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Ephedra for Weight Loss

By Adriane Fugh-Berman, MD, and Amy Allina

THE HERB EPHEDRA (*E. SINICA*), ALSO CALLED MA HUANG, HAS A long history of use in both Western and Eastern herbalism for asthma and other respiratory conditions; there are no reported cases of adverse events related to these traditional uses of this herb. The use of ephedra for weight loss, bodybuilding, boosting energy, or recreational purposes has no traditional precedent and cannot be considered safe. Targeted by the relentless advertising campaigns of the diet and weight loss industries—from diet drugs to gyms to trendy, fad diet books—women particularly are likely to use ephedra in an effort to lose weight.

Ephedra contains 0.5-2.0% alkaloids, primarily ephedrine (50-90% of alkaloids), as well as pseudoephedrine and others. A usual adult dose of ephedra for asthma is about 2 g of herb, which would contain about 13 mg total alkaloids. There is great variation, however, in dosage of products. One analysis of nine commercial supplements demonstrated a range of ephedrine-type alkaloids between 1.08-13.54 mg.[1]

Ephedrine is an orally active sympathomimetic amine, less potent but more long-acting than epinephrine. Ephedrine is an α-1 agonist and a non-selective β-agonist.[2] Systemic effects include bronchodilation, increased peripheral resistance, increased heart rate, increased blood pressure, urinary retention, increased respiratory rate, increased body temperature, and pupillary dilation.[3]

Risks

Sympathomimetic agents can be risky in people with underlying cardiovascular disease, cerebrovascular disease or abnormalities, prostatic hypertrophy, thyroid disorders, or those on monoamine oxidase inhibitors (MAOIs).

Ephedra was in herbal "Ecstasy," used by teenagers to get high. Between 1993 and 1997, the Food and Drug Administration received reports of 34 deaths and about 800 medical and psychiatric complications associated with ephedra-containing products.[3]

Ephedrine-induced psychosis and episodes of mania are

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well-documented. Ephedrine has been associated with chest pain in adolescents.[4] Ephedrine also has been associated with kidney stones. A kidney stone database has analyzed more than 200 stones containing ephedrine, norephedrine, and pseudoephedrine.[5]

Combinations with other sympathomimetics may increase the risk of harm; one ephedra/caffeine product has been linked to the sudden death of a 23-year-old[6] and another product was used successfully for suicide.[7] A case of a severe MAOI interaction has been reported with phenelzine and an ephedrine product that also contained caffeine and theophylline.[8]

Cardiovascular Effects

Increased heart rate has been seen in most trials of ephedrine for weight loss; increases in blood pressure are less consistent and probably are more likely to occur early in use. In one trial, 12 normotensive adults (including six women) ages 23-40 were given four capsules (375 mg each) of a ma huang product. Heart rate and blood pressure were measured at baseline and eight and 17 hours after ingestion. Half of the participants experienced a statistically significant increase in 12-hour heart rate (from approximately 72 beats per minute to 81 beats per minute).[9] Between hours 8 and 11, four participants had statistically significant increases in systolic blood pressure while two had significant decreases in diastolic blood pressure. Significant increases in heart rate were seen approximately 42 minutes after ingestion of ephedrine sulfate (50 mg) in another study.[10]

Most studies of ephedrine for weight loss did not find a significant adverse effect on blood pressure; however, few trials included hypertensives. One trial included participants with diastolic blood pressure up to 110;[11] the report does not state how many subjects were hypertensive, and data on these patients are not broken out. Another trial of an ephedrine/caffeine combination included treated hypertensives and found that diastolic and systolic pressures decreased in both hypertensive and normotensive subjects.[12] Because hypertensive patients are most sensitive to compounds that increase blood pressure, more research must be done in this area.

Clinical Trials for Weight Loss

There are no well-established indications for the use of dietary supplements containing ephedra alkaloids. Ephedra increases thermogenesis, as do many sympathomimetic agents, but trials of ephedra or ephedra/caffeine combinations have not shown consistent or dramatic results on weight loss (*see Table 1*) and have shown significant adverse effects. Most trials are small, and dropout rates have been notably high.

The use of ephedra for the treatment of respiratory conditions probably is not dangerous and, given the bronchodilating effects of ephedrine, probably is effective. However, no methodologically acceptable clinical trials of efficacy of ephedra preparations for respiratory ailments were identified.

There is some evidence that a caffeine/ephedrine combination can improve aerobic exercise performance, but the treatment increases heart rate and the incidence of nausea and vomiting has been as high as 25%.[13,14]

Individual sensitivity can be established only retrospectively, after an adverse event has occurred. Some people are more susceptible than others; as with cocaine, the majority of stroke cases associated with ephedrine occur in people with cerebral vessel abnormalities.[3] However, such abnormalities are not uncommon and rarely are known to those who have them.

While ephedra is associated with more adverse reactions when combined with caffeine or phenylpropanolamine, intracerebral hemorrhage has been associated with the use of ephedra alone.[3] There probably are several subpopulations for whom ephedra is more dangerous, but at this time we do not have enough information to identify these subpopulations. Virtually all adverse effects associated with the use of ephedra alkaloids have occurred when it was used for weight loss, exercise enhancement, energy enhancement, or recreational use.

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Table 1

Randomized controlled trials of ephedra for weight loss*

Author	N/Duration	Treatment	Result	Comment
Astrup[11]	180 obese subjects (141 completed) x 24 weeks	Diet (4.2 MJ) and 20 mg E vs. 200 mg C vs. 20/200 mg E/C	E/C significantly better than C or P; Weight loss (kg): E/C 16.6; E 14.3; C 11.5; P13.2	More AE in both E groups (including dizziness, headache, tremor, psychiatric, insomnia, dry mouth, tachycardia). Withdrawals because of AE: E/C = 3, E = 1, C = 2. No difference in BP or HR.
Astrup[15]	14 obese women x 8 weeks	Diet (4.2 MJ/d) and 20/200 mg E/C tid vs. P	No significant difference in weight loss between groups	E/C group lost significantly more body fat and less fat-free mass.
Buemann[16]	32 overweight women x 8 weeks	Diet (4.2 MJ/d) and 20/200 mg E/C tid vs. P	No significant difference in weight loss between groups	Total cholesterol decreased in both groups; HDL decreased in P but not E/C group.
Breum[17]	103 overweight subjects (81 completed) x 15 weeks	20/200 mg E/C tid vs. 15 mg DF bid	No significant difference between groups; weight loss (kg): DF 6.9; E/C 8.3. In those with BMI > 30, weight loss significantly different (7.0 kg vs. 9.0 kg)	Withdrawals because of AE: E = 6, 1 death; DF = 2. Forty-three percent of DF group and 54% of E/C group had S/E. No differences in HR or BP.
Cesari[18] (abstract only)	20 obese women x 4 months	50 mg E tid (n = 6;) 50 mg E + 100 mg C tid (n = 7); or P (n = 7)	No significant difference in weight loss or BMI	
Daly[19]	29 obese subjects (24 completed) x 8 weeks	P or 75 mg E + 150 mg C + 330 mg ASA/d x 4 weeks, then 150 mg E + 150 mg C + 330 mg ASA/d x 4 weeks`	Significant difference between groups; weight loss (kg): ECA 2.2; P 0.7	No significant difference in BP or HR between groups. One subject in 150 mg group developed hypertension.
Mancini[20] (abstract only)	42 overweight women (32 completed) x 8 weeks	Low-calorie diet and 22 mg E + 20 mg C + 50 mg aminophylline tid	P lost 2.2 kg, ECA lost 4.5 kg (apparently significant)	7/22 ECA dropped out (2 for SE: insomnia, dyspepsia), 3/19 P dropped out.
Pasquali[21]	22 obese women (20 completed) x 4 months	Diet (4,180-5,016 Kj/d) and 50 mg P or E tid or 50/100 mg E/C tid	No significant difference among groups	

E = ephedrine, C = caffeine, P = placebo, ASA = aspirin, AE = adverse event, SE = side effect, HR = heart rate, BP = blood pressure, DF = dexfenfluramine

*Four Danish studies were omitted for lack of translation resources

Conclusion

Ephedra should not be available in products labeled or marketed for weight loss, bodybuilding, energy enhancement, or recreational use; the only indication for which ephedra products should be labeled is respiratory conditions. For traditional uses in traditional forms, ephedra does not seem to be hazardous. The uses of ephedra for weight loss, exercise enhancement, or as an "energizer" are not traditional uses, and any dose at which these effects occur is an overdose.

Ephedrine is available in several oral over-the-counter (OTC) drugs used to treat asthma; recommended dosages on these OTC drugs allow up to 150 mg/d ephedrine. ❖

Dr. Fugh-Berman is Editor of Alternative Therapies in Women's Health *and Ms. Allina is program director, National Women's Health Network, Washington, DC.*

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Clinical Abstracts

With Comments by Adriane Fugh-Berman, MD

Dieting Depresses

Source: Smith KA, et al. Impaired regulation of brain serotonin function during dieting in women recovered from depression. *Br J Psychiatry* 2000;176:72-75.

Design/Setting/Subjects: Nineteen women with at least one episode of DSM IV major depression who were fully recovered and had not taken medication for at least six months. The control group consisted of 23 women with no personal or family history of any Axis I psychiatric disorder. Subjects were placed on a three-week calorie controlled diet of 1,000 kcal/d. Subjects completed a daily diary of what they ate and recorded scores on visual analog scales (happy, sad, and irritable). Neuroendocrine testing utilizing prolactin response to intravenous tryptophan infusion was done at baseline (during the early to mid-follicular phase of the menstrual cycle) and again at the end of the third week of dieting. Subjects waited a week after the first neuroendocrine test before beginning to diet so that neuroendocrine testing could be done in the same time of the cycle.

Results: Twenty-five subjects successfully completed the three-week protocol. Prolactin responses to tryptophan were similar in both groups prior to dieting. Dieting significantly decreased baseline tryptophan levels in both groups. After dieting, however, prolactin response to tryptophan infusion increased in the control group but not in the formerly depressed group. Relative to the control group, VAS ratings in the formerly depressed group were lower

for the " happy" scores; there was no difference in "sad" or "irritable" scores.
Funding: Medical Research Council.
Comment: Some of the mechanics of this interesting study lost me; the protocol for neuroendocrine testing is quite complicated, and apparently women who did not lose at least 2 kg on the diet were dropped from analysis because prior work by the authors showed that such patients do not reliably increase prolactin response to tryptophan. But the authors sound reasonable enough. Depressed patients are known to show blunted endocrine responses to tryptophan, but the authors counter that potential criticism by pointing out that these responses normalize with clinical recovery. The concept that women vulnerable to major depression show impaired regulation of brain serotonin function during calorie-restricted diets has obvious clinical implications. ❖

Citrus aurantium for Weight Loss

Source: Colker CM, et al. Effects of *Citrus aurantium* extract, caffeine, and St. John's wort on body fat loss, lipid levels, and mood states in overweight healthy adults. *Curr Ther Res* 1999;60:145-153.

Design/Setting/Subjects: A double-blind, randomized, placebo-controlled, three-armed study of 23 subjects with a body mass index more than 25 kg/m^2. Subjects were divided into three groups; one group received treatment, one group received a maltodextrin placebo, and one group received nothing. All were counseled by a dietitian on how to follow an 1,800 calorie American Heart Association Step 1 diet and performed a weight circuit training exercise program three days a week under the direction of an exercise physiologist.
Treatment/Dose/Route/Duration: A product containing 975 mg *Citrus aurantium* extract (containing 6% synephrine alkaloid), 528 mg caffeine, and 900 mg St. John's wort (3% Hypericum [sic]) daily for six weeks.
Outcome Measures: Weight, fat loss, mood (Profile of Mood States questionnaire), blood lipids, blood pressure (BP), heart rate, EKG findings, serum chemistries, urinalysis.
Results: Twenty subjects completed the six-week study (nine in the treatment group, seven in the placebo group, and four in the control group). Subjects in the treatment group lost a significant amount of weight (1.4 kg) compared to the placebo group (which lost 0.9 kg) and control group (which lost 0.04 kg). The treated group lost 2.9% of fat while no significant changes in percent body fat lost were seen in the placebo or control groups. No significant changes were seen in any group in the profile of mood states questionnaire, blood lipids, BP, heart rate, EKG, serum chemistries, or urinalysis. The treated group had a significant increase in basal metabolic rate while the placebo group had a significant decrease in basal metabolic rate; there was no change in the control group. No side effects were reported.
Funding: Twin Laboratories, Inc. Hauppage, NY.
Comments: This very small study found an additive effect of a *Citrus aurantium* product in short-term weight loss. No justification is given for having both a placebo and an untreated control group, and the latter comprised only four subjects. It was difficult for me to believe that the difference in weight loss between the treated group (1.4 kg) and the placebo group (0.9 kg) was significant; half a kilo equals 1.1 pounds. I'm still not convinced. Although the text states that the treated group lost a significant amount of weight compared to the placebo and untreated groups, the table appears to indicate that the difference is significant compared to baseline but not in comparison to the other groups.

There is no evidence that St. John's wort has any effect on weight loss or appetite suppression (although there is clear evidence of efficacy for depression). And since dieting can be depressing, maybe this is not an unreasonable addition. I assume that the "3% hypericum" is a typo (hypericum is the same as St. John's wort) and actually means 3% hypericin, in which case the dose of St. John's wort in this product would be a therapeutic antidepressant dose. It should be kept in mind that St. John's wort interacts with a number of drugs, including cyclosporine, digoxin, theophylline, and SSRIs.[1] There is a lot of caffeine in this product; the equivalent of about four cups of coffee or 10 cups of tea. Caffeine has a thermogenic effect, and this effect is synergistic with other sympathomimetic agents. Even 100 mg caffeine has a thermogenic effect lasting one to two hours; dosages higher than 600 mg/d increase 24-hour energy expenditure under respiratory chamber conditions.[2]

Citrus aurantium contains synephrine and octopamine, which are phenolamines found in mammalian organs and sympathetic nerve fibers—in the same region as adrenaline and noradrenaline. Synephrine is structurally similar to adrenaline, and octopamine is similar in structure to noradrenaline (they differ only in the number of hydroxyl groups on the aromatic ring).[3] P-synephrine has antidepressant effects in mice; in oral doses from 1-10 mg/kg, p-synephrine decreased the duration of immobility in the tail suspension test and forced swimming test (doses of 30 mg/kg were ineffective).[4] Administration of an alpha-1 adrenoreceptor antagonist blocked the effect. Besides modulating the activation of alpha adrenoreceptors, both synephrine and octopamine appear to inhibit cyclic adenosine monophosphate production.[3] Beta-3 adrenoreceptors also are activated by synephrine and octopamine. Beta-3 adrenoreceptor agonists are full lipolytic agents in rats, hamsters, and dogs, but are much less active in humans and guinea pigs. Synephrine is partially active in stimulating lipolysis in rats, hamsters, dogs, guinea pigs, and humans.[5] Of agents tested, octopamine was more potent; of several amines, only octopamine fully stimulated lipolysis in rats, hamsters, and dogs; it was inefficient in humans and guinea pigs.

Sympathomimetic agents in sufficient doses speed metabolism and may result in weight loss. Given growing concerns with ephedra, products containing synephrine and octopamine are apt to be the next wave in "natural" weight loss products. However, any sympathomimetic agent taken in sufficient dosages to cause weight loss cannot be

presumed to be safe, especially in those with cardiovascular disease. ❖

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B_{12} Deficiency and Depression

Source: Penninx BW, et al. Vitamin B (12) deficiency and depression in physically disabled older women: Epidemiologic evidence from the Women's Health and Aging Study. *Am J Psychiatry* 2000;157:715-721.

Design/Setting/Subjects: Cross-sectional study in 700 disabled, nondemented community dwelling women over 65 years old (a subset of the Women's Health and Aging Study, a prospective cohort study of the causes and course of physical disability in a sample of physically disabled older women.) The mean age of participants was 77.3 years. Twenty-eight percent were African-American. Serum levels of vitamin B_{12}, folate, methylmalonic acid, and total homocysteine were assayed.

Results: Depressed women were more likely to be less educated, more likely to be white, and had more chronic diseases and disability in activities of daily living. Depressed subjects had significantly higher serum methylmalonic acid levels. Metabolically significant vitamin B_{12} deficiency was present in 14.9% of the 478 nondepressed subjects, 17% of the 100 mildly depressed subjects, and 27% of the 122 severely depressed women; the difference between depressed and nondepressed women was significant. Homocysteine, folate, anemia, and serum vitamin B_{12} were not associated with depression status. The authors conclude that metabolically significant vitamin B_{12} deficiency was associated with a doubled risk of severe depression.

Funding: National Institute on Aging.

Comments: Of course, correlation does not prove causation, but there are several plausible explanations for why low levels of B_{12} might predispose one to depression. The authors point out that vitamin B_{12} deficiency affects serotonin and catecholamine synthesis, and that vitamin B_{12} is required for the synthesis of S-adenosylmethionine (SAM-e, currently a popular dietary supplement for which there is some evidence of efficacy for depression). However, in this study methionine levels were normal in severely depressed women and were not significantly different from subjects who were not depressed. Another explanation for the link is that depression could cause low vitamin B_{12} levels through decreased food intake; this was judged unlikely as serum folate levels (sensitive to food intake) were not different across groups, nor was the number of subjects who reported weight loss during the previous year. Severe B_{12} deficiency can cause a variety of psychiatric manifestations including depression, and lesser states of deficiency may also be implicated. Cobalamin is nontoxic even in high doses and should be tested as a treatment for depression. ❖

Green Tea for Weight Loss

Source: Dulloo AG, et al. Efficacy of a green tea extract rich in catechin polyphenols and caffeine in increasing 24-h energy expenditure and fat oxidation in humans. *An J Clin Nutr* 1999;70:1040-1045.

Objective: To determine whether a green tea extract could increase energy expenditure (EE) and fat oxidation in humans.

Design/Setting/Subjects: Crossover study in 10 healthy men (subjects acted as their own controls) utilizing a respiratory chamber at the University of Geneva, Department of Physiology.

Treatment/Dose/Route/Duration: On separate occasions subjects were given green tea extract (50 mg caffeine and 90 mg epigallocatechin gallate); caffeine (50 mg); or placebo, which they ingested at breakfast, lunch, and dinner.

Outcomes: 24-hour EE, respiratory quotient (RQ), and urinary excretion of nitrogen and catecholamines.

Results: Ingestion of green tea extract resulted in a significant increase in 24-hr EE (4%, $P < 0.01$) and a significant decrease in 24-hr RQ (from 0.88 to 0.85, $P < 0.001$) with no change in urinary nitrogen. Norepinephrine excretion was 40% higher during treatment with green tea than with placebo ($P < 0.05$). Caffeine had no effect on EE, RQ, urinary nitrogen, or urinary catecholamines. No significant changes in heart rate were noted during he first eight hours the subjects were assessed.

Funding: In part by Arkopharma laboratories and by the Swiss National Science Research Fund.

Comment: Well, this should cause widespread shortages of green tea. In the Chinese side of my family—where eating combines art, sport, and religion—copious amounts of tea were considered antidotal to the semi-comatose state induced by banquets. The explanation tendered was that tea "washed the fat off the sides of the stomach." OK, maybe it wasn't the right mechanism, but my relatives may have had a point; green tea does seem to burn calories.

This study seems to show a clinically significant difference. The authors state that thermogenesis is assumed to contribute 8-10% of daily EE in a typical sedentary man. The green tea extract increased 24-hr EE by 4%, which would extrapolate to a 35-43% increase in the thermogenesis compartment of daily energy expenditure. They didn't calculate further, but if I am extrapolating correctly, that means that green tea could cause on the order of a 3% increase in daily EE.

Caffeine is known to be thermogenic (and, for some of us, life-sustaining), but not in the doses used in this study, which

the authors admit; only doses of caffeine > 100 mg can cause a thermogenic effect for 1-2 hours, and 600-1000 mg/d is necessary to affect 24-hr EE in the respiratory chamber. The dosage of caffeine was reasonably chosen to equal the amount in the green tea extract, and this experiment does demonstrate that green tea has some thermogenic qualities that are not caused by caffeine alone. One possible explanation is that flavonoids, called catechins, in tea inhibit COMT, the enzyme that degrades norepinephrine (which helps to control thermogenesis and fat oxidation).

Capsaicin (the compound that provides the heat in chili peppers) has also been shown to stimulate thermogenesis and fat oxidation in humans, but that's probably obvious to anyone who has doffed a jacket and mopped a brow after a good curry. So hot food and green tea may be a good combination for those watching their weight. ❖

CME Questions

17. Ephedrine has been associated with:
a. intracerebral hemorrhage.
b. kidney stones.
c. psychosis.
d. All of the above

18. Adverse effects have been reported with ephedra products:
a. in weight loss and bodybuilding products.
b. in traditional Chinese medicine prescriptions.
c. in weight loss and bodybuilding products and traditional Chinese medicine prescriptions.

19. Traditional use of ephedra is for:
a. weight loss.
b. treating fatigue.
c. respiratory conditions.

20. Synephrine and octopamine are:
a. methylxanthines.
b. sympathomimetic phenolamines.
c. pyrrolizidine alkaloids.

21. A recent study found that vitamin B_{12} deficiency was:
a. more common among depressed patients.
b. less common among depressed patients.
c. equally common among depressed and non-depressed patients.

Label Review

With Comments by Adriane Fugh-Berman, MD

Hollywood 48 Hour Miracle Diet®

Package Information

"Lose up to ten pounds in 48 hours!"

"Lose weight while you cleanse, detoxify and rejuvenate your body!"

"Congratulations on taking the first step! You are just 48 hours away from looking and feeling better. I know, I created this product to help me with my own weight problem. It worked for me and it can work for you too." Jamie Kabler, "The Diet Guru"

Suggested Usage

Day one: Mix one four ounce serving of concentrate with four ounces of bottled water. Sip over the next four hours. Repeat this three more times during the rest of the day. Day two: Repeat above. For best results use once a month.

Important: Do not eat food, alcohol, caffeine or tobacco while on " Hollywood 48 Hour Miracle Diet." Drink eight glasses of water each day. Shake well before each use. Refrigerate after opening. Use before the expiration date on the top of the cap. Always consult physician before beginning any weight loss program.

Supplement Facts

Serving size: 4 fl ounces (237 ml)

Servings per container: 8

Amount per serving
calories: 100 (energy)
calories from fat: 0

	% daily value
total fat 0 g	0%
Cholesterol 0 mg	0%
sodium 20 mg	2%
Total Carbohydrates 25	9%
Sugars 22 g	
Protein 0 g	
Vitamin A	75%
Vitamin C	75%
Vitamin D	75%
Vitamin E	75%
Thiamin	75%
Riboflavin	75%
Niacin	75%
Vitamin B_6	75%
Folic acid	75%
Vitamin B_{12}	75%
Biotin	75%
Pantothenic acid	75%

Ingredients: purified water, pineapple, apple, orange and grapefruit concentrates, apricots, peach and banana purees, vitamin palmitate, vitamin D, vitamin E acetate, ascorbic acid (vitamin C), thiamin mononitrate (vitamin B_1), riboflavin (vitamin B_2) pyridoxine hydrochloride (vitamin B_6), cyanocobalamin (vitamin B_{12}), niacin, folic acid, pantothenic acid, biotin and a special blend of essential oils of bergamot, tangerine, lemon, orange, and lavender.

The statements contained herein have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

Manufactured by Aspen Products, Inc., 1800 E. Sahara Blvd., Ste. 107, Las Vegas, NV 89104

Price: 32 fl. oz. (1 qt; 947 ml), $19.90

Comments

This was the ultimate sacrifice. After unsuccessfully trying to palm this product off on various friends, colleagues, or anyone I met who mentioned that they wanted to lose a few pounds, I came to the grim conclusion that I would have to try this product myself. In the spirit of experimentation I actually consumed nothing but this juice for 24 hours. (My friends, on reading this, are frantically dialing 911; I have never voluntarily skipped one of my five, preferably hot, meals a day.) No, I am not overweight, and, yes, everyone hates me. This background is provided not only to ensure that the readers understand what an enormous sacrifice I have made for you, but also to point out that I have an atypical metabolism, and results from this extremely sloppy experiment should be interpreted in light of that fact.

The product tastes mainly of pineapple and apricots; it is not very sweet, especially diluted with water. It's not bad. It does seem to have an appetite suppressant effect; I did not feel all that hungry. Homicidal, yes, but not particularly hungry. Apologies to anyone I snapped at during the National Women's Health Network board meeting. I ignored the restriction on caffeine (sacrifices have their limit) but I didn't eat for 24 hours. According to the bathroom scale in the building where the meeting was held, I lost four pounds. However, skipping a day of food probably would cause me to lose four pounds even without magic juice. (I have no data to back that statement up and, no, I'm not going to find out!) I believe the weight was regained within a few days, but I don't really know because the meeting ended and I don't own a scale on the grounds that scales are evil devices whose threat to women's self-esteem is rivaled only by fashion and beauty magazines. So, in summary, efficacy was demonstrated in an uncontrolled, n-of-1 study with a noncompliant, metabolically atypical patient using a (literally) unvalidated scale.

So, did I risk anything besides the lives of my fellow meeting-goers? Probably not. This product contains essential oils of bergamot, tangerine, lemon, orange, and lavender, in unspecified amounts. Species names are not given, so one can't tell, for example, whether the "orange" referred to is bitter or sweet. This isn't a specific criticism of this product; citrus oils are considered GRAS (generally recognized as safe) and commonly are used as food flavorings and additives. Manufacturers are not required to state the amount present nor the botanical name (in fact, the only clue on some labels that essential oils are present may be the term "natural flavoring").

Bitter orange (*Citrus aurantium*) contains synephrine and octopamine, sympathomimetic phenolamines that probably are the active ingredients in this drink.[1] Bitter orange also contains 89-96% d-limonene. Bergamot orange (*Citrus bergamia*), the flavoring in Earl Grey tea, contains linalyl acetate 36-45%, limonene 28-32%, and linalool 11-22%. Lemon (*Citrus limon*) contains primarily d-limonene 70%. Tangerine (*Citrus reticulata*) contains tangaretin. Lavender contains linalool, linalyl acetate, and camphor; true lavender (*Lavandula angustifolia*) is low in camphor. Other lavender species (*L..intermedia, L. stoechas*) can contain up to 30% camphor, but, according to *Alternative Therapies in Women's Health* board member Tieraona Low Dog, MD, camphorous lavender generally is not sold because it smells bad! A good thing, since camphor is notably epileptogenic.

None of the other ingredients are particularly toxic. D-limonene, the most common isomer of limonene, is nontoxic in humans and most animals (toxicity has been demonstrated only in one strain of male rat). Several compounds could cause photosensitivity. The psoralens bergapten is found in some preparations of bergamot and lemon oil (however, most companies use bergapten-free oil), and bitter orange contains phototoxic oxypeucedanin.

Linalool is known to have some sedative effects. Besides synephrine and octopamine, no other compounds in this mixture have been linked to appetite suppression or weight loss to my knowledge (and no information on such an effect was identified in a MEDLINE search).

Little is known about the effects of synephrine or octopamine in humans. One trial of a weight loss product containing synephrine has been published.[2] (*See page 85.*) Sympathomimetics would be expected to increase heart rate and blood pressure, and cannot be presumed safe in those with cardiovascular disease. Products containing synephrine or octopamine should at least be labeled with the amount. Short- and long-term safety of these amines should be established before we can recommend their use by patients. ❖

References

1. Tisserand R, Balacs T. *Essential Oil Safety*. Edinburgh: Churchill Livingstone; 1995.
2. Colker CM, et al. Effects of *Citrus aurantium* extract, caffeine, and St. John's wort on body fat loss, lipid levels, and mood states in overweight healthy adults. *Curr Ther Res* 1999; 60:145-153.

In Future Issues:

Omega-3 Fatty Acids and High-Risk Pregnancy
Menstrual Disturbances and Vegetarianism