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LETTER TO THE EDITORS

Synthetic cannabinoid 5F-ADB detected in hair samples from patients seeking addiction treatment in São Paulo's open drug use scene

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In 2023 and 2024 there was a surge in consumption of synthetic cannabinoids in São Paulo's open drug use scene, locally referred to as "K Drugs." This was promptly identified through epidemiological surveillance at the São Paulo Medical Development Association (Associação Paulista para o Desenvolvimento da Medicina) health care addiction center, which reported K Drug consumption by 37.8% of its patients in April 2024.[1] However, this was just the beginning of a sharp upward trend that peaked in September 2024, when 80.4% of patients reported K drug consumption.

This phenomenon poses a major challenge for health care providers, as synthetic cannabinoids vary widely in potency and toxicity,[2] leading to unpredictable and severe effects that often overlap with those of other substances, for which clinical management strategies differ significantly. These unpredictable effects add further complexity to already difficult cases, such as individuals who use crack cocaine and live in open drug use scenes.

The broad spectrum of the effects of synthetic cannabinoids, including the cardiovascular, psychiatric, and neurological symptoms associated with intoxication and withdrawal, often resemble those of other new psychoactive substances, opioids (e.g., generalized body pain), or even the pesticide strychnine, which has occasionally been found as a contaminant or adulterant in crack cocaine. The overlapping features of strychnine intoxication and the symptoms increasingly reported by users of so-called "K drugs" have been particularly notable, especially seizure-like activity accompanied by intense muscle spasms and rigidity, and the characteristic presentation of opisthotonus, in which the body arches backward due to extreme muscle contractions.[3]

The combination of rising case numbers and the clinical complexity associated with overlapping symptoms (for which management strategies vary depending on the involved substance) underscored the importance of confirming whether substances marketed as K2, K9, and related variants were indeed synthetic cannabinoids in order to guide appropriate clinical care and public health responses.[4] As a response, a surveillance strategy was implemented in the above mentioned addiction center, integrating cycles of hair sample collections from patients who reported synthetic cannabinoid consumption during clinical risk assessments (ethical approval certificate 39437220.4.0000.5505).

Validation of the screening method through liquid chromatography-tandem mass spectrometry resulted in the addition of a total of 19 new substances to the traditional toxicological screening panel. The task of identifying specific types of synthetic cannabinoids has become increasingly complex, since over 220 new synthetic drugs have recently been classified as cannabinoid receptor agonists.[5] Based on government seizure reports, only three synthetic cannabinoids were screened: UR-144, JWH-073, and synthetic cannabinoid 5F-ADB (5F-MDMB-PINACA).[6] Nevertheless, toxicology surveillance detected a broad variety of substances, such as: opioids (morphine, acetylmorphine, heroin, codeine, methadone, tramadol, and fentanyl); entactogens (MDMA, MDA, MDEA, MBDB); various phenethylamines, including 25B-NBOMe, 25C-NBOMe, and 25E-NBOH, as well as 2C drugs (2C, 2C-B) and tryptamines like 5-MeO-DMT; synthetic cathinones (mephedrone, ethylone, 3,4-MDPHD); dissociatives (ketamine and phencyclidine, 3-MeO-PCP); and hallucinogens, including lysergic acid diethylamide, dimethyltryptamine.

The new panel was added to the standard assessment, which already included 32 psychoactive drugs. This also allowed identification of potentially lethal adulterants in crack cocaine, such as strychnine and other common adulterants such as phenacetin and levamisole. To date, two sample collection cycles have been conducted, with batches of 10 hair samples from patients seeking treatment in May 2023 and February 2024. Among the 20 patients who reported using K drugs, 15 also reported crack use. Four patients had not used crack but reported intranasal cocaine use. At least one adulterant (phenacetin and/or levamisole) was detected in the hair samples of five of these 15 crack users. The analysis also ruled out strychnine as an adulterant in any of the samples. Tetrahydrocannabinol was only identified in 3 of the 20 samples. Cannabinol, another natural cannabinoid, was detected in two samples, while cannabidiol was not found in any sample. One patient, whose hair sample tested negative for both cocaine and crack, had consumed at least two opioids: fentanyl and tramadol. Fentanyl (a synthetic opioid) and tramadol (a natural opioid) were only detected in this user, who also tested positive for the synthetic cannabinoid 5F-MDMB-PINACA, which was detected in five of the 20 samples. No other synthetic drugs were detected in the samples.

Although 5F-MDMB-PINACA shares several adverse effects with other compounds in the synthetic cannabinoid class, the intensity and range of its symptoms are particularly concerning.[7] These pharmacological characteristics are consistent with the severe clinical presentations observed among patients treated at the open drug scene. However, 5F-MDMB-PINACA was detected in

only approximately one-quarter of the samples. This discrepancy suggests that other highly potent psychoactive substances may have been in circulation in the open drug scene during the same period, potentially contributing to the observed clinical severity.

Notably, during the same period, São Paulo law enforcement reported a marked increase in the seizure of a new class of synthetic opioid known as nitazenes, a highly potent benzimidazole with an estimated potency ranging from 1.5 to 20 times that of fentanyl.[8-10] Although these substances were increasingly detected in law enforcement and forensic toxicology settings, the toxicological panel used in this preliminary phase of our surveillance was not yet equipped to identify nitazenes. This limitation raised the possibility that undetected nitazenes may have contributed to the severe clinical presentations observed in some cases. In response, efforts are now underway to expand the toxicological panel to include newly circulating synthetic cannabinoids and nitazenes.

The confirmed detection of 5F-MDMB-PINACA, even in a limited subset of cases, marked a critical milestone in understanding the substances circulating in São Paulo's open drug use scene. This finding has already proven fundamental for improving clinical care, enabling more accurate risk assessments, more precisely targeted interventions, and ultimately better treatment outcomes for this high-risk population. Moreover, it underscores the profound challenges inherent to monitoring new psychoactive substances in highly dynamic and polysubstance environments such as open drug scenes, where patterns of use, adulteration, and drug availability shift rapidly and unpredictably. These findings reinforce the urgent need for agile, adaptive toxicological surveillance systems capable of keeping pace with the evolving drug landscape.

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Disclosure

The authors report no conflicts of interest.

Data availability statement

The data that support this study are available from the authors upon request.

Author contributions

CSM: Conceptualization, Project administration, Funding acquisition, Investigation, Writing – original draft.
KISB: Project administration, Data curation, Resources.
AYS: Data curation, Methodology, Validation.
GZ: Validation, Resources, Supervision.
VCR: Investigation, Methodology.
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ACA: Project administration, Data curation.
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MC: Writing – review & editing.
TB: Resources, Methodology.
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