Supplement Performance
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Low-Dose Ephedra/Caffeine Mixture is an Effective and Reasonably Safe Fat-loss Aid

“While ephedra might be more dangerous than, say, a multivitamin, its risks, which stem mainly from stimulating the cardiovascular system, are well within the range considered acceptable for OTC [over-the-counter] drugs. The FDA, the medical establishment and the pharmaceutical industry all want to prevent the emergence of an alternative drug market in which consumers can obtain cheap, effective and reasonably (though not completely) safe products without permission from the government’s gatekeepers.” —Jacob Sullum, The Washington Post

Basic Facts about Ephedrine/Ephedra

Ephedrine is classified as a sympathomimetic drug and central nervous system stimulant. Its ability to suppress appetite and increase thermogenesis (production of heat) has led to its use in weight loss/fat loss. Ephedrine alone isn’t very effective as a fat-loss agent; however, caffeine clearly enhances its effectiveness. It’s been estimated that about 80 percent of weight loss from a ephedrine/caffeine mixture is due to the appetite suppressing and 20 percent is due to a thermogenic effect. There’s also evidence that ephedrine spares muscle mass and prevents a drop in the resting metabolic rate associated with calorie restriction.

In addition, ephedrine is used as a performance-enhancing substance (ergogenic aid). For example, Jacobs and colleagues reported that ephedrine ingestion, either alone or in combination with caffeine, can lead to a significant increase in the number of repetitions that can be performed and the total amount of weight that can be lifted during weight training. In fact, the magnitude of the ergogenic effect is highly significant for gym rats since only 90 minutes after ingesting caffeine plus ephedrine a 16 percent improvement in bench press performance was reported.

In most dietary supplements, ephedrine used to appear as an extract from one of two sources: ephedra or ma huang. Although the ephedra species have a long tradition of use (more than 5,000 years) for respiratory ailments, in 2004, the U.S. Food and Drug Administration (FDA) decided to ban ephedra-containing supplements. According to Health and Human Services Secretary Tommy G. Thompson, “This FDA rule reflects what the scientific evidence shows—that ephedra poses an unreasonable risk to those who use it.”

Some feel ephedra extract is safer than pharmaceutical ephedrine based on the fact that the LD50, which refers to the amount of a material that causes death in 50 percent of test animals, is lower for the botanical extract (5.4 grams per kilogram of bodyweight) as compared to the LD50 for pharmaceutical ephedrine (64.9 milligrams per kilogram). Nevertheless, the FDA didn’t ban ephedrine. This decision may have something do with fact that the FDA has strong financial connections with the pharmaceutical industry.

Ephedrine as a Fat-loss Agent

The history of ephedrine as a weight-loss/fat-loss agent is rather interesting. In 1972, Dr. Erikson, a Danish general practitioner in Elsinore, Denmark, noted unintentional weight loss when he prescribed a compound containing ephedrine, caffeine and Phenobarbital to patients he was treating for asthma. By 1977, over 70,000 patients were taking the “Elsinore Pill,” and one Danish pharmaceutical house was reportedly producing one million tablets a week!

As you may know, MD Publisher and Editor-in-Chief Steve Blechman is a former TwinLab® big boss and he launched the first commercial ephedra-containing fat-loss supplement (Ripped Fuel), which was extremely popular among serious gym rats simply because it worked and had few, if any, adverse effects when used as directed. Indeed, numerous well-controlled clinical studies support this contention. The latest study was just published in the International Journal of Obesity, a leading peer-reviewed scientific journal in the area of obesity research.

New Study Confirms Safety of Low-Dose Ephedra/Caffeine Mixture

The purpose of the recent study by Hackman and co-workers at the University of California was to determine the safety and efficacy of a low-dose ephedrine/caffeine mixture in 61
overweight/obese women. This study was a nine-month, double-blind, randomized control study comparing the efficacy and safety of a dietary supplement containing ephedra, caffeine (guarana), high potency vitamins and minerals, omega-3 fatty acids and a host of other botanical extracts to a control supplement (i.e., an inactive fake supplement containing only some vitamins/minerals). The active supplement provided 40 milligrams per day of ephedrine and 100 milligrams per day of caffeine.

As expected, women receiving the ephedra/caffeine mixture lost significantly more bodyweight (7.18 kilograms) and body fat (5.33 kilograms) than the control group (2.25 and 0.99 kilograms, respectively) and showed significant improvements in blood lipids. Furthermore, the ephedra/caffeine group reported more energy and decreased appetite compared to controls and scored higher on a quality of life domain assessing vitality. Importantly, the ephedrine/caffeine mixture didn’t cause any major adverse side effects. However, minor symptoms included dry mouth, insomnia, nervousness and palpitations. The incidence of dizziness and headache were similar between groups. The authors concluded that “a low-dose of ephedra alkaloids and caffeine combined with a broad spectrum multinutrient supplement and other botanical extracts may be a useful option to help physicians and patients with safe and effective weight loss.”

As pointed out by the authors, the mean weight loss in the group of women taking the ephedrine/mixture in this study was similar to the mean weight loss found in obese patients treated with orlistat in addition to calorie restriction. In other words, this study clearly demonstrated that the ephedra/caffeine mixture is a more effective fat-loss agent than orlistat, a prescription drug approved by the FDA. Orlistat blocks the absorption of almost one-third of ingested fat. The side effects of orlistat are rather annoying: flatulence, increased defecation, fecal urgency, fatty/oily stool, etc. So, if you’ve just started to date some hot babe, orlistat is clearly not your drug of choice. I would rather have a dry mouth than excessive gas in the alimentary canal!

It’s worth noting that the formula used by Hackman et al., also contains hydroxycitric acid (HCA), which is a popular ingredient in fat-loss supplements, but studies on its fat-loss enhancing effects are controversial. In a recent study by Drs. van der Haar and co-workers, the effects of three different HCA-containing preparations (Regulator, Citrin K, CitriMax®) on food intake and bodyweight were studied in rats. The conclusion was that these commercially available HCA preparations exert striking differences in efficacy in inhibiting voluntary food intake in rats. Specifically, Regulator and Citrin were potent suppressants of food intake, whereas CitriMax exerted much smaller effects on food intake.

Are the Adverse Effects Greatly Exaggerated?

In a comprehensive study by Blechman and colleagues at the New York School of Medicine and City and County of San Francisco Hall of Justice, the investigators reviewed all autopsies in their medical examiners’ jurisdictions, from 1994 to 2001, where ephedrine or any of its isomers were detected. Toxicology testing results were tabulated and anatomic findings in ephedra cases were compared to those in a control group of drug-free trauma victims.

Of 127 ephedra cases, 33 were due to trauma, i.e., an injury caused by an extrinsic (outside of a body) agent. Furthermore, more than 88 percent (113/127) of the decedents also tested positive for other drugs, the most common being cocaine and morphine. The authors stated, “What is most surprising about the results of this study is that of the cases where only ephedrine alkaloids were detected, only one possible case of ephedrine toxicity occurred in San Francisco from 1994 to mid-1999. This data contradicts the recent, well-publicized case reports suggesting that large numbers of ephedrine-related deaths were occurring and that only a fraction are being reported to the FDA.”

More recently, Ray and co-workers reported that the ingestion of an ephedrine/caffeine mixture (plus other herbal extracts and omega-3 fatty acids) for one year doesn’t significantly alter normal blood chemistry or induce any irreversible histological changes in the mouse heart, even
though their study employed up to 10 times the normal human consumption dose of ephedra. Collectively, these studies suggest that the adverse effects of ephedra are greatly exaggerated.

In contrast, some clinicians feel that ephedra may pose significant risk. Andrews and co-workers at the Beth Israel Medical Center reviewed the available literature and concluded that more stringent oversight by regulatory authorities is required to minimize the incidence of adverse events. The authors rightly stated, however, that, “No clinical trial has reported major adverse cardiovascular events (stroke, myocardial infarction, or malignant arrhythmias) associated with the use of ephedra alkaloids for weight loss.”

They also cited numerous case reports purportedly showing that adverse cardiovascular and cerebrovascular effects, including stroke, myocardial infarction and sudden death, are related to ephedra use. Many of these case reports are very dubious and some of them had nothing to do with ephedra products. For example, Andrews et al., stated, “Myocardial ischemia has also been reported when ephedra alkaloids are combined with other medications that cause increased adrenergic tone, such as bupropion,” citing the case report by Pedersen. In reality, the patient’s medication history revealed recent commencement of bupropion (Zyban®) for smoking cessation and pseudoephedrine as a non-prescription influenza remedy. In sum, the review paper by Andrews et al., was poorly peer reviewed.

Surprisingly, there’s a recent study showing that a single dose of an ephedra/caffeine supplement can produce significant increases in blood pressure and resting heart rate in healthy young adults. Call me a skeptic, but this report smells like old fish. You see, the first and third authors of this paper have served as “expert witnesses” in litigation involving manufacturers of dietary supplements that contain ephedra. These authors are outspoken critics of ephedrine supplements and just happen to be the authors of the only published study purportedly showing that a single dose of ephedra/caffeine (taken in recommended doses) can produce significant cardiovascular and metabolic changes. However, some 20 percent of patients have blood pressures significantly higher in the doctor’s office than at home (“white coat hypertension”) simply because emotions increase the cardiac output and peripheral resistance and thus arterial pressure. Thus, one can’t draw any conclusions based on such a single-dose study.

Finally, the purpose of the recent “study” by Dr. Wool and colleagues was to compare toxicity from botanical products containing ephedra to non-ephedra products. They utilized the Toxic Exposure Surveillance System (TESS; a national poison center database) to determine the number and outcomes of cases involving botanical products reported from 1993-2002. The authors concluded, “Hazard rate analysis suggests poison center-reported events involving ephedra-containing botanical products were much more likely to result in severe medical outcomes than those involving nonephedra-containing botanical products.”

These well-meaning authors apparently didn’t read the comment published in the Annals of Internal Medicine in 2003 blasting another ephedrine-related TESS study. In their comment, researchers at the PROSAR International Poison Control Center and International Toxicology Consultants stated, “The TESS report does not provide the percentages of individual products or categories in which the exposure is coded as unrelated, rendering the results presented in Bent and colleagues’ work invalid. Furthermore, Bent and colleagues don’t make clear that most of the ephedra cases described in TESS involve botanicals with many active ingredients. There’s no consideration of severity, ephedrine dose, duration of use, purity, contaminants, underlying health status, or other substances contemporaneously consumed. Comparing ephedrine with ‘other herbs,’ the actions and indications of which are distinct, is toxicologic nonsense.” In other words, such TESS-studies can’t be taken seriously.

**Bottom Line**

A low-dose ephedra/caffeine mixture is an effective and reasonably safe fat-loss agent. However, ephedra isn’t for everyone and must be used responsibly. It’s very important to read product labels, warnings and cautions and follow the directions. Someone should never, under any circumstances, use ephedra-containing supplements with heart disease or high blood pressure. Remember, you can’t have the best of both worlds; there’s no such thing as “very effective and perfectly safe.” It’s all about the risk-to-benefit ratio. You have to decide whether potential fat loss benefits outweigh potential adverse effects.
The author of this article has no financial relationship with companies selling fat loss supplements.

References:
5. Int J Obes (Lond), 2006 Mar 21; [Epub ahead of print].