

RESEARCH LETTER

ONLINE FIRST

DMAA as a Dietary Supplement Ingredient

The pharmaceutical amphetamine derivative 1,3-dimethylamylamine (DMAA) was introduced in 1948 as a nasal inhaler for rhinitis by Eli Lilly & Co. By the 1970s, it had been withdrawn as an approved pharmaceutical. Surprisingly, DMAA is currently used as an ingredient in roughly 200 sports supplements, many sold in major franchises throughout the United States, with sales topping \$100 million in 2010 alone (**Table**).¹⁻⁴

For DMAA to be legally sold as a dietary supplement, it must be a naturally occurring substance with a documented history of use prior to 1994. Remarkably, the evidence to support the sale of DMAA-containing supplements hinges on a single study.⁵ In this 1 study, published in the now defunct *Journal of the Guizhou Institute of Technology*, geranium oil (extracted from the fresh leaves and stems of *Pelargonium graveolens*) was found to contain less than 0.7% DMAA based on a gas chromatography and mass spectrometry analysis. The researchers do not describe their methodology but presumably based their conclusions on matching an unknown peak spectrum of geranium oil with the library mass spectrum of DMAA. The appropriate confirmatory test, using a standardized

preparation of DMAA to confirm its presence, was not described.

Since the publication of this study, more than a half-dozen peer-reviewed reports have been unable to confirm this finding.⁶ Health Canada, for one, has concluded that "there is no credible scientific evidence that DMAA is captured as an isolate of a plant."⁶ This lack of evidence has not deterred multiple supplement companies from marketing DMAA as if it were isolated from geranium. For example, the popular Jack3d product (US-Plabs) sold at GNC (General Nutrition Centers) is labeled as containing "1,3-dimethylamylamine (Geranium [Stem])" (label available from the author on request).

Given its wide availability, physicians should understand DMAA's potential health effects. Supplements containing DMAA have been implicated as potentially contributing agents in multiple serious adverse events, including panic attacks, seizures, stress-induced cardiomyopathy,⁷ and 2 deaths.² In Europe and New Zealand, DMAA use as a party drug has been implicated in at least 1 hemorrhagic stroke.⁸ Causality has yet to be proven, but these adverse effects are consistent with DMAA's known pharmacologic actions. In *The Dispensatory of the United States of America 1950 Edition*,⁹ DMAA's systemic toxic effects in animals was described as "greater than that of ephedrine and less than that of amphetamine,"^{9(p2049)} and the authors counseled that if DMAA's use as a nasal inhaler "produces side effects such as headache, nervousness, mental stimulation, or tremors, the drug should be discontinued."^{9(p2049)} Small trials have also demonstrated that DMAA-containing supplements increase blood pressure and heart rate.¹⁰

Last summer, Health Canada banned DMAA from all supplements,⁶ and last December, the US military removed DMAA-containing supplements from all military exchanges worldwide (Table).¹ As of March 2012, the US Food and Drug Administration (FDA) had yet to act. Given that DMAA is a potentially dangerous ingredient and that manufacturers' claims that it is naturally derived are unsubstantiated, manufacturers and distributors should immediately recall all DMAA-containing supplements. Without delay, the FDA should clarify its position on DMAA and aggressively prosecute all violations of the law.

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Table. List of DMAA-Containing Supplements Withdrawn From All Military Exchanges as of December 7, 2011¹

Supplement Proprietary Name	Manufacturer
Jack3d (tropical fruit and lemon lime)	USPlabs
OxyELITE Pro	USPlabs
Lipo 6 Black	Nutrex Research Inc
Lipo 6 Black Ultra	Nutrex Research Inc
Hemo Rage Black	Nutrex Research Inc
PWR Ultra Concentrated Pre Workout Revolution	iSatori Technologies LLC
Neurocore Powder	MuscleTech
HydroxyStim	MuscleTech
Lean EFX	Fahrenheit Nutrition
Napalm	Muscle Warfare
K Otic	All American EFX
Nitric Blast	Sports Nutrition International
SSIN Juice Concentrate	BioRhythm-ADS
Code Red	MuscleMeds Performance Technologies
MethylHex4,2	SEI Pharmaceuticals
Arson Fat Burner Capsule	Muscle Asylum Project
SpiroDEX	Gaspari Nutrition

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1. Allied Communications Publication. ALFOODACT 036-2011 UPDATE/CORRECTION for ALFOODACT 034-2011 Dimethylamylamine (DMAA) is placed on medical hold due to possible serious adverse health effects. <http://www.troopssupport.dla.mil/subs/fso/alfood/2011/alf03611.pdf>. Accessed March 22, 2012.
2. Lattman P, Singer N. Army studies workout supplement after deaths. *New York Times*. February 3, 2012;B1.
3. Therapeutic Research Faculty. Natural medicines comprehensive database [registration required]. <http://naturaldatabase.therapeuticresearch.com/home.aspx?cs=&ts=ND>. Accessed March 28, 2012.
4. Nutrition Business Journal. Moving the needle: 'geranium extracts' exit the marketplace. <http://newhope360.com/research/moving-needle-geranium-extracts-exit-marketplace?page=1>. Accessed March 28, 2012.
5. Ping Z, Jun Q, Qing L. A study on the chemical constituents of geranium oil [in Chinese]. *J Guizhou Inst Tech*. 1996;25(1):82-85.
6. Health Canada, Health Products and Food Branch. Classification of 1,3-dimethylamylamine (DMAA). <http://www.scribd.com/doc/82744576/DMAA-Health-Canada-2011>. Accessed March 22, 2012.
7. Salinger L, Daniels B, Sangalli B, Bayer M. Recreational use of bodybuilding supplement resulting in severe cardiotoxicity. *Clin Toxicol*. 2011;49(6):573-574.
8. Gee P, Jackson S, Easton J. Another bitter pill: a case of toxicity from DMAA party pills. *N Z Med J*. 2010;123(1327):124-127.
9. Osol A, Farrar G, eds. *The Dispensatory of the United States of America 1950 Edition*. Philadelphia, PA: J.B. Lippincott Co; 1950.
10. McCarthy CG, Farney TM, Canale RE, Alleman RJ, Bloomer RJ. A finished dietary supplement stimulates lipolysis and metabolic rate in young men and women. *Nutr Meta Insights*. 2012;5(1):23-31.