Concerns regarding toxicity associated with caffeine-containing pre-workout supplements

To the Editor: We are concerned about methylxanthine-mediated toxicity associated with multi-ingredient pre-workout supplements (MIPS) in South Africa (SA). Marketed as exercise performance enhancers, these products are often sold as proprietary blends with incompletely disclosed ingredients, and frequently contain stimulants such as caffeine and theobromine.[1] Labelling inaccuracy was highlighted in an Australian study, in which measured caffeine ranged from 59% to 178% of the labelled amount, with significant variability between product batches.[2] This raises concerns for dose-dependent and additive toxicity.

Recently, an adult patient presented to the emergency unit with a sympathomimetic toxidrome following ingestion of a MIPS and an energy drink. The patient presented with chest pain, palpitations, difficulty breathing and vomiting, consistent with methylxanthine toxicity. Examination findings included diaphoresis, sinus tachycardia, mild hypertension and bilateral mydriasis. There was no history of prescription or illicit drug use. Urine toxicology was negative for amphetamines and cocaine. Supportive care with intravenous fluids and benzodiazepines led to complete resolution of the presenting symptoms.

Caffeine, and other methylxanthines, produce sympathomimetic-like toxicity, although gastrointestinal effects are more prominent. Toxicity includes vomiting, central nervous system stimulation (e.g. tremor, agitation), tachypnoea, sinus tachycardia and hypokalaemia. Severe toxicity may result in arrhythmias, seizures and rhabdomyolysis. Case reports and case series have showcased the harms associated with caffeine toxicity from MIPS.[3,4]

This case highlights the importance of a detailed supplement history and high index of suspicion for MIPS-related toxicity in patients presenting with sympathetic overactivity. Furthermore, it underscores a critical regulatory gap in SA. Caffeine intended for injection is a schedule 3 medicine, subject to full regulatory oversight by the SA Health Products Regulatory Authority (SAHPRA).[5] Caffeine, only as part of multiple substance formulations, is also permitted under SAHPRA's Category D complementary medicines and health supplements guidance, subject to a maximum daily dose of 300 mg.[6] Despite this, manufacturers of MIPS that contain caffeine may position these products as foodstuffs, placing them outside of SAHPRA's rigorous regulatory processes. Healthcare workers and consumers should be alerted to the unregulated nature of these products and the risks of harm, especially when co-ingesting multiple caffeinated products. The increasing popularity and availability of these products obligates enhanced regulatory oversight.[7]

J Taylor; G Tatz; N Madikizela; M Blockman
Division of Clinical Pharmacology, Department of Medicine, University of Cape Town, South Africa
Marc.blockman@uct.ac.za

Ethical considerations. Informed consent was obtained from the patient for publication of this correspondence. This correspondence was approved by the University of Cape Town Human Research Ethics Committee (ref. no. HREC 296/2026).

1. Jagim A, Harty P, Camic C. Common ingredient profiles of multi-ingredient pre-workout supplements. Nutrients 2019;11(2):254. https://doi.org/10.3390/nu11020254
2. Desbrow B, Hall S, O'Connor H, et al. Caffeine content of pre-workout supplements commonly used by Australian consumers. Drug Test Anal 2019;11(3):523-529. https://doi.org/10.1002/dta.2501
3. Harris B, Winn C, Ableman T. Hemorrhagic stroke in a young healthy male following use of pre-workout supplement Animal Rage XL. Military Med 2017;182(9-10):e2030-e2033. https://doi.org/10.7205/MILMED-D-17-00013
4. Kamijo Y, Takai M, Fujita Y, et al. A retrospective study on the epidemiological and clinical features of emergency patients with large or massive consumption of caffeinated supplements or energy drinks in Japan. Intern Med 2018;57(15):2141-2146. https://doi.org/10.2169/internalmedicine.0333-17
5. National Department of Health, South Africa. Medicines and Related Substances Act No. 1010 of 1965. Consolidated Schedules 1 August 2025.Goverment Gazette No. 53099: 6464. 2025. https://www.sahpra.org.za/wp-content/uploads/2025/08/Consolidated-Schedules_01-August-2025.pdf (accessed 18 June 2026).
6. South African Health Products Regulatory Authority. Complementary medicines guidance on specified substances. Pretoria: SAHPRA, 2022. https://www.sahpra.org.za/wp-content/uploads/2022/02/7.06_CMs_Specified_Substances_Jan22_v3_2.pdf (accessed 18 June 2026).
7. Garthe I, Maughan R. Athletes and supplements: Prevalence and perspectives. Int J Sport Nutr Exercise Metab 2018;28(2):126-138. https://doi.org/10.1123/ijsnem.2017-0429

S Afr Med J 2026;116(6):e5186. https://doi.org/10.7196/SAMJ.2026.v116i6.5186