-receptors, which has stimulatory effects by increasing the release of NE (Giampreti et al., 2009).	None.	None.	GI distress, increased HR, HTN, anxiety, and agitation (Haller et al., 2008; Kearney et al., 2010). Giampreti et al. (2009) describe severe acute neurotoxic effects of a 5-g dose on a bodybuilder.	Evidence does not support yohimbe as an effective weight-loss supplement.

Note. ConsumerLab.com used as a resource for some safety issues related to supplements. GT = green tea; CNS = central nervous system; NE = norepinephrine; HTN = hypertension; FDA = Food and Drug Administration; EGCG = epigallocatechin gallate; HR = heart rate; RCT = randomized, double-blind, placebo-controlled clinical trial; GI = gastrointestinal.

& Walker, 2003; Andraws et al., 2005; Haller, Benowitz, & Jacob, 2005; Shekelle et al., 2003; Soni, Carabin, Griffiths, & Burdock, 2004).

Numerous studies have examined the effect of ephedra on weight loss. A meta-analysis concluded that ephedrine/ephedra helps with short-term weight loss (~0.6–1.0 kg/month) but stresses the cardiovascular system and raises blood pressure (Shekelle et al., 2003). Ephedra is also used by athletes and active individuals to help with weight loss and improve sport performance (Bents & Marsh, 2006; Dhar et al., 2005; Hespel, Maughan, & Greenhaff, 2006; Shekelle et al., 2003). Unfortunately, the consequences can be deadly. To date, three deaths in college and professional sports have been attributed, at least in part, to ephedra (Keisler & Hosey, 2005), including the death of a U.S. Major League Baseball pitcher in 2003 (Mihoces, 2003). Adolescent athletes use ephedrine as a quick way to increase athletic ability and decrease body fat (Dorsch & Bell, 2005) and are the least concerned with safety and health issues. Bents and Marsh found that 49% of the athletes in an American college hockey conference had used ephedra at least once to improve performance, and 20% had used pseudoephedrine in the last 30 days. At the time of the study, 55% of the athletes knew ephedra was banned by the FDA and by most amateur and professional sporting leagues.

Ephedra + Caffeine

The combined effects of ephedra and caffeine produce significant cardiovascular, metabolic, and hormonal responses that are greater than observed when each is taken separately (Diepvens et al., 2007). These synergistic effects are the reason caffeine and ephedra are frequently combined in weight-loss supplements (Coffey, Steiner, Baker, & Allison, 2004). Two double-blind RCTs lasting 6–9 months reported greater weight loss (~3–5 kg) and fat loss (~1.5–4.3 kg) with ephedrine alkaloids (40–90 mg/day) and caffeine (100–192 mg/day) versus a placebo in overweight or obese individuals (Boozer et al., 2002; Hackman et al., 2006). However, both treatment groups reported adverse events. Boozer et al. reported significant increases in blood pressure and heart rate over controls, while Hackman et al. reported minor issues (e.g., dry mouth, nervousness, and palpitations). Similar metabolic effects are reported in healthy, young, normal-weight adults using equivalent doses of caffeine and ephedra (Vukovich, Schoorman, Heilman, Jacob, & Benowitz, 2005).

In the United States, combining caffeine and ephedrine for weight loss is not practical because of the FDA ban on ephedra alkaloids and the adverse negative side effects (Dhar et al., 2005; Haller, Meier, & Olson, 2005; Soni et al., 2004).

Green Tea

Green tea, frequently in the form of green tea extracts, is a commonly used dietary supplement in the United States (Sharpe et al., 2006). Caffeine and catechins are considered the two active substances in green tea associated with weight loss. Catechins are polyphenols with antioxidant and anti-inflammatory properties (Basu & Lucas, 2007). Green tea has several hypothesized biological mechanisms whereby it may help reduce obesity, including reduced adipocyte lipogenesis, decreased fat absorption, increased fat oxidation, and increased thermogenesis (Wolfram, Wang, & Thielecke, 2006). Epigallocatechin gallate, or EGCG, a primary catechin in tea, inhibits catechol-o-methyl-transferase and thus prolongs the action of norepinephrine (Westerterp-Plantenga, 2010). In this way, caffeine and green tea catechins may work synergistically to increase thermogenesis (Cabrera, Artacho, & Giménez, 2006; Hursel & Westerterp-Plantenga, 2010; Shixian, VanCrey, Shi, Kakuda, & Jiang, 2006; Westerterp-Plantenga, 2010). Numerous studies have documented the increase in thermogenesis with green tea or green tea extracts (Hursel & Westerterp-Plantenga, 2010).

In addition to increased thermogenesis, green tea catechins may alter lipid metabolism by inhibiting fatty-acid synthase (Tian, Li, Wu, & Chen, 2004) and increasing fat oxidation through sympathetic nervous system stimulation (Dulloo et al., 1999). In sedentary young men (8–30% body fat), green tea extract (270 mg/day EGCE, 150 mg/day caffeine) significantly increased fat oxidation by 9.9% over 24 hr compared with the caffeine-only (150 mg/d caffeine) or the placebo group (Dulloo et al., 1999). Data from a metabolic chamber showed that green tea extract significantly decreased respiratory quotient from 0.88 to 0.85 over 24 hr ($p < .001$). In normal-weight, active men (VO_{2max} = 50.9 ml · kg^{-1} · min^{-1}), green tea extract significantly increased fat oxidation by 17% (~16 kcal more fat oxidized) during 30 min of cycling at 60% maximal oxygen consumption compared with placebo (Venables, Hulston, Cox, & Jeukendrup, 2008). In that study, green tea extract (340 mg catechins with 136 mg EGCE, no caffeine) was given at each meal for the 24-hr period before exercise. In summary, green tea catechins increased fat oxidation over a 24-hr period in both sedentary and active lean individuals during exercise, but the physiological significance of this increase still needs to be determined.

Currently the interest in green tea as an aid for weight loss or weight maintenance is high (Kao, Chang, Lee, & Chen, 2006; Wolfram, 2007; Wolfram et al., 2006). Two recent meta-analyses have examined the effect of green tea on weight loss and weight maintenance. Hursel, Viechtbauer, and Westerterp-Plantenga (2009) examined 49 studies, with 11 RCTs meeting their inclusion criteria (weight loss = 9, weight maintenance = 2). In the weight-loss studies, participants consumed an EGCG-caffeine mixture (~50–300 mg/day of EGCG, ~0–100 mg/day caffeine) or placebo/low-green-tea-catechin dose for 12 weeks. In the weight-maintenance studies (n = 2), subjects consumed ~500 kcal/day for 4 weeks and then were randomized into either the placebo or ECGC-caffeine treatment (104–150 mg/day caffeine, 270–323 mg/day ECGC) groups for 12–13 weeks to determine whether green tea helped with weight maintenance (Kovacs, Lejeune, Nijs, & Westerterp-Plantenga,

2004; Westerterp-Plantenga, Lejeune, & Kovacs, 2005). Results showed that green tea catechins significantly decreased body weight during the weight-loss period and significantly helped maintain body weight during weight maintenance ($\mu = 1.31$ kg, $p < .001$). However, the results were influenced by habitual caffeine use. High users of caffeine (>300 mg/day) had less of an effect (0.27 kg weight loss) than low users (1.60 kg weight loss). They also found the effect of green tea catechins to be less in Whites (0.82 kg weight loss) than in Asians (1.51 kg weight loss), indicating that ethnicity may be a moderating factor. However, the authors did indicate that the studies in Asians all used lower caffeine intakes than the studies in Whites. More data are needed to determine how ethnicity may moderate catechin effectiveness. A second meta-analysis including 15 studies (n = 1,243 participants) examined the effect of green tea catechins with or without caffeine on body weight (Phung et al., 2010). Those authors found that green tea catechins plus caffeine significantly reduced body weight compared with either matched caffeine (1.38 kg weight loss) or caffeine-free (0.44 kg weight loss) groups. However, when they compared green tea catechins alone to a no-caffeine group, there was no effect. Both meta-analyses conclude that green tea may significantly decrease body weight, but the clinical significance is small (<2 kg). However, a number of factors can influence study results, such as timing of green tea supplementation relative to meals, which can influence green tea catechin absorption; dose (length of treatment, amount, and frequency); type of green tea catechins used; and study population characteristics including age, ethnicity, health status, and body size (Phung et al., 2010). Currently, we do not know the ideal dose, timing, or population most likely to benefit from green tea supplementation for weight loss or weight maintenance.

Finally, no research has added green tea to a combined diet-and-exercise weight-loss program. However, two studies examined adding green tea to 12 weeks of exercise-only programs aimed at either weight loss (Maki et al., 2009) or fitness (Hill et al., 2007). Hill et al. added EGCG (300 mg/day) to an exercise program (135 min/week of walking or running) for overweight and obese premenopausal women and found no additional effect. Maki et al. randomly assigned overweight or obese adults to either treatment (625 mg/day of green tea catechins, 39 mg/day of caffeine) or control (39 mg/day of caffeine) groups. All participated in ≥180 min/week of moderate, supervised exercise. There were no differences in fat-mass or weight loss between groups (~1 kg greater weight loss in catechin group). However, the green tea catechin group lost significantly more abdominal body fat, both total and subcutaneous, and had lower fasting serum triglycerides than the control group.

Sarma et al. (2008) systematically reviewed the safety of green tea extracts. Of the 216 green tea case reports they examined, 34 were related to liver damage, with 27 categorized as possible causality. Sarma et al. found that health problems associated with green tea extracts were more likely to occur if the product was taken on an empty stomach. To address these concerns, Frank et al. (2009) made their own green tea catechin extract (714 mg/day) and fed it to healthy men for 3 weeks and found no elevations in liver enzymes or liver dysfunction. These data, combined with the results of Sarma et al., would suggest there may be other contaminants in some commercially available green tea extracts that are contributing to liver damage. Green tea extracts are not regulated, so product safety is not assured. Conversely, drinking green tea has a number of reported health benefits (Basu & Lucas, 2007; Cabrera et al., 2006; Kao et al., 2006; Wolfram, 2007).

Bitter Orange

There are a number of other stimulants added to weight-loss supplements that are associated with adverse health effects (Pittler, Schmidt, & Ernst, 2005; see Table 2). Only bitter orange is addressed here. Bitter orange (citrus aurantium), which contains synephrine alkaloids, has been used to replace ephedra in many weight-loss supplements (Fugh-Berman & Myers, 2004; Haaz et al., 2006). In addition to its stimulatory effects, researchers have identified a citrus-based polyphenolic compound in bitter orange that may have lipolytic effects in humans (Dallas, Gerbi, Tenca, Juchaux, & Bernard, 2008). Reviews indicate that the effectiveness of bitter orange as a weight-loss supplement is limited (Haaz et al., 2006; Haller, Benowitz, & Jacob, 2005). Current studies are short (2–8 weeks), sample sizes are small (n = 4–30), varying diets and exercise protocols are used, and bitter orange is combined with other stimulants and botanicals such as caffeine, ephedra, guarana, St. John's wort, and ginkgo biloba.

As bitter orange is added to more weight-loss products, the incidence of adverse effects has increased (Haaz et al., 2006). Adverse events associated with bitter orange are increased blood pressure and heart rate (Bui, Nguyen, & Ambrose, 2006), myocardial infarction (Nykamp, Fackih, & Compton, 2004), angina (Gange, Madias, Felix-Getzik, Weintraub, & Estes, 2006), and ischemic colitis (Sultan, Spector, & Mitchell, 2006).

Changing Body Composition: Nutrient Partitioning

Substances that fall into the nutrient partitioning category are hypothesized to work by changing either fat or carbohydrate metabolism, thus increasing lean body mass and reducing body fat (see Table 3). Only calcium, conjugated linoleic acid, and chromium picolinate are discussed here.

Calcium

Higher calcium (Ca) intakes, through supplements or dairy consumption, are associated with lower body weight or decreased weight gain (Major et al., 2008). The specific mechanisms by which Ca/dairy intake may play a role in regulating body weight are still unknown, but a number have been proposed:

Table 3 Weight-Loss Supplements With Hypothesized Mechanisms Involving Changing Body Composition Through Alterations in Energy or Nutrient Partitioning

Supplement	Proposed mechanisms or use	Current level of evidence	Scientific findings	Potential side effects and safety issues	Current status
Ca supplements or dairy products	A low-Ca diet increases adipose Ca uptake and stimulates fat accretion. A high-Ca diet increases fecal fat excretion. Appetite control may improve while on a high-Ca diet.	Impact of Ca on weight has been extensively studied (49 RCTs) and reviewed (Lanou & Barnard, 2008). One meta-analysis using 15 RCTs examining effect of Ca on fat excretion (Christensen et al., 2009).Two RCTs (Major et al., 2009; Major et al., 2008) examining effect of Ca on appetite with equivocal results.	Only 4 RCTs show Ca contributes to greater weight loss with energy-restricted diet (~2–4 kg; Zemel, 2004, 2005, 2008). One meta-analysis was not supportive (Lanou & Barnard, 2008). Meta-analyses showed increased fecal fat loss (~2 g/day) with increased Ca intake and 5.2 g/day loss with increased dairy (Christensen et al., 2009).Ca may only help with appetite control when Ca intake is low (<600 mg/day; Major et al., 2009).	Generally regarded as safe. Supplements or increased dairy intake will improve overall Ca intake.	May only be beneficial for those who typically consume a low-Ca diet (<600 mg/day).
CLA	Reduction of fat mass by reducing adipocyte differentiation and metabolism. Outcome may depend on the form of the isomer fed.	Extensively studied, with reviews (Li et al., 2008; Churruca et al., 2009; Egras et al., 2011) and 2 meta-analyses (Larsen et al., 2003; Whigham et al., 2007).	Limited data supporting decreases in fat mass (1–2 kg) or gains in lean tissue (~1 kg) 12 weeks to 24 months (~3–6 g/day CLA).	GI distress; may negatively increase blood insulin and reduce insulin sensitivity.	Effects in animals have not been clearly duplicated in humans.
L-carnitine	Essential for transport of fatty acids into the mitochondria. Synthesized in the liver from lysine and methionine.	Extensively studied and subjected to numerous reviews (Brass, 2004; Karlic & Lohninger, 2004; Spriet et al., 2008).	Earlier research showed little evidence that L-carnitine supplementation significantly increases skeletal-muscle carnitine and fat oxidation while decreasing body fat in normal healthy individuals (Brass, 2004; Villani et al., 2000). In 2011, research showed that L-carnitine supplementation combined with carbohydrate increases skeletal-muscle carnitine and reduces muscle glycogen use during exercise, indirectly indicating increased fat oxidation (Wall et al., 2011).	Generally considered safe.	No current evidence to show clinically significant weight loss. More research required based on new research findings.
Cr picolinate (Cr^{+3})	Essential trace metal that potentiates the action of insulin. Hypothesized to increase lean mass and promote fat loss.	Extensively studied with 2 meta-analyses (Pittler & Ernst, 2004; Pittler et al., 2003) and 1 review (Vincent, 2003).	No benefit of Cr picolinate on weight loss or muscle-mass increases under controlled feeding conditions (Lukaski et al., 2007).	The AI for Cr is 30 µg/day for men and 20 µg/day for women, 51–70 years. No UL has been set for Cr; doses <200 µg/d are typically safe. Cr^{+6} is a human carcinogen and toxin (Institute of Medicine & Food and Nutrition Board, 2001).	Supportive evidence is minimal. Cr picolinate is unlikely to produce clinically significant changes in body composition or weight loss (<1 kg).
HCA, a botanical extract from plants native to India, especially *Garcinia cambogia*	HCA inhibits ATP-citrate-lyase, the enzyme that cleaves citrate into oxaloacetate and acetyl-CoA for endogenous fat synthesis (Watson et al., 1969; Watson & Lowenstein, 1970). HCA may suppress fatty-acid synthesis and food intake while decreasing weight gain.	Reviews and RCTs are generally not supportive of the hypothesis (Heymsfield et al., 1998; Kovacs, Westerterp-Plantenga, & Saris, 2001; Kovacs, Westerterp-Plantenga, Saris, et al., 2001; Kriketos et al., 1999).	No benefit of HCA on weight loss, fat oxidation, or appetite.	Numerous safety issues including liver injury. In 2009, the FDA warned consumers to stop using Hydroxycut products that contained HCA (Fong et al., 2010).	No strong data supporting significant weight loss, especially when considering safety issues. HCA is typically combined with other substances in weight-loss products, which could contribute to safety issues.
Pyruvate	Hypothesized to improve exercise performance and enhance body composition through increasing fat oxidation via lower RER.	Two reviews (Pittler & Ernst, 2004, 2005) and 1 RCT (Koh-Banerjee et al., 2005) showed no effect.	No benefit of pyruvate on long-term weight loss or changes in body composition.	Generally considered safe. Large doses (>5 g/day) may cause GI distress (Egras et al., 2011).	No data supporting significant weight loss.

Note. Ca = calcium; RCT = randomized, double-blind, placebo-controlled clinical trial; CLA = conjugated linoleic acid; GI = gastrointestinal; Cr = chromium; AI = adequate intake; UL = upper tolerable intake level; HCA = hydroxy-citric acid; FDA = Food and Drug Administration; RER = respiratory-exchange ratio.

- The "Ca hypothesis" suggests that adequate dietary Ca, through its influence on plasma 1,25-dihydroxyvitamin D_3 levels, suppresses intracellular adipocyte Ca levels, which in turn enhances fat lipolysis and decreases fat synthesis (Zemel, 2004, 2005).
- High dietary Ca may alter fat metabolism (Melanson et al., 2003) and/or increase fecal fat excretion through the formation of insoluble Ca–fatty-acid complexes that increase fat lost in the stool by ~5.2 g/day or 47 kcal/day (Bendsen, Hother, Jensen, Lorenzen, & Astrup, 2008; Christensen et al., 2009; Jacobsen, Lorenzen, Toubro, Krog-Mikkelsen, & Astrup, 2005), which may translate into ~2 kg/year weight loss (Astrup, Chaput, Gilbert, & Lorenzen, 2010).
- Increased dairy Ca intake, especially in those with low intake, may improve appetite control in athletes consuming an energy-restricted diet. This hypothesis suggests that the body may have a "taste" or appetite for Ca and that a low-Ca diet (<600 mg/day of Ca) may increase the motivation to seek out and choose Ca-rich foods (Major, Alarie, Doré, & Tremblay, 2009; Major et al., 2008; Tordoff, 2001).

The role that dairy intake or Ca supplementation may play in weight control has been extensively researched. A recent review (Lanou & Barnard, 2008) identified 49 RCTs examining the effect of dairy intake or Ca supplementation on body weight with and without an energy-restricted diet. Overall, 41 showed no effect, two showed weight gain, one showed a lower rate of weight gain, and five showed weight loss. Of the RCTs without energy restriction, 37 of 38 did not support weight loss with either dairy or Ca supplementation. Of the 11 RCTs in which energy was restricted, seven showed no effect, while four found a significant association between increased Ca or dairy intake and weight loss. Only one of those studies included exercise in the weight-reduction protocol and found no differences between groups (Bailey, Sullivan, Kirk, Hall, & Donnelly, 2007). Studies published since this review have shown no effect of dairy or Ca supplementation on weight without energy restriction (Wennersberg et al., 2009; Yanovski et al., 2009). Based on the Ca hypothesis, Ca or dairy supplementation does not affect weight loss unless combined with an energy-restricted diet (Zemel, 2008). Overall, adding more dairy or Ca to a weight-loss diet is not likely to result in large weight losses (~2–4 kg), and this effect may only be seen in individuals who typically have low Ca intakes (<600 mg/day; Astrup et al., 2010). However, adding low-fat dairy or Ca to the diet may help prevent or slow the typical weight gain one observes with age (Tremblay, 2008).

Researchers have also examined the impact of Ca supplementation or dairy Ca intake on fat oxidation, both at rest and during exercise (Melanson, Donahoo, Dong, Ida, & Zemel, 2005; Melanson et al., 2003; Teegarden et al., 2008; White, Lyle, Flynn, Teegarden, & Donkin, 2006). Unfortunately, research in this area has been equivocal. Some researchers find that both supplemental and dairy Ca increase fat oxidation (Melanson et al., 2003), while others find this effect only with Ca supplements (Teegarden et al., 2008). White et al. found no acute effects of dairy Ca intake on fat oxidation during exercise.

Conjugated Linoleic Acid

Conjugated linoleic acid is an isomer of linoleic acid, one of two essential fatty acids required in the diet. It is hypothesized that CLA, primarily the *cis*-9, *trans*-11, trans-10, and *cis*-12 isomers, can increase lean-tissue mass and decrease body fat based on extensive animal research (Bhattacharya, Banu, Rahman, Causey, & Fernandes, 2006; Churruca, Fernández-Quintela, & Portillo, 2009; Li, Huang, & Xie, 2008). Research in humans has not produced the dramatic results observed in animals. Extensive reviews and two meta-analyses have examined the effect of CLA supplementation on fat loss or weight regain after a weight-loss program and report either no or moderate outcomes. One meta-analysis found a small, but significant, decrease in fat mass (0.05 kg/week) with 3.2 g/day of CLA over 6–24 months (Whigham, Watras, & Schoeller, 2007). Conversely, a second meta-analysis found no significant difference in either body weight or fat mass in CLA users (3.4 g/day for 1year) compared with a placebo group (Larsen, Toubro, & Astrup, 2003). A review by Li et al. reports that most studies fail to show a decrease in body weight after supplementing with CLA (0.7–6.8 g/day), while seven studies showed small changes in fat mass. Finally, a recent review including RCTs using CLA alone found little or no change in body weight with CLA supplementation (3.4–6.8 g/day for 4weeks to 24 months; Egras, Hamilton, Lenz, & Monaghan, 2011).

Research published after these meta-analyses continues to show equivocal results. Norris et al. (2009) reported that CLA contributed to a small decrease in weight (~1 kg) in obese postmenopausal women, while Diaz, Watkins, Li, Anderson, and Campbell (2008) found no effect of CLA (1.8 g/day) on body composition or weight in overweight women on an energy-reduced diet (–500 kcal/day) plus 30 min exercise 5 days/week for 3 months. Conversely, two recent studies have shown small improvements in body composition (~1.2 kg gain in lean tissue vs. controls) in normal-weight young (Pinkoski et al., 2006) and older (Tarnopolsky et al., 2007) adults using CLA (5–6 g/day for 7–24 weeks) and participating in resistance exercise. Finally, there appears to be no effect of CLA on exercise performance (Campbell & Kreider, 2008).

The inconsistency between human clinical trials and animal studies may be due to differences in age, gender, and CLA dose and isomer form (Li et al. 2008; Plourde, Jew, Cunnane, & Jones, 2008). Most animal studies are done in young growing animals, while the human research is done in adults, primarily overweight women. Human-research studies typically feed a single CLA isomer or a

mixture of isomers, while weight-loss supplements are typically mixtures of isomers. CLA supplementation can also have negative consequences. Research shows that some CLA isomers negatively affect blood lipids and increase insulin resistance (Raff et al., 2009; Salas-Salvadó, Márquez-Sandoval, & Bulló, 2006; Thrush et al., 2007). Currently, the efficacy of CLA for weight and fat loss is limited.

Chromium Picolinate

Chromium (Cr) picolinate is an essential trace metal hypothesized to increase lean muscle mass and promote fat loss while enhancing the effects of insulin. Two meta-analyses have examined Cr supplementation (6–14 weeks) and weight loss in a variety of subjects (overweight, normal weight, athletes). One reported <0.2 kg/week weight loss with Cr supplementation (Pittler, Stevinson, & Ernst, 2003), while the second (Pittler & Ernst, 2004), focusing only on overweight individuals in 10 RCTs, found a 0.08- to 0.2-kg/week weight loss (1.1–1.2 kg greater weight loss than controls). A 2003 review of Cr picolinate reported no benefit of supplementation on weight loss or muscle development, even when combined with exercise training (Vincent, 2003). Research done since those reviews has found no effect of Cr picolinate on body weight or composition (Diaz et al., 2008; Lukaski, Siders, & Penland, 2007; Yazaki et al., 2010). Only Lukaski et al. tested the effect of Cr picolinate supplementation on weight changes, using a carefully controlled diet and dual X-ray absorptiometry (DXA) to assess change in body composition. In their double-blind RCT, 83 premenopausal women were fed controlled diets and supplemented with Cr picolinate (1,720 µg/day) or a placebo for 12 weeks. Lukaski et al. found no effect of Cr supplementation on body composition or weight.

Appetite Suppressants: Soluble Fibers

Appetite suppressants include soluble fibers, *Hoodia gordonii,* and protein (see Table 4). The use of protein as a weight-loss aid has been extensively reviewed by others, so it is not covered here (Paddon-Jones et al., 2008; Westerterp-Plantenga, Nieuwenhuizen, Tomé, Soenen, & Westerterp, 2009). Only soluble fibers are discussed.

Soluble fibers are hypothesized to affect body weight in two ways. First, they absorb water in the gut and increase the sense of satiety and fullness, which results in decreased food and energy intake (Anderson et al., 2009). Second, short-chain fatty acids produced from soluble-fiber fermentation in the gut may have satiety-producing effects through their impact on gut-hormone production (e.g., leptin, PPY, GLP-1; Hosseini, Grootaert,

Table 4 Weight-Loss Supplements With Hypothesized Mechanisms Involving Appetite Suppression

Supplement	Proposed mechanisms or use	Current level of evidence	Scientific findings	Potential side effects and safety issues	Current status
Soluble fibers (e.g., psyllium, guar gum, beta glucans, or glucomannan)	Soluble fibers hold water and increase satiety and fullness. SCFA can influence production of satiety hormones (Anderson et al. 2009; Hosseini et al., 2011).	Numerous reviews and RCTs examining either high-fiber diets or fiber supplements (Anderson et al. 2009; Keithley & Swanson, 2005; Pittler & Ernst, 2001).	A high-fiber diet is associated with lower body weight. Use of fiber supplements may contribute to weight loss, but the amount is small (1–2 kg). Type and amount of fiber may be factors.	GI upset, bloating, and gas.	A high-fiber diet may contribute to small decreases in weight (1–2 kg). Newer water-holding fibers are being developed, which may be more effective for weight loss or maintenance.
Hoodia gordonii (e.g., Hoodia, Kalahari cactus, Xhoba)	Native plant of the Kalahari Desert in southern Africa associated with reduced hunger. Appetite suppression attributed to a plant compound called P57, a steroidal alkaloid (Madgula et al., 2010).	There is no scientific evidence or human clinical trials. Studies in mice show ~50% bioavailability, found in kidney, liver, and brain and eliminated rapidly (Madgula et al., 2010).	None.	Safety is unknown. No published studies.	No evidence to support Hoodia as a weight-loss supplement.

Note. SCFA = short-chain fatty acids; RCT = randomized, double-blind, placebo-controlled clinical trial; GI = gastrointestinal.

Verstraete, & Van de Wiele, 2011). Epidemiological studies show that higher fiber diets are associated with lower body weight and adiposity (Anderson et al., 2009; Kromhout, Bloemberg, Seidell, Nissinen, & Menotti, 2001; Slavin, 2005), but the specific amount and type of fiber required to produce weight loss are less definitive. Anderson et al. reviewed RCTs (n = 5) examining the effect of high-fiber diets (no supplements) on weight and found that higher fiber diets resulted in ~1 kg more weight loss than control diets.

Research on dietary fiber supplements for weight loss is growing (Giacosa & Rondanelli, 2010). A 2001 meta-analysis (n = 20 placebo controlled RCTs) found no effect of guar gum supplementation on body weight (Pittler & Ernst, 2001). A more recent review by Anderson et al. (2009) identified 16 RCTs (n = 391 controls, n = 423 treatment) that primarily used fiber tablets (3×/day, 4.5–20 g/day, 4–12 weeks) of guar gum or glucomannan, a highly viscous soluble fiber. Results showed a greater weight loss with fiber (~1.3–2.5 kg) than controls. A fiber-specific review examined the impact of glucomannan supplementation only on weight loss (Keithley & Swanson, 2005). It found seven studies (n = 28–60) lasting 4–16 weeks and providing 2–5 g/day of glucomannan. Overall, the studies reported small differences in weight loss (~1–2 kg) in the fiber versus the placebo group. The researchers concluded that glucomannan may have properties that can promote weight loss, but better controlled trials are needed. Studies published since that review report equivocal results (Birketvedt, Shimshi, Erling, & Florholmen, 2005; Kraemer et al., 2007; Salas-Salvadó et al., 2008), which may be due to differences in protocols and the use of glucomannan either alone or with other fibers. Most recently, researchers report using a highly viscous polysaccharide, manufactured by reacting glucomannan with other soluble polysaccharides, for weight loss in 29 sedentary overweight and obese adults (Lyon & Reichert, 2010). They report significant changes in weight (5.8 kg weight loss) and body composition (2.4% body-fat reduction) over a 14-week period, but no control group was included in the study. Whether this new variation of glucomannan will be helpful as a weight-loss aid needs further research.

Summary

Dietary weight-loss supplements vary in the evidence supporting their claims. Some products have been extensively tested and show modest effects (<2 kg weight loss), but many have had either no or limited RCT trials examine their effectiveness. A number of factors confound the research literature related to the effectiveness of weight-loss supplements, such as small sample sizes, short intervention periods, little or no follow-up to see if the weight loss is maintained, and differences in protocols, especially whether the supplement is given in combination with an energy-restricted diet or increases in exercise expenditure. Currently, there is no strong body of research evidence indicating that one specific supplement will produce significant weight loss (~2–4 kg), especially in the long term. A number of supplements such as green tea, fiber, and low-fat dairy products may complement a healthy lifestyle to prevent weight gain over time. With no effective weight-loss supplements on the market, it is the responsibility of the health profession to educate the public on diet, exercise, and lifestyle changes for weight loss or maintenance. Athletes and active individuals also need to be educated on how best to reach their performance and weight goals without resorting to stimulants. Finally, many of the weight-loss supplements can have serious health effects, for little or no benefit, and many are banned substances.

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