# Content versus label claims in ephedra-containing dietary supplements

BILL J. GURLEY, STEPHANIE F. GARDNER, AND MARTHA A. HUBBARD

**Abstract:** The content of ephedra alkaloids in herbal dietary supplements containing ephedra (ma huang) was studied.

The ephedra alkaloid content of 20 ephedra-containing supplements was determined by high-performance liquid chromatography. Contents of (–)-ephedrine, (+)-pseudoephedrine, (–)-methylephedrine, (–)-norephedrine, and (+)-norpseudoephedrine were measured.

Ephedra alkaloid content varied considerably among products. Total alkaloid content ranged from 0.0 to 18.5 mg per dosage unit. Ranges for (–)-ephedrine and (+)-pseudoephedrine were 1.1–15.3 mg and 0.2–9.5 mg, respectively. (+)-Norpseudoephedrine, a Schedule IV controlled substance, was often present. Significant lot-to-lot variations in alkaloid content were observed for four products. For one product, lot-to-lot variations in the content of (–)-ephedrine, (+)-pseudoephedrine, and (–)-methylephedrine exceeded 180%, 250%, and 1000%, respectively. Half of the products exhibited discrepancies between the label claim for ephedra alkaloid content and actual alkaloid content in excess of 20%. One product was devoid of ephedra alkaloids.

Assay of 20 ephedra-containing dietary supplements showed that alkaloid content often differed markedly from label claims and was inconsistent between two lots of some products.

**Index terms:** Analysis; Canthine; Chromatography, liquid; Concentration; Content uniformity; Control, quality; Dietary supplements; Ephedra alkaloids; *Ephedra sinica*; Ephedrine; Labeling; l-Norephedrine; Methylephedrine; Pseudoephedrine

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With the passage of the Dietary Supplement Health and Education Act (DSHEA) in 1994, herbal dietary supplements have taken the American health care system by storm. Sales of dietary supplements in the United States have doubled every two years since 1991, and projected sales for 2000 exceed $12 billion.[1,2] As stipulated by DSHEA, dietary supplements are exempt from rigorous FDA regulation. This is in stark contrast to federal regulations regarding the manufacture and sale of conventional prescription and nonprescription products. In fact, DSHEA places the burden of proof for dietary supplement safety squarely on the shoulders of FDA and not the supplement manufacturer.[2] As a result, consumers of herbal supplements must depend on self-regulation within the nutraceutical industry for assurance of product quality, consistency, potency, and purity.[3]

Consumers have grown accustomed to the high quality inherent in the manufacture of conventional drug products and usually accept without question the consistency, purity, and potency of prescription and nonprescription medications. Consequently, consumers have little reason to doubt the package label claims on conventional medications.

To date, a small number of studies conducted by investigators outside the supplement industry have revealed that quality control standards for dietary supplements run the gamut from good to nonexistent. A recent analysis

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of melatonin supplements found significant discrepancies in disintegration, dissolution, and in vitro release characteristics.[4] Substantial deviations in content from the product label claim have been documented for dehydroepiandrosterone,[5] ginseng,[6,7] feverfew,[8] and kava.[9] Moreover, as a result of species misidentification, botanical supplements have been contaminated with harmful herbs.[10] Even more disturbing is the adulteration, either intentionally or otherwise, of botanical supplements with undeclared conventional pharmaceuticals or heavy metals.[11] Taken together, these examples illustrate an apparent lack of interest in product quality by many nutraceutical manufacturers.

The number of adverse reactions and deaths associated with herbal products is on the rise.[12-14] One category of supplements frequently associated with adverse events is that containing ephedra alkaloids.[15-24] The plant genus *Ephedra* (also known by its Chinese name, ma huang) is a natural source for the alkaloids (–)-ephedrine, (+)-pseudoephedrine, (–)-methylephedrine, (+)-norpseudoephedrine, and (–)-norephedrine.[25] Many nonprescription, FDA-regulated products contain (–)-ephedrine, (+)-pseudoephedrine, or (–)-norephedrine (in the racemic mixture phenylpropanolamine) as bronchodilators, decongestants, or appetite suppressants. No conventional drug product in the United States, however, contains (–)-methylephedrine or (+)-norpseudoephedrine; in fact, (+)-norpseudoephedrine is classified as a Schedule IV controlled substance.

Because of the sympathomimetic activity of these compounds, supplement manufacturers market ephedra products as "energy boosters," or thermogenic dietary aids. No published clinical trials substantiate the safety or efficacy of these supplements. Adverse effects associated with ephedra supplements are well documented and range from nervousness, anxiety, tachycardia, hypertension, insomnia, and appetite suppression to nephrolithiasis, psychosis, seizures, heart attack, stroke, and death.

Package labels for ephedra supplements often make a claim for total alkaloid content, yet the quantities of individual alkaloids are not specified. Current labeling guidelines do not require that quantities of individual ephedra alkaloids be reported. As a result, consumers are unaware of the quantity and potency of specific alkaloids ingested. Knowledge of specific alkaloid content may be useful to both consumers and health care providers because ephedra alkaloids not only vary in pharmacologic activity and potency but may have additive or synergistic effects in certain combinations.[26,27]

To assess the content and consistency of ephedra alkaloids among ephedra dietary supplements, we analyzed 20 commercially available products by high-performance liquid chromatography (HPLC).[28]

## Methods

**Supplements analyzed.** The 20 ephedra-containing products examined were purchased mostly in 1999 (a few may have been bought in 1998) from local retailers or via the Internet. Selection was based on availability, ei-

Table 1.
**Products Analyzed**

| Product | Trade Name | Manufacturer or Distributor | Lot No. | Dosage Form |
|---|---|---|---|---|
| A | Diet Pep | Pep Products, Inc., Castle Rock, CO | 582U27 | Tablet |
| B | Diet Phen | Source Naturals, Inc., Scott's Valley, CA | 729007 | Tablet |
| C | Energel | General Nutrition Corp., Pittsburgh, PA | 55134FX | Soft-gelatin capsule |
| D | Ephedra | Solaray, Inc., Ogden, UT | 105374 | Capsule |
| E | Escalation | Enzymatic Therapy, Green Bay, WI | 230R621QF | Capsule |
| F | Exandra Lean | The Kutting Edge, Corinth, MS | None given on label | Capsule |
| G | Excel | Excel Corp., Salt Lake City, UT | NL1306D | Capsule |
| H | Herbal Phen-Fen | HPF L.L.C., Horsham, PA | 3430H7 | Tablet |
| I | Herbal PF Stage 2 | HPF L.L.C., Trevose, PA | 5775C8 | Tablet |
| J | Metabolean | Premier Marketing, Pinehurst, NC | 3902 | Tablet |
| K | Metabomax | Nature's Sunshine Products, Spanish Fork, UT | 9056969 | Tablet |
| L | Ma Huang | Nature's Answer, Inc., Hauppauge, NY | 9812EE | Liquid extract |
| M | Natural Trim | Starlight International Products, Monterey, CA | Illegible | Capsule |
| N | Turbotrim Plus | Trim International, Inc., Pensacola, FL | 0391023 | Tablet |
| O | Up Your Gas | National Health Products, Orlando, FL | 9105 | Tablet |
| P | Xenadrine | Cytodyne Technologies, Lakewood, NJ | 64124 | Capsule |
| $Q_1$ | Herbal Ecstacy | Global World Media Corp., Venice, CA | 21F8 | Tablet |
| $Q_2$ | Herbal Ecstacy | Global World Media | Illegible | Tablet |
| $R_1$ | Metabolife | Metabolife International Inc., San Diego, CA | A909 | Tablet |
| $R_2$ | Metabolife | Metabolife International | L866 | Tablet |
| $S_1$ | Ripped Fuel | Twin Laboratories, Inc., Ronkonkoma, NY | 89983 | Capsule |
| $S_2$ | Ripped Fuel | Twin Laboratories | 55419 | Capsule |
| $T_1$ | Trim Fast | Preferred Price Plus, Owensboro, KY | 10936 | Capsule |
| $T_2$ | Trim Fast | Preferred Price Plus | None given on label | Capsule |

ther locally or through the Internet. Two separate lots of 10 of the products were obtained for a comparison of lot-to-lot variability. (One of the products studied for lot-to-lot variability had no lot number indicated. The two bottles purchased for the study were obtained from different stores and were assumed to be from different lots.) Brief descriptions of the products analyzed are presented in Table 1. Eleven of the 20 supplements (55%) were claimed to contain herbal sources of other stimulants, namely caffeine and synephrine.

**Analytical methodology and sample preparation.** A validated HPLC method for the determination of ephedrine-type alkaloids was used to quantitate (–)-ephedrine, (+)-pseudoephedrine, (–)-methylephedrine, (–)-norephedrine, and (+)-norpseudoephedrine.[28] Details about assay conditions, validation procedures, and sample preparation have been previously described.

Fifteen samples of each product were analyzed. For those products selected for lot-to-lot variability comparisons, 15 samples from each lot were analyzed. Individual dosage forms of each product (tablets, hard-gelatin capsules, soft-gelatin capsules, or liquid extract) were weighed or a specific volume obtained. Each tablet was then pulverized in a mortar and pestle, and the contents were scrupulously recovered and the material weighed again. Hard-gelatin capsules were emptied, and the contents were weighed. Soft-gelatin capsules were left intact. For liquid dosage forms, 1-mL portions were obtained for analysis. The procedure for extracting ephedra alkaloids from each dosage form was that used by Gurley et al.[28]

## Results

The ephedra alkaloid content of each product is presented in Tables 2 and 3. Of the 20 products, 19 contained (–)-ephedrine; however, the quantity varied greatly, with product C containing the least (1.09 mg per capsule) and product M the most (15.33 mg per capsule). The second most common alkaloid, (+)-pseudoephedrine, was present in 16 of the supplements. The quantity ranged from 0.16 mg per capsule (product C) to 9.45 mg per capsule (product G). Nine supplements contained measurable amounts of (–)-methylephedrine. (+)-Norpseudoephedrine and (–)-norephedrine were the least prevalent alkaloids, with quantities consistently below 0.5 mg per dosage form. Four products (D, E, G, and L) contained measurable quantities of all five alkaloids, while three (H, I, and O) contained only (–)-ephedrine. None of the assayed alkaloids were detected in product F.

Six of the products (E, F, H, I, O, and P) tested for lot-to-lot variability showed virtually no difference in alkaloid content between lots. The content of only a single lot of these supplements is reported in Table 2. The four other supplements (Q, R, S, and T) examined for lot-to-lot vari-

Table 2.
**Ephedra Alkaloid Content per Dosage Unit or per Milliliter for Study Products**

| Product | Mean ± S.D. Alkaloid Content ($n$ = 15)[a] | | | | |
|---|---|---|---|---|---|
| | NPSE | NEPH | PSE | EPH | MEPH |
| A | ND[b] | ND | 1.38 ± 0.07 | 11.27 ± 0.43 | ND |
| B | ND | ND | 0.53 ± 0.04 | 3.03 ± 0.28 | ND |
| C | ND | ND | 0.16 ± 0.03 | 1.09 ± 0.09 | ND |
| D | 0.31 ± 0.04 | 0.17 ± 0.03 | 1.49 ± 0.09 | 2.84 ± 0.44 | 0.28 ± 0.03 |
| E | 0.21 ± 0.03 | 0.19 ± 0.05 | 0.81 ± 0.17 | 13.57 ± 0.98 | 0.20 ± 0.05 |
| F | ND | ND | ND | ND | ND |
| G | 0.38 ± 0.06 | 0.25 ± 0.11 | 9.45 ± 0.64 | 12.78 ± 0.75 | 0.61 ± 0.06 |
| H | ND | ND | ND | 8.10 ± 0.75 | ND |
| I | ND | ND | ND | 9.34 ± 0.93 | ND |
| J | ND | 0.16 ± 0.01 | 1.10 ± 0.05 | 9.58 ± 0.56 | 0.18 ± 0.03 |
| K | ND | ND | 1.49 ± 0.08 | 10.14 ± 0.34 | 0.22 ± 0.01 |
| L | 0.42 ± 0.02 | 0.20 ± 0.02 | 3.37 ± 0.96 | 2.58 ± 0.08 | 0.33 ± 0.01 |
| M | ND | ND | 3.11 ± 0.14 | 15.33 ± 0.49 | ND |
| N | ND | ND | 1.37 ± 0.08 | 8.90 ± 0.50 | 0.39 ± 0.03 |
| O | ND | ND | ND | 11.60 ± 1.14 | ND |
| P | 0.20 ± 0.01 | 0.19 ± 0.01 | 3.44 ± 0.13 | 8.53 ± 0.33 | ND |
| $Q_1$ | ND | ND | 8.44 ± 0.69 | 6.25 ± 0.50 | 0.20 ± 0.02 |
| $Q_2$ | ND | ND | 7.52 ± 0.27 | 2.63 ± 0.09 | 2.71 ± 0.11 |
| $R_1$ | ND | ND | 1.47 ± 0.17 | 9.70 ± 1.09 | ND |
| $R_2$ | ND | ND | 2.17 ± 0.23 | 9.72 ± 1.01 | ND |
| $S_1$ | ND | ND | 1.84 ± 0.10 | 9.08 ± 0.47 | 0.22 ± 0.03 |
| $S_2$ | ND | ND | 5.29 ± 0.54 | 2.51 ± 0.26 | 2.58 ± 0.27 |
| $T_1$ | ND | ND | 2.81 ± 0.62 | 9.91 ± 1.65 | ND |
| $T_2$ | ND | ND | 4.31 ± 0.16 | 14.23 ± 0.46 | ND |

[a]NPSE = (+)-norpseudoephedrine, NEPH = (–)-norephedrine, PSE = (+)-pseudoephedrine, EPH = (–)-ephedrine, MEPH = (–)-methylephedrine.
[b]ND = none detected or quantity below limit of detection (0.15 mg per dosage unit or milliliter).

Table 3.
**Measured Ephedra Alkaloid Content of Products versus Label Claims**

| Product | Labeled Ephedra Content (mg/Unit) | Labeled (–)-Ephedrine Content (mg/Unit) | Mean Measured (–)-Ephedrine Content in mg/Unit (% of Claimed) | Labeled Total Alkaloid Content[a] (mg/Unit) | Mean Measured Total Alkaloid Content in mg/Unit (% of Claimed) |
|---|---|---|---|---|---|
| A | . . .[b] | None | 11.3 | None | 12.7 |
| B | 150 | 4.0 | 3.0 (75) | 4.0 | 3.6 (90) |
| C | 125 | None | 1.1 | 7.5 | 1.3 (17) |
| D | 375 | None | 2.8 | None | 5.1 |
| E | 250 | 15.0 | 13.6 (91) | 15.0 | 15.0 (100) |
| F | . . . | None[c] | 0.0 | None | 0.0 |
| G | 406 | 24.0 | 12.8 (53) | None | 23.5 |
| H | . . . | None | 8.1 | 26.0 | 8.1 (31) |
| I | 125 | 10.0 | 9.3 (93) | 10.0 | 9.3 (93) |
| J | 150 | None | 9.6 | 12.0 | 11.0 (92) |
| K | . . . | None | 10.1 | 12.0 | 11.9 (99) |
| L | . . . | None | 2.6 | None | 6.9 |
| M | 275 | None | 15.3 | 22.0 | 18.4 (84) |
| N | 150 | None | 8.9 | 12.0 | 10.3 (86) |
| O | 285 | None | 11.6 | 17.0 | 11.6 (68) |
| P | 167.5 | 10.0 | 8.5 (85) | None | 12.4 |
| $Q_1$ | . . . | 6–10 | 2.6 (26–43) | 10–12 | 13.3 (111–133) |
| $Q_2$ | . . . | 6–10 | 6.3 (63–105) | 10–12 | 14.7 (123–147) |
| $R_1$ | . . . | None | 9.7 | 12.0 | 11.9 (99) |
| $R_2$ | . . . | None | 9.7 | 12.0 | 11.2 (93) |
| $S_1$ | 167 | None | 9.1 | 10.0 | 10.9 (109) |
| $S_2$ | 167 | 10.0 | 2.5 (25) | None | 10.4 |
| $T_1$ | 150 | None | 9.9 | 12.0 | 12.7 (106) |
| $T_2$ | 150 | None | 14.2 | 12.0 | 18.5 (154) |

[a]Claimed ephedra (or ma huang) content times claimed alkaloid percentage.
[b]Label did not indicate ephedra content.
[c]Label claim is for (–)-norephedrine, not (–)-ephedrine.

ability exhibited marked differences in alkaloid content. Products Q and S, for example, showed variations in (–)-methylephedrine content in excess of 1000% (relative to the less potent lot), and differences in (–)-ephedrine content exceeded 135% and 260%, respectively. Separate lots of product S also exhibited a 188% difference in the amount of (+)-pseudoephedrine. Lot-to-lot differences in (–)-ephedrine and (+)-pseudoephedrine content for product T were 44% and 53%, respectively. A similar variation in (+)-pseudoephedrine content (48%) was noted for product R.

Table 3 lists label claims for ephedra content and compares claims for (–)-ephedrine and total alkaloid content with the amounts determined by HPLC. Only 13 of the 20 supplement labels indicated the ephedra content. The label claims of ephedra content were not correlated with the measured amounts of (–)-ephedrine or total alkaloids. For example, products B and $T_2$ both claimed 150 mg of ephedra, but product B actually contained 3.0 mg of (–)-ephedrine (3.6 mg of total alkaloids) and product $T_2$ contained 14.2 mg of (–)-ephedrine (18.5 mg of total alkaloids). Product D claimed 375 mg of ephedra but contained only 2.8 mg of (–)-ephedrine (5.1 mg of total alkaloids); product E claimed less ephedra (250 mg) than product D but contained more (–)-ephedrine (13.6 mg) and total alkaloids (15.0 mg) than that product.

Label claims for total alkaloids were often not indicative of the amount present (Table 3). Products A, D, and L made no claim for total alkaloid content, even though they contained 12.7, 5.1, and 6.9 mg of ephedra alkaloids, respectively. Product C's label claim for total alkaloid content was 7.5 mg, while product H claimed 26 mg; however, the actual quantities determined by HPLC were 1.3 and 8.1 mg, respectively. Accordingly, total alkaloid content for product C was only 17% of the label claim, while product H's total content was 31% of the label claim. (Product G's label was somewhat difficult to interpret but, if taken literally, indicated that a 325-mg dose contained "8% alkaloids" or 26 mg.) Measured total-alkaloid contents for products $Q_1$, $Q_2$, and $T_2$, on the other hand, were 33%, 47%, and 54% higher than the respective label claims.

Product G claimed 24 mg of ephedrine, but HPLC analysis revealed only 12.8 mg of (–)-ephedrine present; therefore, the ephedrine content was 53% of the label claim. It appears that the 24-mg label claim was more indicative of product G's total alkaloid composition (23.5 mg) than of its ephedrine content alone. A similar finding was made for product $S_2$, which claimed that its ephedra content was

standardized to yield 6% ephedrine (or 10 mg); however, only 2.5 mg of ephedrine (25% of the label claim) was present. Had the label claim for product $S_2$ specified "ephedra alkaloids" (total alkaloid content, 10.4 mg), then almost 100% of the label claim would have been realized. Product F claimed to contain 12.5 mg of norephedrine per capsule, yet no evidence of norephedrine was found. In total, 11 (55%) of the 20 supplements either failed to make a label claim for alkaloid content or exceeded a 20% difference between alkaloid content and label claim (range for percentage of claimed content actually present, 0% [product F] to 154% [product O]).

## Discussion

Hundreds of ephedra-containing supplements are currently available in the United States. Ironically, ephedra supplements vastly outnumber conventional prescription and nonprescription medications containing (–)-ephedrine, (+)-pseudoephedrine, or racemic norephedrine (phenylpropanolamine). With their widespread and easy availability, it is not surprising that hundreds of adverse drug reactions and several deaths have been attributed to ephedra.[14-24] Our study suggests that poor quality control may contribute to the problems associated with the safety and efficacy of ephedra supplements. While we evaluated only 20 products, the results indicate that product inconsistency is pervasive among ephedra supplement manufacturers.

Our findings raise several issues regarding this particular class of dietary supplements that should be brought to the attention of American consumers. These issues include (1) the presence in these products of multiple alkaloids that vary in pharmacologic potency, (2) the presence of ephedra alkaloids in combination with other stimulants (caffeine and synephrine), (3) the frequent and significant differences between label claims and actual contents of ephedra alkaloids, and (4) the dramatic variance in alkaloid content within and among specific products.

**Presence of multiple alkaloids and other stimulants.** Currently, there are no FDA-regulated medications that contain multiple ephedra alkaloids. The reasoning lies in the potential for additive or synergistic effects contributing to sympathomimetic toxicities.[26,27,29] Toxicity, in turn, may hinge upon the types and amounts of ephedra alkaloids ingested, as well as their relative potencies with respect to cardiovascular and central nervous system (CNS) stimulant effects. Numerous cases documenting the hazards of combining multiple nonprescription stimulants have been reported.[26,27,29,30] Combinations deemed unsafe incorporated caffeine, (–)-ephedrine, phenylpropanolamine, and (+)-pseudoephedrine. Known as amphetamine look-alikes, these combination products were banned by FDA in 1983.[31]

Caffeine potentiates the amphetamine-like stimulant effects of both (–)-ephedrine and phenylpropanolamine and augments the toxicity of these alkaloids.[32-34] Illicit amphetamine look-alike combinations have typically contained 40–300 mg of caffeine, 12.5–50 mg of (–)-ephedrine, and 25–50 mg of phenylpropanolamine.[35] Many ephedra supplements claim to incorporate herbal sources of caffeine; if the claims are to be believed, the caffeine content can exceed 200 mg per dose. Likewise, quantities of (–)-ephedrine can easily fall within the 12.5- to 50-mg range when certain supplements are taken as directed. (–)-Norephedrine, the more potent enantiomer of phenylpropanolamine, can be present in small amounts (Table 2). (+)-Pseudoephedrine and the more potent CNS stimulants, (–)-methylephedrine and (+)-norpseudoephedrine, can be present in substantial amounts (as in products G, L, $Q_2$, and $S_2$) and thus could pose more serious problems than phenylpropanolamine when coupled with caffeine and (–)-ephedrine. Evidence suggests, too, that mixtures of caffeine and (–)-methylephedrine produce stimulant effects similar to those of methamphetamine.[36] Alone, (+)-norpseudoephedrine and (–)-methylephedrine have a high abuse potential and have been linked to a number of neurologic toxicities.[37-38] Taken together, the evidence suggests that supplements combining ephedra and caffeine are merely "natural" alternatives to previously banned amphetamine look-alike drugs.

In addition to incorporating caffeine-containing herbs, many ephedra supplements contain *Citrus aurantium*. A natural source of the adrenergic agonists synephrine and octopamine, *C. aurantium* can elevate mean arterial blood pressure and may augment the cardiovascular effects of ephedra alkaloids.[39] In laboratory animals, oral ingestion of *C. aurantium* produced dose-dependent mortality and electrocardiographic abnormalities indicative of ventricular arrhythmia.[40] Thus, ephedra supplements containing caffeine and synephrine may have a greater propensity for adverse effects. Until controlled human studies are conducted, the safety and efficacy of multistimulant supplements will remain unclear.

An unanticipated finding involved supplements containing substantial quantities of (+)-norpseudoephedrine, a Schedule IV controlled substance. FDA prohibits conventional nonprescription medications from containing controlled substances as active ingredients, yet herbal dietary supplements, under the auspices of DSHEA, are apparently exempt from such prohibitions.

**Unhelpful labeling and product variation.** Label claims for total ephedra alkaloids are typically expressed as a standardized percentage of total herb content (e.g., "standardized to 6% ephedra alkaloids"). Many consumers are probably unaware that total alkaloids are calculated as

the product of ephedra content and the stated percentage (e.g., 334 mg of ephedra × 6% = 20 mg of total alkaloids). Even if consumers were to correctly compute total alkaloid composition, their results would often not be representative of actual content. We found that total alkaloid content could vary from as little as 0% to more than 154% of the label claim (Table 3). For conventional pharmaceutical products, such discrepancies would likely result in a product being misbranded and ultimately recalled by the manufacturer.

From the standpoint of alkaloid content, it appears that no two ephedra supplements were the same, even though label claims for ephedra content were identical. Moreover, the quantity of ephedra did not appear to correspond with (–)-ephedrine or total alkaloid content. Ephedra alkaloid content is dependent on the ephedra formulation. The ephedra found in dietary supplements usually consists of powdered "stems and aerial portions" of the herb or dried herbal extracts. (In our survey, 17 of the 20 products were formulated with extracts.) Preparations of powdered stems and aerial portions typically contain lower concentrations of ephedra alkaloids. Extraction procedures, however, remove alkaloids from the plant matrix and concentrate them in aqueous or alcoholic solutions. When dried, extracts yield higher concentrations of alkaloids per gram of material. Another distinction between ephedra supplements formulated with extracts and those containing powdered herb is the rate at which botanical ephedrine is absorbed from the gastrointestinal tract. A comparison of two studies investigating the pharmacokinetics of botanical ephedrine indicates that (–)-ephedrine is absorbed faster from supplements formulated with ephedra extracts[41] than from those containing only the powdered herb.[42]

From the product labels, it appears that the terms "ephedrine" and "ephedrine [or ephedra] alkaloids" are considered by some manufacturers to be synonymous. Individual ephedra alkaloids differ not only with respect to physicochemical properties, but pharmacologic activity as well. Equating "ephedrine" and "ephedrine [or ephedra] alkaloids" is misleading and may confound both consumer and health care professional when assessing these supplements.

While considerable variability might be expected among ephedra products, the excessive lot-to-lot variability within the same product is alarming. Conventional pharmaceuticals exhibiting lot-to-lot differences for (–)-ephedrine in excess of 100% would never be released for public consumption, yet ephedra supplements with such variability currently fill the shelves of our nation's pharmacies and health food stores.

**Regulation and implications for practitioners.** It is obvious that ephedra supplement manufacturers have had difficulty in achieving product consistency. Within the pharmaceutical industry, product consistency is maintained through the implementation of good manufacturing practices (GMPs). Adherence to GMPs for drug production, in turn, ensures product quality. Currently there are no GMP regulations specifically designed for dietary supplements, although a proposed draft of such guidelines modeled after food GMPs has been submitted to FDA.[2] This is not to say that, until specific GMPs are implemented, all supplement manufacturers will neglect efforts to ensure product quality. The National Nutritional Foods Association, together with other organizations in the supplement industry, has mandated a set of GMPs to be implemented by its members before 2003.[43]

In June 1999, Texas adopted regulations with respect to ephedra supplements sold within its borders. The Texas rule requires that every batch of products containing ephedra be analyzed to ensure uniformity with the amount of total ephedra alkaloids stated on the product label.[44]

Health care professionals should be aware of the variability among various herbal products when making recommendations for nutraceuticals. Some manufacturers have taken a proactive stance and can provide data substantiating their label claims. Medication histories should include very specific questions about the patient's consumption of herbal supplements, especially those containing ephedra.

In summary, a potential to cause adverse events, the presence of potentially toxic combinations of stimulants, variations within and among products, deviations from label claims, and even the presence of controlled substances are problems encountered with ephedra supplements. Until GMPs are in place, consumers intent on purchasing an ephedra supplement are best advised to heed the adage of caveat emptor—let the buyer beware.

## Conclusion

Assay of 20 ephedra-containing dietary supplements showed that alkaloid content often differed markedly from label claims and was inconsistent between two lots of some products.

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