Dietary supplements for body-weight reduction: a systematic review¹,²

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ABSTRACT
Background: Compliance with conventional weight-management programs is notoriously poor, and a plethora of over-the-counter slimming aids are sold with claims of effectiveness.

Objective: The objective of this study was to assess the evidence from rigorous clinical trials, systematic reviews, and meta-analyses on the effectiveness of dietary supplements in reducing body weight.

Design: The study was a systematic review. Literature searches were conducted on Medline, Embase, Amédè, Cinahl, and the Cochrane Library until March 2003. Hand searches of medical journals, the authors’ own files, and bibliographies of identified articles were conducted. There were no restrictions regarding the language of publication. The screening of studies, selection, validation, data extraction, and the assessment of methodologic quality were performed independently by the two reviewers. To be included, trials were required to be randomized and double-blind. Systematic reviews and meta-analyses of dietary supplements were included if they were based on the results of randomized, double-blind trials.

Results: Five systematic reviews and meta-analyses and 25 additional trials were included and reviewed. Data on the following dietary supplements were identified: chitosan, chromium picolinate, Ephedra sinica, Garcinia cambogia, glucomannan, guar gum, hydroxy-methylbutyrate, plantago psyllium, pyruvate, yerba maté, and yohimbine. The reviewed studies provide some encouraging data but no evidence beyond a reasonable doubt that any specific dietary supplement is effective for reducing body weight. The only exceptions are E. sinica and ephedrine-containing supplements, which have been associated with an increased risk of adverse events.

Conclusions: The evidence for most dietary supplements as aids in reducing body weight is not convincing. None of the reviewed dietary supplements can be recommended for over-the-counter use. Am J Clin Nutr 2004;79:529–36.

KEY WORDS Overweight, obesity, weight reduction, complementary medicine, alternative medicine, herbal medicine, dietary supplements, chitosan, guar, chromium, ephedra, psyllium, garcinia

INTRODUCTION
The number of persons whose body weight is greater than their ideal is increasing, particularly in developed countries. In the United States, for instance, more than half of the adult population must now be classified as overweight or obese. On the basis of a normal body mass index (BMI; in kg/m²) ranging from 18.5 to 24.9, 31% of the US adult population is obese (BMI ≥ 30), and an additional 34% is overweight (BMI ≥ 25; 1). Excess body weight is one of the most important risk factors for all-cause morbidity and mortality. The likelihood of developing conditions such as type 2 diabetes, heart disease, cancer, and osteoarthritis of weight-bearing joints increases with body weight (2–5), and these conditions lead to substantial economic costs in the total health care budget (6). One factor responsible for overweight and obesity is a continuous decrease in energy expenditure from physical activity during recent decades (7, 8). Compliance with conventional weight-management programs is notoriously poor, which indicates a need for safe, effective, and acceptable therapeutic options. It is therefore not surprising to see the marketing of a plethora of over-the-counter slimming aids with claims of effectiveness (9, 10). The aim of this systematic review is to critically assess the evidence from rigorous clinical trials, systematic reviews, and meta-analyses on the effectiveness of dietary supplements in reducing body weight.

METHODS
Systematic literature searches were conducted to identify all randomized clinical trials (RCTs), systematic reviews, and meta-analyses of dietary supplements for body weight reduction. Data sources were Medline, Embase, Amédè, Cinahl, and the Cochrane Library. The search terms used were dietary supplements, food supplements, herbal products, phytotherapy, overweight, obesity, weight loss, slimming, and derivatives of these. Each database was searched from its inception until March 2003. Hand searches of relevant medical journals and of the authors’ own files were conducted. The bibliographies of all articles located were searched for further studies. There were no restrictions regarding the language of publication (11).

To be included, trials were required to state that they were randomized and double-blind. Systematic reviews and meta-analyses of dietary supplements were included if based on the results of randomized, double-blind trials. Studies assessing acute effects only were excluded. All studies were selected according to defined criteria, and data were validated and extracted in a systematic manner. Methodologic quality was evaluated by using the system developed by Jadad et al (12). The screening and selection of studies, data extraction, validation, and the assessment of methodologic quality were performed independently by the 2

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reviewers. Disagreements in the evaluation of studies were largely due to reading errors and were resolved through discussion.

RESULTS

Five systematic reviews and meta-analyses based on the results of double-blind RCTs and 25 additional double-blind RCTs met all inclusion criteria. The identified evidence relates to ayurvedic herbal preparations, chitosan, chromium picolinate, *Ephedra sinica*, *Garcinia cambogia*, glucomannan, guar gum, hydroxy-methylbutyrte, plantago psyllium, pyruvate, yerba maté, and yohimbe (Tables 1 and 2).

Ayurvedic preparations

We identified one double-blind RCT assessing ayurvedic herbal preparations (13). Included patients whose body weight was ≥ 20% greater than their ideal according to the Life Insurance Corporation of India received daily either indistinguishable placebo or ayurvedic preparations (Table 1) plus 750 mg Triphala/d. Patients in the treatment group experienced a reduction in body weight ranging between 7.9 and 8.2 kg, which differed significantly from the reduction seen with placebo.

Chitosan

Chitosan is a cationic polysaccharide, which is produced from chitin, a substance derived from the exoskeleton of crustaceans. It is promoted as a remedy to reduce fat absorption (41), and data from preclinical studies exist to support this notion (42–44). However, data from our meta-analysis of 5 double-blind RCTs, which included patients who were described as either obese, overweight, or having 10–25% excess body weight, indicated serious methodologic limitations of the clinical evidence (36). The meta-analysis concluded that the effectiveness of chitosan for body-weight reduction is not established beyond a reasonable doubt. We identified 5 further double-blind RCTs (Table 1) assessing overweight or obese patients that had been published since the meta-analysis. Overall, the evidence available in the literature indicates that there is considerable doubt that chitosan is effective for reducing body weight in humans. Adverse events most frequently included gastrointestinal symptoms such as constipation and flatulence (Tables 1 and 2).

Chromium picolinate

Chromium, an essential trace mineral and cofactor to insulin, enhances insulin activity and has been the subject of studies assessing its effects in carbohydrate, protein, and lipid metabolism (45–47). Reported effects include an increase in lean body mass, a decrease in percentage body fat, and an increase in the basal metabolic rate (19, 45, 48). Chromium picolinate is an organic compound of trivalent chromium and picolinic acid, a naturally occurring derivative of tryptophan. Our meta-analysis included 10 double-blind RCTs (Table 2). The results suggest a relatively small reduction of 1.1–1.2 kg (ie, 0.08–0.2 kg/wk) compared with placebo during an intervention period of 6–14 wk in patients with an average BMI of 28–33 (37). By comparison, a diet with a provision of 3300 kJ/d achieves a mean weight loss of ≈1.5–2.5 kg/wk, and a more moderate energy restriction to 5000 kJ/d results in a weight loss of 0.5–0.6 kg/wk (49). Therefore, it seems that the observed effect with chromium picolinate is, although statistically significant, not clinically meaningful.

All 3 trials that reported on adverse events and an additional trial using niacin-bound chromium (Table 1) reported no adverse events in patients receiving chromium.

*Ephedra sinica*

*E. sinica*, or ma-huang, is an evergreen shrub native to central Asia (50). Ephedrine, the primary active constituent of the botanical *E. sinica*, has been studied alone and in combination with caffeine. A systematic review of 5 double-blind trials, including 2 trials whose format was randomized or nonrandomized is not clear, concluded that the combination of ephedrine and caffeine is effective for reducing body weight and appears to outweigh the risks (Table 2) (38). The most rigorous review to date (39) assessed human studies with ≥ 8 wk of follow-up and concluded that *E. sinica* and ephedrine promote a modest short-term weight loss of ≈0.9 kg/100 mo more than does placebo (Table 2). The intake of those supplements, however, is associated with a 2.2- to 3.6-fold increase in odds of psychiatric, autonomic, or gastrointestinal symptoms and heart palpitations. Because of safety concerns, the FDA is now taking several regulatory actions with regard to ephedra and ephedrine-containing supplements (51, 52).

*Garcinia cambogia*

Hydroxycitric acid is obtained from extracts of *G. cambogia* and has been shown to inhibit citrate cleavage enzyme, suppress de novo fatty acid synthesis and food intake, and decrease body weight gain (20). We identified a double-blind RCT, which tested the effects of 3 g *G. cambogia* extract/d, which contained 50% hydroxycitric acid, in patients with an average BMI of 32 (20). The results suggest the absence of a significantly greater weight loss in the treatment group than in the placebo group. Two further double-blind RCTs report effects in favor of treatment with *G. cambogia* compared with placebo (Ramos et al, unpublished observations; cited in 20, 21). This is supported by a trial testing the effects of hydroxycitric acid (22). Other double-blind RCTs, however, that tested *G. cambogia* extract– or hydroxycitric acid– containing combination preparations with or without dietary alterations (Kaats et al, unpublished observations; cited in 20, 23–25) report conflicting results. Overall, the evidence for *G. cambogia* is not compelling. Adverse events are reported in the reviewed trials and are listed in Table 1.

*Glucomannan*

Glucomannan is a component of konjac root, derived from *Amorphophallus konjac* C. Koch. Its chemical structure is similar to that of galactomannan from guar gum (see below) and comprises a polysaccharide chain of glucose and mannose (53). We identified one double-blind RCT including patients with body weight ≥20% over their ideal (26). The report suggests significantly greater weight loss in the treatment group than in the placebo group. There were no adverse events in the treatment group. Independent replication of this trial is warranted.

*Guar gum*

Whether guar gum, a dietary fiber derived from the Indian cluster bean (*Cynamopsis tetragonolobus*), is effective in lowering body weight was assessed in our meta-analysis (40). Twenty double-blind, placebo-controlled RCTs were included, and the data from 11 trials were statistically pooled. The results of the
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<tr>
<th>Reference</th>
<th>Design and Jadad score</th>
<th>Intervention</th>
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<tr>
<td>Paranjpe et al (13)</td>
<td>Parallel, 3</td>
<td>Gokshuradi guggul Sinhanad guggul Chandraprabha vari</td>
<td>750 mg</td>
<td>Placebo</td>
<td>3 mo</td>
<td>70/48</td>
<td>P &lt; 0.05 for all intervention groups</td>
<td>Diarrhea and nausea (8)</td>
<td>Patients received advice on diet and exercise; dietary intake was not controlled</td>
</tr>
<tr>
<td>Wuolijski et al (14)</td>
<td>Parallel, 3</td>
<td>Chitosan</td>
<td>2.4 g</td>
<td>Placebo</td>
<td>8 wk</td>
<td>51/51</td>
<td>NS</td>
<td>Constipation (5), diarrhea (1), swollen heels or wrists (2), headache (1) Gastrointestinal discomfort including flatulence, stool bulkiness, bloating, nausea, heartburn</td>
<td>Patients were instructed not to change their eating habits</td>
</tr>
<tr>
<td>Schiller et al (15)</td>
<td>Parallel, 5</td>
<td>Chitosan</td>
<td>3 g</td>
<td>Placebo</td>
<td>8 wk</td>
<td>69/59</td>
<td>P &lt; 0.0001</td>
<td>Patients were instructed not to change their eating or exercise habits</td>
<td></td>
</tr>
<tr>
<td>Pittler et al (16)</td>
<td>Parallel, 5</td>
<td>Chitosan</td>
<td>2 g</td>
<td>Placebo</td>
<td>4 wk</td>
<td>34/30</td>
<td>NS</td>
<td>Constipation (6)</td>
<td>Patients were instructed not to change their eating habits</td>
</tr>
<tr>
<td>Ho et al (17)</td>
<td>Parallel, 3</td>
<td>Chitosan</td>
<td>3.1 g</td>
<td>Placebo</td>
<td>12 wk</td>
<td>88/68</td>
<td>NS</td>
<td>Gastrointestinal symptoms (7)</td>
<td>No dietary restriction</td>
</tr>
<tr>
<td>Girola et al (18)</td>
<td>Parallel, 5</td>
<td>Chitosan, <em>Garcinia cambogia</em> and chrome bound</td>
<td>480, 110, and 38 mg</td>
<td>Half-dose or placebo</td>
<td>4 wk</td>
<td>150/144</td>
<td>P &lt; 0.01</td>
<td>Nausea (3), headache (1)</td>
<td>Patients received a diet based on 4200 kJ/d</td>
</tr>
<tr>
<td>Crawford et al (19)</td>
<td>Crossover, 3</td>
<td>Chromium, niacin-bond</td>
<td>600 µg</td>
<td>Placebo</td>
<td>2 mo</td>
<td>20/18</td>
<td>NS</td>
<td>None</td>
<td>Patients received dietary consultation and exercised for 60 min &gt; 3 times/wk</td>
</tr>
<tr>
<td>Heymsfield et al (20)</td>
<td>Parallel, 5</td>
<td><em>G. cambogia</em></td>
<td>3 g</td>
<td>Placebo</td>
<td>12 wk</td>
<td>135/135</td>
<td>NS</td>
<td>Headache (9), upper respiratory tract symptoms (16), gastrointestinal symptoms (13)</td>
<td>Patients were provided with a high-fiber, 5040-kJ/d diet and asked not to change exercise habits</td>
</tr>
<tr>
<td>Ramos et al¹</td>
<td>NR; NA</td>
<td><em>G. cambogia</em></td>
<td>1.5 g</td>
<td>Placebo</td>
<td>8 wk</td>
<td>40/NA</td>
<td>P &lt; 0.05</td>
<td>NR</td>
<td>Patients were provided with a low-fat, 4200–6300-kJ/d diet</td>
</tr>
<tr>
<td>Mattes and Borman (21)</td>
<td>Parallel, 4</td>
<td><em>G. cambogia</em></td>
<td>2.4 g</td>
<td>Placebo</td>
<td>12 wk</td>
<td>167/89</td>
<td>P = 0.03</td>
<td>NR</td>
<td>Patients were advised to consume a 5000-kJ/d diet and were instructed to exercise 3 times/wk</td>
</tr>
<tr>
<td>Thom (22)</td>
<td>Parallel, 3</td>
<td>Hydroxycitric acid (G. cambogia)</td>
<td>1.32 g</td>
<td>Placebo</td>
<td>8 wk</td>
<td>60/60</td>
<td>P &lt; 0.001</td>
<td>Stomach pain (1)</td>
<td>Patients consumed a low-fat, 5000-kJ/d diet and were advised to exercise 3 times/wk</td>
</tr>
<tr>
<td>Rothacker and Waitman (23)</td>
<td>Parallel, 3</td>
<td><em>G. cambogia</em>, caffeine, and chromium polynicotinate</td>
<td>2.4 g, 150 mg, and 120 µg</td>
<td>Placebo</td>
<td>6 wk</td>
<td>50/48</td>
<td>NS</td>
<td>None</td>
<td>Patients were advised to consume a 5000-kJ/d diet</td>
</tr>
<tr>
<td>Kaats et al¹</td>
<td>NR; NA</td>
<td><em>G. cambogia</em>, chromium picolinate, and l-carnitine</td>
<td>1.5 g, 600 µg, and 1.2 g</td>
<td>Placebo</td>
<td>4 wk</td>
<td>200/NA</td>
<td>Body weight not reported; P &lt; 0.01 for fat mass loss</td>
<td>NR</td>
<td>Patients were provided with a low-fat, high-fiber diet</td>
</tr>
<tr>
<td>Antonio et al (24)</td>
<td>Parallel, 4</td>
<td><em>G. cambogia</em>, calcium phosphate, guggul extract, and l-tyrosine</td>
<td>750, 750, and 750 mg</td>
<td>Placebo or no treatment</td>
<td>6 wk</td>
<td>20/18</td>
<td>NS</td>
<td>None</td>
<td>All patients were provided with a 7500-kJ/d diet plan and exercised 3 times/wk</td>
</tr>
</tbody>
</table>

(Continued)
<table>
<thead>
<tr>
<th>Reference</th>
<th>Design and Jadad score</th>
<th>Intervention</th>
<th>Daily dose</th>
<th>Control</th>
<th>Duration</th>
<th>Subjects</th>
<th>Body weight results (intergroup differences)</th>
<th>Adverse events in intervention group (no. of cases)</th>
<th>Control of lifestyle factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thom (25)</td>
<td>Parallel, 5</td>
<td>G. cambogia, Phaseolus vulgaris, and inulin fiber</td>
<td>0.3, 1, 2, and 1.2 g</td>
<td>Placebo</td>
<td>12 wk</td>
<td>40/40</td>
<td>NR, ( P = 0.001 ) compared with baseline</td>
<td>None</td>
<td>Patients were advised to consume a low-fat, 5000-kJ/d diet</td>
</tr>
<tr>
<td>Walsh et al (26)</td>
<td>Parallel, 3</td>
<td>Glucomannan fiber</td>
<td>3 g</td>
<td>Placebo</td>
<td>8 wk</td>
<td>20/NR</td>
<td>( P &lt; 0.005 )</td>
<td>None</td>
<td>Patients were advised not to change their eating or exercise habits</td>
</tr>
<tr>
<td>Nissen et al (27)</td>
<td>Parallel, 3</td>
<td>( \beta )-Hydroxy-( \beta )-methylbutyrate</td>
<td>3 g</td>
<td>Placebo</td>
<td>4 wk</td>
<td>40/40</td>
<td>( P &lt; 0.05 ) for fat mass decrease and lean mass increase</td>
<td>NR</td>
<td>Patients exercised 3 d/wk</td>
</tr>
<tr>
<td>Vukovich et al (28)</td>
<td>Parallel, 2</td>
<td>( \beta )-Hydroxy-( \beta )-methylbutyrate</td>
<td>3 g</td>
<td>Placebo</td>
<td>8 wk</td>
<td>31/NR</td>
<td>( P = 0.04 ) for fat mass decrease and ( P = 0.06 ) for lean mass increase</td>
<td>NR</td>
<td>Patients exercised 2 d/wk</td>
</tr>
<tr>
<td>Rodriguez-Moran et al (29)</td>
<td>Parallel, 4</td>
<td>Plantago psyllium</td>
<td>15 g</td>
<td>Placebo</td>
<td>6 wk</td>
<td>125/123</td>
<td>NS</td>
<td>Good tolerance of psyllium</td>
<td>Patients were advised to consume a 105-kJ ( \cdot ) kg ( ^{-1} ) ( \cdot ) d ( ^{-1} ) diet</td>
</tr>
<tr>
<td>Kalman et al (30)</td>
<td>Parallel, 4</td>
<td>Pyruvate</td>
<td>6 g</td>
<td>Placebo</td>
<td>6 wk</td>
<td>26/26</td>
<td>NR, ( P &lt; 0.001 ) compared with baseline</td>
<td>NR</td>
<td>Subjects exercised 3 d/wk and were instructed to consume an 8400-kJ/d diet</td>
</tr>
<tr>
<td>Kalman et al (31)</td>
<td>Parallel, 3</td>
<td>Pyruvate</td>
<td>6 g</td>
<td>Placebo or no treatment</td>
<td>6 wk</td>
<td>53/51</td>
<td>NS</td>
<td>None</td>
<td>Subjects exercised 3 d/wk and were instructed to consume an 8400-kJ/d diet</td>
</tr>
<tr>
<td>Andersen and Fogh (32)</td>
<td>Parallel, 3</td>
<td>Yerba maté, guarana, and damiana</td>
<td>672, 570, and 216 mg</td>
<td>Placebo</td>
<td>45 d</td>
<td>47/47</td>
<td>Decrease of 5.1 kg (treatment) and 0.3 kg (placebo); ( P &lt; 0.005 )</td>
<td>NR</td>
<td>Patients were instructed not to change their eating habits</td>
</tr>
<tr>
<td>Kacio et al (33)</td>
<td>Parallel, 2</td>
<td>Yohimbine</td>
<td>20 mg</td>
<td>Placebo</td>
<td>3 wk</td>
<td>20/20</td>
<td>( P &lt; 0.005 )</td>
<td>None</td>
<td>Patients were advised to consume a 4200-kJ/d diet</td>
</tr>
<tr>
<td>Sax (34)</td>
<td>Parallel, 4</td>
<td>Yohimbine</td>
<td>16-43 mg</td>
<td>Placebo</td>
<td>6 mo</td>
<td>47/33</td>
<td>NS</td>
<td>Impaired sleep (3), nervousness (1), headache (1), arthralgia (1)</td>
<td>Patients were advised to consume a 7500-kJ/d diet and exercise 3 times/wk</td>
</tr>
<tr>
<td>Berlin et al (35)</td>
<td>Parallel, 2</td>
<td>Yohimbine</td>
<td>18 mg</td>
<td>Placebo</td>
<td>8 wk</td>
<td>19/19</td>
<td>NS</td>
<td>Undesirable events similar to those during intervention with placebo</td>
<td>Patients were advised to consume a 4200-kJ/d diet</td>
</tr>
</tbody>
</table>

\( ^{1} \) NR, not reported; NA, not applicable.  
\( ^{2} \) Quantification of the likelihood that bias is inherent in a trial, based on the description of randomization, blinding, and withdrawals (12).  
\( ^{3} \) n randomly assigned/\( n \) analyzed.  
\( ^{4} \) Unpublished observations, cited in reference 20.

Meta-analysis suggest that guar gum is not effective in reducing body weight. The agreement between the individual RCTs confirms the overall result of the meta-analysis. Adverse events reported in the reviewed trials predominately relate to the gastrointestinal system (Table 2).

**Hydroxy-methylbutyrate**

\( \beta \)-Hydroxy-\( \beta \)-methylbutyrate is a metabolite of leucine that has shown anabolic actions through inhibiting protein breakdown (54). \( \beta \)-Hydroxy-\( \beta \)-methylbutyrate is available as a dietary supplement and is primarily used by bodybuilders as a supportive measure to induce changes in body composition. The searches yielded 4 RCTs reported in 3 articles (54, 27, 28). Two double-blind RCTs reported significant intergroup differences with respect to fat mass (27, 28), while at least a trend toward an increase in lean body mass was reported from all trials, including those in which it is unclear whether the patients and care providers were blinded. Thus, there are encouraging data that require further independent replication. Only 2 of the 4 trials provided data on adverse events (54), and they reported no such events in patients treated with \( \beta \)-hydroxy-\( \beta \)-methylbutyrate.

**Plantago psyllium**

Psyllium is a water-soluble fiber derived from the husks of ripe seeds from *Plantago ovata* (50). We identified one double-blind RCT, which included patients with type 2 diabetes and a mean BMI of 29 (29). There were no significant changes in body
weight in either the treatment or placebo group. The authors report excellent tolerance of psyllium.

Pyruvate

Pyruvate is generated in the body via glycolysis, and supplementation with pyruvate seems to enhance exercise performance and improve measures of body composition (55, 56). Two double-blind RCTs, which included patients with BMIs of 25, assessed the effects of pyruvate supplementation (30, 31). None of these studies reported significantly greater effects on weight reduction than were seen with placebo. One (30) reported a significant body-weight reduction of 1.2 kg from baseline, while both reported significant reductions in fat mass and percentage body fat from baseline. Considering the evidence available from rigorous clinical trials, the case of pyruvate as an aid to body-composition changes and weight loss is weak. No adverse events are reported in one trial, and the other did not report on adverse events (Table 1).

Yerba maté

Yerba maté (Ilex paraguariensis) is an evergreen tree that is native to South America. In a combination preparation also containing guarana (Paullinia cupana) and damiana (Turnera diffusa), it was tested in patients with a BMI of 26–30 (32). I. paraguariensis and in particular P. cupana contain relatively large amounts of caffeine and have been shown by ultrasound scanning to prolong gastric emptying time (32). The descriptive results of that study indicated that this combination preparation might potentially be effective in lowering body weight. Adverse events were not reported.

Yohimbine

Yohimbine (Pausinystalia yohimbe) is a tall evergreen tree that is native to Central Africa. Yohimbine, an α-2 receptor antagonist, is the main active constituent of the ground bark of P. yohimbe. Most clinical studies relate to the effects of this isolated constituent of yohimbic bark. We identified 3 double-blind RCTs, which included patients who were >15–20% over their ideal body weight or had a BMI ranging between 28 and 48 (33–35). These trials report conflicting results (Table 1). At present, therefore, it is unclear whether yohimbine is effective in reducing body weight. Few adverse events were reported.

DISCUSSION

The data from published double-blind RCTs, systematic reviews, and meta-analyses are encouraging in some cases, but they provide little convincing evidence that any specific dietary supplement is effective in reducing body weight. The only exceptions are E. sinica– and ephedrine-containing dietary supplements. These remedies, however, have been associated with an increased risk of adverse events. The relative paucity of compelling evidence to suggest the effectiveness of dietary supplements in weight loss confirms the findings of earlier reviews (57).

**TABLE 2**

Systematic reviews and meta-analyses of dietary supplements for body-weight reduction

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<th>Reference</th>
<th>Design</th>
<th>Intervention</th>
<th>Daily dose</th>
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<tr>
<td>Ernst and Pittler (36)</td>
<td>Meta-analysis of double-blind, placebo-controlled RCTs</td>
<td>Chitosan</td>
<td>4 tablets (^d)</td>
<td>4 wk</td>
<td>386/366</td>
<td>−3.3 (1.5, 5.1)</td>
<td>Nausea (3), flatulence (4)</td>
<td>Patients in all trials were advised to consume a 400–5000 kJ/d diet</td>
</tr>
<tr>
<td>Pittler et al (37)</td>
<td>Meta-analysis of double-blind, placebo-controlled RCTs</td>
<td>Chromium picolinate</td>
<td>188–924 μg</td>
<td>6–14 wk</td>
<td>601/516</td>
<td>−1.1 (−1.8 to −0.4)</td>
<td>None</td>
<td>Patients in most trials were instructed not to change their eating habits and to exercise regularly</td>
</tr>
<tr>
<td>Greenway (38)</td>
<td>Systematic review of controlled and uncontrolled studies (^\text{i})</td>
<td>Ephedrine and caffeine</td>
<td>30–150 and 150–600 mg</td>
<td>8–24 wk</td>
<td>294/NR</td>
<td>NA</td>
<td>Dysrhythmia (84), dizziness (65), nausea (64), insomnia (32), tremor (24) (^\text{ii})</td>
<td>NR</td>
</tr>
<tr>
<td>Shekelle et al (39)</td>
<td>Meta-analysis of placebo-controlled RCTs</td>
<td>Ephedrine</td>
<td>60–150 mg</td>
<td>12–24 wk</td>
<td>393/NR</td>
<td>−0.6/mo (−0.2 to −1.0/mo)</td>
<td>Psychiatric symptoms (59), autonomic hyperactivity (138), heart palpitations (51), hypertension (7), upper gastrointestinal symptoms (88), headache (16), tachycardia (6) (^\text{ii})</td>
<td>NR</td>
</tr>
<tr>
<td>Pittler and Ernst (40)</td>
<td>Meta-analysis of double-blind, placebo-controlled RCTs</td>
<td>Guar gum</td>
<td>7.5–30 g</td>
<td>3 wk–6 mo</td>
<td>203/192</td>
<td>−0.04 (−2.2, 2.1)</td>
<td>Diarrhea, flatulence (28), gastrointestinal complaints (8)</td>
<td>Patients in most trials were instructed not to change their eating habits</td>
</tr>
</tbody>
</table>

\(^d\) RCTs, randomized controlled trials; NR, not reported; NA, not applicable.

\(^\text{i}\) n randomly assigned/n analyzed.

\(^\text{ii}\) Not defined in original trials.

\(^\text{iii}\) Data from double-blind, placebo-controlled trials are presented; it is unclear whether 2 of the 5 studies were randomized.

\(^\text{iv}\) Data from all identified studies are presented.

\(^\text{v}\) Data from controlled trials are presented.
Lifestyle changes including dieting and regular physical exercise are the basis for successful long-term weight loss, and limited evidence exists to support the effectiveness of pharmacotherapeutic options other than orlistat and sibutramine (58, 59). Notoriously poor compliance with conventional weight-management programs and the popularity of complementary and alternative medicine have created a ready market for nonprescription weight-loss products. Data from a US survey of a random population sample of almost 15,000 adults, for instance, showed the common use of nonprescription weight-loss products, particularly among young obese women. It is interesting that 8% of women with no excess body weight were also reported to use such products (9).

Although these preparations are popular, the lack of convincing data on effectiveness (60), even minor adverse events shift the delicate risk-benefit balance against their use. There is no convincing evidence, for instance, that guar gum is more effective than placebo (Table 2), whereas adverse events such as diarrhea, nausea, and flatulence were severe enough for 3% of the patients in trials included in our meta-analysis to withdraw. These findings are corroborated by other reports in the literature (61–63). In addition, it has been suggested that guar gum may cause possible drug interactions such as a potentiation of the effects of insulin and a decreased absorption of oral contraceptives (64). There are similar findings with respect to chromium picolinate (Table 2), whose data suggest risks caused by chromosome damage (65). This possibility was not confirmed later in animal experiments (66) or in studies involving humans (67). More recently, however, it was suggested that chromium picolinate enhances the rate of appearance of lethal mutations and female sterility in *Drosophila melanogaster* (68). Two clinical cases of young men who developed acute rhabdomyolysis were linked with chromium picolinate taken as part of an exercise regimen (69, 70). Severe renal impairment was reported in a 33-year-old woman who took chromium picolinate (71). Another case involved a 32-year-old man who ingested 1 mg chromium picolinate/d for 4 d and subsequently presented with acute generalized exanthematous pustulosis (72). Case reports are rarely conclusive evidence for establishing causality. These examples, however, indicate that risks may be involved when taking dietary supplements.

We aimed to identify all double-blind RCTs and all systematic reviews and meta-analyses based on double-blind RCTs. The potential incompleteness of the citation tracking is one of the limitations of this systematic review and, indeed, of systematic reviews in general. Although strong efforts were made to retrieve all relevant data, it is conceivable that some studies were not found. The distorting effects on systematic reviews arising from publication bias and location bias are well documented (73–75). In complementary medicine journals, positive findings may be overrepresented (76, 77), and positive conclusions may be favored at the expense of methodologic quality (78). There is also evidence for the tendency of positive findings to be published in English-language journals, (79) and for some European journals not to be indexed in major medical databases (80). It is therefore problematic to restrict literature searches to the language of publications and databases used. For this study we searched databases with a focus on the American and European literature and those that specialize in complementary medicine. There were no restrictions in terms of publication language. We are therefore confident that the search strategy minimized bias. The appraisal of the evidence involved a degree of judgment in some cases, which is another potential source of bias. However, we used a standard scale (12) to assess important criteria of methodologic quality. This scale was also used in 4 of the 5 systematic reviews and meta-analyses. The methodologic quality of the evidence was combined in an informal process with the type of evidence (eg, RCT or meta-analysis) and the volume of evidence to produce an indication of weight. This process of appraising the clinical evidence was performed independently by the 2 reviewers, which further minimized bias.

In conclusion, according to our findings, the evidence for most dietary supplements as aids in reducing body weight is not convincing. None of the reviewed dietary supplements can be recommended for over-the-counter use.

MP was responsible for the conception and design of the study. MP and EE were responsible for the drafting of the manuscript, critical revision of the manuscript for important intellectual content, and for final approval of the manuscript. Neither of the authors had any conflicts of interest.

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