RE: Phytochemical Analyses Fail to Identify Methylhexaneamine as a Natural Component of Pelargonium Oils or Sweet-scented "Rose" Geranium Leaves or Stems


Although Pelargonium and Geranium are two different plant genera in the Geraniaceae family, oil from Pelargonium species is often labeled according to the common name as geranium oil. One previous study on sweet-scented "rose" geranium (P. graveolens) oil reported the presence of a compound known as 4-methyl-2-hexaneamine (MHA), in addition to other compounds such as terpenes and sesquiterpenes. Also known as dimethylamylamine (DMAA), MHA had a new drug application approved by the Food and Drug Administration (FDA) and was used as a nasal decongestant until its manufacturer, Eli Lilly and Company, took it off the market in 1983. Recent incidents of adverse side effects associated with using this stimulant have resulted in restrictions in Canada and New Zealand, and the World Anti-Doping Agency has recently banned its use.

According to regulations outlined in the Dietary Supplement Health and Education Act of 1994 (DSHEA), botanical and herbal substances are allowed to be sold as dietary supplements; this would apply to products that contain MHA if the compound is present in a plant, such as geranium. If a compound or product does not fall under these DSHEA definitions, it is subject to the FDA New Dietary Ingredient (NDI) notification system, and safety data must be submitted to this agency for its usage. As synthetically derived MHA is widely available and recent studies have not confirmed the presence of MHA in geranium, the authors of this analytical study investigated whether MHA could be found in either the leaves, stems, or the essential oil of rose geranium.

Authentic sweet-scented geranium plant material was procured from both the Indian Institute of Integrative Medicine in Jammu, India and the National Center for Natural Products Research (NCNPR) at the University of Mississippi, Oxford, Mississippi. Essential oil was made by steam distillation of leaves for a yield of 0.16% of fresh weight. Additional samples of commercial essential oils procured for the study consisted of this and other geranium, i.e., wild geranium (G. maculatum) and apple geranium (P. odoratissimum), oils. Commercial sports supplements with claims that the products contained "dimethylamylamine (geranium
stem)" or "1,3-dimethylamylamine" were also analyzed. All materials were extracted and partitioned as necessary, prior to being analyzed by using gas chromatography-mass spectrometry (GC-MS), liquid chromatography-tandem mass spectrometry (LC-MS-MS), and/or LC-high-resolution-MS (LC-QTOF-MS). An MHA standard was used for quantification, and an internal standard (2-amino-6-methylheptane) was used to validate the extraction and detection methods. In addition, a spiking experiment was conducted to ensure that any absence of MHA was not due to lack of MHA recovery in the extraction processes.

In total, 20 commercial oils (including 1 sample each of the other 2 species), 3 authenticated oils, and authenticated fresh and dried sweet-scented geranium leaves and stems were assessed. The GC-MS method had a limit of detection (LOD; the concentration above which a compound can be detected by the instrumentation) of 0.1 ppm; MHA was not detected above this concentration in any of the oils using this method. Oils were then analyzed using the LC-MS-MS method with a much lower LOD of 2.5 ppb, and concentrations of MHA above this LOD were also not observed. When all plant and oil samples were analyzed with the LC-QTOF-MS method, no MHA was detected above the LOD of 10 ppb. Specifically, leaves of sweet-scented geranium at various growth stages showed no detectable MHA above 10 ng/ml at any point; this was also observed when analyzing the dried plant material.

Of the commercial products analyzed, however, concentrations greater than 1 mg/g of MHA were detected; taken together with the above results, it is unlikely that geranium leaves, stems, or oil are the source of MHA in these products. As bulk MHA is commercially available, it is suggested that the MHA in sports supplements may be of synthetic origin. If this is the case, as strongly asserted by the data presented herein, MHA may fall under the NDI guidelines requiring safety data or established history of use showing that the compound and supplement "will reasonably be expected to be safe."

The use of MHA in sports supplements sold in the United States is receiving broad scrutiny of late. In light of the reported serious adverse side effects associated with the use of MHA, such as cerebral hemorrhage, raised blood pressure with no concurrent heart rate increase, and coma and death, the safety of MHA consumption is in question. This study conducted a thorough and broad investigation of not only their own preparations of authenticated geranium material and essential oil, but also of commercial oil and products containing MHA. The study also addressed whether plant development and preparation affected the presence of MHA. In addition, multiple instruments and methods were used, and rigorous use of standards and method validation were employed. Thus, the study reports extremely robust evidence that the MHA in the commercial supplements analyzed is of synthetic origin. Widespread and deserved attention to this article will ideally help prevent further toxicity from the consumption of MHA.

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References


The American Botanical Council has chosen not to reprint the original article.