TABLE 1 Prevalence of Coronary Artery Disease, Lower Extremity Peripheral Arterial Disease (PAD), and Cerebrovascular Disease in 110 Men With an Abdominal Aortic Aneurysm

	No. of Patients
Coronary artery disease	78 (71%)
Lower extremity PAD	50 (46%)
Cerebrovascular disease	30 (27%)

TABLE 2 Prevalence of Coexistent Coronary Artery Disease (CAD), Lower Extremity Peripheral Arterial Disease (PAD), and Cerebrovascular Disease in 110 Men With an Abdominal Aortic Aneurysm

	No. of Patients
CAD plus lower extremity PAD plus cerebrovascular disease	26 (24%)
CAD plus lower extremity PAD	24 (22%)
CAD plus cerebrovascular disease	4 (4%)
CAD only	24 (22%)
No CAD, lower extremity PAD, or cerebrovascular diseasee	32 (29%)

sectional area of ≥1 major coronary artery by atherosclerotic plaque.

In the present study of 110 men with an AAA, 71% had CAD, 46% had lower extremity PAD, and 27% had cerebrovascular disease. Twenty-four percent of the patients with an AAA had CAD plus lower extremity PAD plus cerebrovascular disease, 22% had CAD plus lower extremity PAD and no cerebrovascular disease, 22% had only CAD, 4% had CAD plus cerebrovascular disease and no lower extremity PAD, and 29% had no CAD, lower extremity PAD, or cerebrovascular disease.

These data show that there is a high prevalence of coexistent atherosclerotic vascular disease in patients with an AAA. Patients with an AAA should be screened for coexistent atherosclerotic vascular disease and should receive intensive risk factor modification.

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Safety and Efficacy of Citrus Aurantium for Weight Loss

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To examine the safety and efficacy of citrus aurantium, an herb now commonly used as a substitute for ephedra in dietary supplements marketed to promote weight loss, we conducted a systematic review. An extensive search of MEDLINE, EMBASE, BIOSIS, and the Cochrane Collaboration Database identified only 1 eligible randomized placebo controlled trial, which followed 20 patients for 6 weeks, demonstrated no statistically significant benefit for weight loss, and provided limited information about the safety of the herb. ©2004 by Excerpta Medica, Inc.

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On April 11, 2004, the Food and Drug Administration (FDA) banned the sale of dietary supplements containing ephedrine alkaloids because they present an "unreasonable risk of illness or injury."[1] This FDA action followed the publication of several studies that highlighted the potential dangers of ephedra.[2–4] Before the announcement of the FDA ban, it was estimated that approximately 2 million adults took ephedra-containing products daily.[5] In response to the ban, many manufacturers changed their supplement formulations to "ephedra-free" products by eliminating ephedra and substituting the herb citrus aurantium (also known as "bitter orange" and "sour orange"). For example, 8 of the former leading manufacturers of ephedra-containing dietary supplements now sell weight loss products that include citrus aurantium.[6] Citrus aurantium extract contains m-synephrine (phenylephrine),[7] a sympathomimetic drug, which primarily stimulates α-1 adrenergic receptors.[8] Because many former ephedra users may now be using citrus aurantium-containing products, we

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TABLE 1 Reported Weight Outcomes in the One Eligible Study of a Citrus-aurantium–containing Herbal Product for Weight Loss

Treatment Group*	Baseline Weight (kg)	Week 6 Weight (kg)	Percent Change	p Value†
Citrus aurantium (n = 9)	90.9 ± 17.5	89.5 ± 16	−1.5%	0.05
Placebo (n = 7)	83.6 ± 17.5	82.7 ± 18	−1.1%	0.10
No-placebo control (n = 4)	78.1 ± 11.5	77.7 ± 10.5	−0.5%	Not reported

*Exact contents of the treatments are noted in the text.
†The p values, as reported in the study, are from tests of within-group changes in weight.
Values are expressed as mean ± SD.

sought to examine the evidence regarding the safety and efficacy of this herbal remedy for weight loss.

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We searched MEDLINE, EMBASE, the Cochrane Collaboration Database, and BIOSIS for abstracts and articles of studies examining the efficacy of citrus aurantium for weight loss in humans from 1966 to 2004. In each database, we used a title word search for "citrus aurantium or bitter orange or sour orange" with no language restriction. Two reviewers (SB and AP) independently reviewed all titles and retrieved articles that were deemed potentially relevant. Articles were eligible for inclusion if they were randomized controlled trials examining the use of citrus aurantium alone or with other ingredients compared with a placebo and reporting the outcome of change in weight. Studies examining products containing citrus aurantium and ephedrine alkaloids were excluded, because ephedrine alkaloids are known to promote weight loss[2] and are now banned substances in dietary supplements. Two reviewers independently rated the quality of each included study with a frequently used, 5-point measure of study quality.[9]

The search identified 157 titles of which 7 were randomized controlled trials of products containing citrus aurantium. Six studies (3 of which were published in abstract form only) were excluded because the products contained ephedrine in addition to citrus aurantium (3 studies)[10–12] or weight loss was not reported (3 studies).[7,13,14] One study satisfied all inclusion criteria and was a 6-week, randomized, placebo-controlled trial involving 23 healthy subjects with a body mass index of >25 kg/m^2.[15] Patients were randomized to 1 of 3 groups: (1) an herbal mixture containing citrus aurantium (6% synephrine alkaloid) 975 mg, St. John's Wort (3% hypericum) 900 mg, and caffeine 528 mg; (2) a maltodextrin placebo; or (3) a control group without placebo. Subjects in all groups engaged in a 3-day/week exercise program and received dietary counseling. Outcomes were assessed at baseline, 3 and 6 weeks, and included change in weight, percent body fat, fat mass, and basal metabolic rate. The study received a quality score of 3 of 5 because the randomization technique was not described and reasons for the withdrawal of 3 subjects were not stated.

Table 1 lists changes in weight in the 3 treatment groups. The group receiving the citrus aurantium-containing product lost an average of 1.4 kg compared with an average loss of 0.9 kg in the placebo group and 0.4 kg in the no-placebo control group. The investigators performed statistical tests of within-group changes in weight and presented the p values for these tests (Table 1). They did not report a statistical test of a comparison of the change in weight between groups. The data presented in the study does not support the authors' statement that, "compared with subjects in the placebo and control groups, subjects in the treatment group lost a significant amount of body weight."[15] The study reported that there were no significant changes in the laboratory tests, blood pressure, heart rate, or electrocardiograms, but the data were not presented. No information about patient reports of adverse events was reported.

One randomized, controlled study that used a crossover design was excluded from the systematic review because it did not report a weight loss outcome, but it did present blood pressure and pulse changes in 12 subjects after consumption of fresh citrus aurantium juice compared with a water placebo (patients were not blinded).[7] Blood pressure and pulse were assessed hourly for 5 hours after consumption of the juice, which contained "approximately 13 to 14 mg of synephrine." Using a 2-way analysis of variance, the investigators stated that the citrus aurantium juice had no significant effects on blood pressure or pulse, but they did not provide confidence intervals to exclude clinically important changes in these hemodynamic measures.

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This systematic review found no evidence that the herb, citrus aurantium, is effective for weight loss. Safety information is extremely limited, and, because citrus aurantium contains the sympathomimetic drug m-synephrine (phenylephrine),[7] consumption of the herb may lead to increases in blood pressure, pulse, and the risk of adverse cardiovascular events.

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