Ephedrine: Innocent Until Proven Guilty

Ephedrine is classified as a sympathomimetic drug and central nervous system stimulant. Its ability to act as a sympathetic agonist and increase thermogenesis (production of heat) has led to its use in weight loss/fat loss. In most dietary supplements, ephedrine used to appear as an extract from one of two herbs: ephedra or Ma Huang.

Although ephedra species have a long tradition of use (more than 5,000 years) for respiratory ailments, the U.S. Food and Drug Administration (FDA) recently decided to ban ephedra-containing supplements. The pharmacokinetics of ephedrine following ingestion of supplements formulated as concentrated ephedra extracts is distinguishable from that of synthetic ephedrine found in conventional dosage forms. Nevertheless, the FDA did not ban ephedrine.

Ephedrine has also been coupled with both caffeine and aspirin to further enhance its effectiveness (i.e., ECA). Ephedrine stimulates release of norepinephrine (noradrenaline), which in turn stimulates the synthesis of prostaglandins by the activated tissues. Aspirin inhibits the synthesis of prostaglandins and serves as a prostaglandin blocker, and thereby may prevent inhibition of norepinephrine release.

In addition, ephedrine is used as a performance-enhancing substance (ergogenic aid). For example, Dr. I. 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 could be performed and the total amount of weight that could 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.

History of Ephedrine as a Weight/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 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-caffeine 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 studies support this contention. For example, Dr. C. Boozer and colleagues at the New York Obesity Research Center reported that in a six-month placebo-controlled trial, ephedra plus caffeine
promoted bodyweight and body fat reduction and improved blood lipids without significant adverse effects.

More recently, Dr. F. Greenway and co-workers at the Pennington Biomedical Research Center examined the effect of a supplement containing herbal caffeine and ephedrine on metabolic rate, weight loss, body composition and safety parameters. Results indicated that ephedra plus caffeine promoted more weight and fat loss than placebo (fake supplement) and was well tolerated. According to the authors, “Dietary herbal supplements containing [ephedra and caffeine] should remain available to obese individuals trying to control their weight.”

**Can Ephedrine be as Toxic as Reported?**

Dr. S. Bent and coworkers published a questionable paper on ephedra and other herbals in the *Annals of Internal Medicine*. They concluded that the risk for an adverse reaction after the use of ephedra is substantially greater than with other herbal products. However, there were serious methodological flaws, negative bias and failure of peer review on this article. Thus, three rebuttals were recently published in that same journal.

First, Dr. J. Whitaker felt that Dr. Bent’s data were extremely inaccurate. To estimate ephedra consumption, Dr. Bent and colleagues used marketing data from SPINS, Inc. on ephedra consumed in the category "Herbal Formulas and Singles," which accounted for 403,976 units per year. However, as pointed out by Dr. Whitaker, “They ignored the ephedra-containing products used for weight loss or energy— their stated concern— categorized by SPINS as ‘Vitamins and Supplements.’ This category accounted for 12,568,641 units per year, which is 31 times the amount on which Bent and colleagues based their conclusions. This oversight grossly exaggerates the relative risks of ephedra.”

Secondly, according to Drs. R. Kingston and S. Borron, “Comparing ephedra with ‘other herbs,’ the actions and indications of which are distinct, is toxicologic nonsense... The authors also ignored the difficulties of assigning a cause-and-effect relationship to events spontaneously reported to poison centers.”

Finally, Dr. A. Dickinson pointed out that “the authors relied on sales data that fail to encompass the bulk of the ephedra market, and therefore their calculations of relative risk are severely flawed.” Also, it should be noted that Dr. Bent and colleagues have a clear financial conflict of interest, as they have presented “expert” testimony against Twinlab, Cytodyne, MuscleTech, GNC, Phoenix Labs, etc.

More recently, Dr. G. Soni and co-workers published excellent review on ephedra and purported adverse effects in the respected *Toxicology Letters*. They concluded that the adverse event reports raise concerns about the risks associated with ephedra usage, but did not establish a direct causal relationship between intake of ephedra and reported injuries. They also pointed out that the published preclinical and clinical studies, and the long history of safe use of ephedra, support the safety-in-use of ephedra when used as directed. According to Dr. Soni et al., the problems associated with the adverse events appear to be the result of overuse, inconsistent potency, individual sensitivity, contaminations, etc.

While exercise does not appear to alter the pharmacological action of the sympathomimetic drugs, it’s worth noting that the pressor effects (increases in
blood pressure, vasodilation) of ephedrine/ephedra may be additive with the pressor effects of resistance exercise. Blood pressure as high as 480/350 has been recorded in the brachial artery of a bodybuilder during a double leg press. Because ephedrine may augment exercise-induced increases in blood pressure, it’s possible that bodybuilders who concomitantly use ephedrine in higher-than-recommended doses may experience serious vascular events.

**Citrus Aurantium: A Replacement for Ephedra?**
Many supplement companies are now substituting Citrus aurantium for ephedra in their diet formulations. Citrus aurantium, an agent containing beta agonists, has been reported to aid in weight loss in two studies and increase thermogenesis, at least to some extent, in three studies. Thus, it may be the best thermogenic substitute for ephedra. However, more research is needed before firm conclusions can be drawn. For more detailed information on Citrus aurantium and weight loss, see the recent review by Dr. H. Preuss and coworkers in the *Journal of Medicine*.

**Water: The Ultimate Thermogenic “Supplement”?**
In 14 healthy, normal-weight subjects, Dr. M. Boschmann and colleagues assessed the effect of drinking 500 milliliters of water on energy expenditure and substrate burning rates. Interestingly, drinking 500 milliliters of water increased metabolic rate by 30 percent. The increase occurred within 10 minutes and reached a maximum after 30-40 minutes. In men, fats mainly fueled the increase in metabolic rate. The authors concluded that drinking two liters of water per day would augment energy expenditure by about 400 kilojoules (about 95 calories).

**Bottom Line**
Ephedrine-caffeine supplementation promotes fat loss, improves exercise performance and is relatively safe when used as directed. However, ephedrine/ephedra is not for everyone and must be used responsibly. It’s very important that you read product labels, warnings and cautions, and follow the directions.

Dr. Steven Karch, an Assistant Medical Examiner in San Francisco, stated, “When used in recommended doses, ephedra-containing products have proven themselves extremely safe… ephedra-containing supplements can promote weight loss and improve athletic performance. They should never, under any circumstances, be used by someone with heart disease or high blood pressure, and the recommended dose should not be exceeded.”

Dr. Karch should know what he’s talking about, as he is the author of *The Pathology of Drug Abuse* and the editor of the *Drug Abuse Handbook*. *The Pathology of Drug Abuse* is considered the standard reference on that subject and is used by courts and medical examiners around the world.

**WARNING:** Do not use ephedrine/ephedra if you have heart disease, high blood pressure, thyroid disease, diabetes, or difficulty in urination due to enlargement of the prostate gland unless directed by a physician. Do not use this product if you have been hospitalized for asthma or if you are taking any prescription drug for
asthma, unless directed by a physician. Do not continue to use this product, but
seek medical assistance immediately, if symptoms are not relieved within one hour
or if they become worse. Some users of this product may experience nervousness,
tremors, sleeplessness, nausea or loss of appetite. If these symptoms persist or
become worse, consult your physician. A persistent cough may be a sign of a
serious condition. If cough persists for more than one week, tends to recur, or is
accompanied by a fever, rash, or persistent headache, consult a physician. Do not
take this product for persistent or chronic cough such as occurs with smoking,
asthma, chronic bronchitis or emphysema, or where cough is accompanied by
excessive mucus (phlegm) unless directed by a physician. In case of accidental
overdose, seek professional assistance or contact a poison control center
immediately. As with any drug, if you are pregnant or nursing a baby, seek the
advice of a health professional before using this product. Do not use this product if
you are presently taking any prescription drug without first consulting your doctor.

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