CASE REPORT

Unexpected Detection of Psilocybin in a 100 mg Tramadol Tablet: A Forensic Case Report

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Abstract

***Background*:** Tramadol is a synthetic opioid analgesic prescribed for moderate pain. Psilocybin (4-phosphoryloxy-N,N-dimethyltryptamine) is a naturally occurring psychoactive compound found in certain mushrooms, often referred to as "magic mushrooms" and is classified as a Schedule I substance. This case report aimed to present the unexpected detection of psilocybin in a 100 mg tramadol tablet.
***Case Presentation*:** This case report presents the forensic identification of psilocybin in a tablet labeled as tramadol 100 mg. Analysis was conducted using Gas Chromatography–Mass Spectrometry (GC-MS). A high concentration of psilocybin was confirmed, and additionally, 60 mg of tramadol was detected in the analyzed tablet.
***Discussion*:** Active compounds of some mushrooms, such as Psilocybe cubensis and Paneolus, have psychotropic agents with hallucinogenic effects. Psilocybin is a prodrug of psilocin, meaning it's converted into psilocin in the body, and Psilocin then acts as a serotonin receptor agonist, particularly on the 5-HT2A receptor, leading to visual hallucinations, euphoria, and altered cognition. These effects can be particularly dangerous when combined with other opioids and psychoactive substances that do not have a determined dosage and intensify each other's effects.
***Conclusion*:** This case underscores the importance of drug monitoring and advanced toxicological analysis in combating the public health threat posed by drug adulteration.

Keywords: Tramadol, Psilocybin, Drug Adulteration, Gas Chromatography–Mass Spectrometry (GC-MS), Hallucinogens

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INTRODUCTION

Tramadol is a synthetic opioid analgesic frequently prescribed for moderate to moderately severe pain [1]. Despite being a controlled substance, it is considered relatively safe compared to stronger opioids, leading to widespread use and occasional abuse [2]. Psilocybin, on the other hand, is a hallucinogenic tryptamine compound found in Psilocybe mushrooms and is classified as a Schedule I substance in many countries, including Iran [3]. Its psychoactive effects include altered perception, hallucinations, and changes in mood and cognition, typically occurring within 30–60 minutes of ingestion [4, 5]. The presence of psilocybin in a medication assumed to be tramadol is unprecedented and poses serious risks to unsuspecting users. This report outlines the analytical process and public health implications of this adulteration case identified in Iran.

The increasing complexity of illicit drug distribution networks has facilitated the emergence of counterfeit medications that mimic the appearance of legitimate pharmaceuticals. In particular, the blending of psychoactive substances with therapeutic drugs poses a unique challenge to both clinical and forensic settings [6, 7]. This trend underscores the necessity for robust analytical techniques, such as GC-MS, to accurately identify hazardous adulterants and prevent adverse outcomes in the population.

CASE PRESENTATION

A tablet, visually indistinguishable from standard 100mg tramadol formulations, was submitted to the toxicology unit

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of the North Khorasan legal medicine in Bojnourd. This case was obtained from the illicit market, not through a licensed pharmacy or medical prescription. The submission followed a report of atypical psychoactive effects (including hallucinations and confusion) in a user who had ingested what was believed to be a routine dose of tramadol. The individual had no prior psychiatric history or known exposure to hallucinogens.

Analysis

The substance was analyzed using Gas Chromatography–Mass Spectrometry (GC-MS) at the forensic laboratory of the North Khorasan legal medicine.

Procedure

- The tablet was crushed, dissolved in methanol, centrifuged, and filtered.
- GC-MS was performed using an Agilent 7890A GC with 5977B MS detector, under electron ionization (EI) conditions [8, 9].
- Data were matched with reference spectra from the NIST MS library.

Findings

- A strong chromatographic peak matched the profile of psilocybin, confirmed by its retention time and mass spectrum.
- Estimated concentration: approximately 15 mg of psilocybin per tablet.
- Additionally, 60 mg of tramadol was detected in the analyzed tablet.

DISCUSSION

This case illustrates an alarming incident of drug adulteration in Iran involving a pharmaceutical-grade opioid substituted with a psychedelic compound. Such substitutions are hazardous; the detection of psilocybin in routine forensic or clinical screening presents significant challenges. Standard immunoassay-based drug screening panels, which are commonly used in both clinical and law enforcement settings, typically do not include psilocybin or its active metabolite, psilocin, due to their unique chemical structure and limited cross-reactivity with antibodies used in these assays. As a result, cases involving psilocybin may go undetected unless more sophisticated analytical techniques are employed. Confirmatory methods, such as GC-MS or liquid chromatography–tandem mass spectrometry (LC-MS/MS), offer the specificity and sensitivity required to reliably identify and quantify psilocybin and related tryptamines [10]. The pharmacological effects of psilocybin are mediated by agonism at serotonin 5-HT2A receptors, leading to visual hallucinations, euphoria, and altered cognition [11, 12]. These effects can be particularly dangerous in unsuspecting individuals who believe they are consuming a therapeutic agent. This is the first reported case in Iran of psilocybin being found in a tramadol-labeled product. The forensic identification using GC-MS was critical, as standard drug immunoassays are unlikely to detect psilocybin [13]. While this case represents the first reported detection of psilocybin in a tramadol tablet in Iran, similar incidents of drug adulteration have been documented globally and highlight a growing public health concern. Studies have shown that adulteration of pharmaceutical and over-the-counter products—including dietary and sexual enhancement supplements—is a widespread issue that often involves the unauthorized addition of pharmacologically active substances, posing significant risks to users unaware of such modifications [14, 15]. In particular, the addition of psychoactive compounds to products marketed for entirely different purposes reflects a disturbing trend that complicates clinical management and undermines drug safety regulations [16]. These international findings underscore the forensic and public health relevance of our case, emphasizing the need for increased surveillance and analytical scrutiny to detect and prevent such adulterations. The unexpected combination of psilocybin, a serotonergic psychedelic, with tramadol, an opioid analgesic with serotonergic activity, raises significant concerns about potential pharmacological interactions. Both substances influence the central serotonergic system, which may increase the risk of serotonin syndrome—a potentially life-threatening condition characterized by agitation, confusion, tachycardia, hypertension, hyperthermia, and neuromuscular abnormalities [17, 18].

Moreover, this case sheds light on the evolving tactics employed by drug traffickers, where psychoactive compounds are stealthily introduced into otherwise routine pharmaceuticals. One possible hypothesis is that such adulteration may be intended to increase the psychoactive effects of the product, potentially leading to greater user appeal or repeated use, though further research is needed to confirm any specific motives behind this practice, further complicating public health responses [19]. Interdisciplinary collaboration between forensic laboratories, healthcare providers, and law enforcement is essential to address this multifaceted threat effectively.

CONCLUSION

This case report emphasizes the necessity for comprehensive chemical screening of suspicious or counterfeit pharmaceuticals, particularly in regions with increasing reports of drug adulteration. To address the risks associated with drug adulteration exemplified by this case, we recommend the implementation of targeted screening protocols in forensic laboratories, including routine analysis of seized pharmaceutical products using advanced analytical techniques such as GC-MS, LC-MS/MS, or high-resolution mass spectrometry (HRMS). These methods should be calibrated to detect a broad spectrum of psychoactive substances, including emerging hallucinogens like psilocybin. Additionally, national toxicology databases should be updated regularly to include novel adulterants and combinations. We recommend the expansion of forensic

toxicology capabilities and clinician awareness regarding the hallucinogenic substitution of commonly used medications such as tramadol.

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Ethical Approval: This study is deem exempt from Ethics Committee review, as it qualifies as non–human subjects research; therefore, the requirement for informed consent was waived.

Conflict of interest: The authors declare that they have no financial conflicts of interest or personal affiliations that could have influenced the objectivity or integrity of the results presented in this manuscript.

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REFERENCES

1. Grond S, Sablotzki A. Clinical pharmacology of tramadol. Clinical pharmacokinetics. 2004;43(13):879-923.
2. Alrashdi S, Paudyal V, Elnaem MH, Cheema E. Causes, nature and toxicology of tramadol-associated deaths reported in the peer-reviewed literature: a systematic review of case studies and case series. Drugs Ther Perspect. 2021;37(9):422-32.
3. Milano G, Saenz E, Clark N, Busse A, Gale J, Campello G, et al. Report on the International Workshop on Drug Prevention and Treatment in Rural Settings Organized by United Nation Office on Drugs and Crime (UNODC) and World Health Organization (WHO). Subst Use Misuse. 2017;52(13):1801-7.
4. Carhart-Harris RL, Bolstridge M, Day CMJ, Rucker J, Watts R, Erritzoe DE, et al. Psilocybin with psychological support for treatment-resistant depression: six-month follow-up. Psychopharmacology. 2018;235(2):399-408.
5. Nichols DE. Psychedelics. Pharmacological reviews. 2016;68(2):264-355.
6. Hasler F, Grimberg U, Benz MA, Huber T, Vollenweider FX. Acute psychological and physiological effects of psilocybin in healthy humans: a double-blind, placebo-controlled dose-effect study. Psychopharmacology. 2004;172(2):145-56.
7. Tylš F, Páleníček T, Horáček J. Psilocybin--summary of knowledge and new perspectives. Eur Neuropsychopharmacol. 2014;24(3):342-56.
8. Cozzi NV, Daley PF. Synthesis and characterization of high-purity N,N-dimethyltryptamine hemifumarate for human clinical trials. Drug Test Anal. 2020;12(10):1483-93.
9. Moeller MR, Kraemer T. Drugs of abuse monitoring in blood for control of driving under the influence of drugs. Therapeutic drug monitoring. 2002;24(2):210-21.
10. Dinis-Oliveira RJ. Metabolism of psilocybin and psilocin: clinical and forensic toxicological relevance. Drug Metab Rev. 2017;49(1):84-91.
11. Rickli A, Kopf S, Hoener MC, Liechti ME. Pharmacological profile of novel psychoactive benzofurans. Br J Pharmacol. 2015;172(13):3412-25.
12. Griffiths RR, Richards WA, McCann U, Jesse R. Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. Psychopharmacology. 2006;187(3):268-83; discussion 84-92.
13. Pasin D, Cawley A, Bidny S, Fu S. Current applications of high-resolution mass spectrometry for the analysis of new psychoactive substances: a critical review. Anal Bioanal Chem. 2017;409(25):5821-36.
14. Yéléhé-Okouma M, Pape E, Humbertjean L, Evrard M, El Osta R, Petitpain N, et al. Drug adulteration of sexual enhancement supplements: a worldwide insidious public health threat. Fundamental & clinical pharmacology. 2021;35(5):792-807.
15. Czepielewska E, Makarewicz-Wujec M, Różewski F, Wojtasik E, Kozłowska-Wojciechowska M. Drug adulteration of food supplements: A threat to public health in the European Union? Regulatory toxicology and pharmacology : RTP. 2018;97:98-102.
16. Vahdati Hassani F, Abnous K, Mehri S, Jafarian A, Birner-Gruenberger R, Yazdian Robati R, et al. Proteomics and phosphoproteomics analysis of liver in male rats exposed to bisphenol A: Mechanism of hepatotoxicity and biomarker discovery. Food Chem Toxicol. 2018;112:26-38.
17. Volpi-Abadie J, Kaye AM, Kaye AD. Serotonin syndrome. Ochsner J. 2013;13(4):533-40.
18. Ahmadi H, Ramezani M, Yazdian-Robati R, Behnam B, Razavi Azarkhiavi K, Hashem Nia A, et al. Acute toxicity of functionalized single wall carbon nanotubes: A biochemical, histopathologic and proteomics approach. Chem Biol Interact. 2017;275:196-209.
19. Palamar JJ, Keyes KM. Trends in drug use among electronic dance music party attendees in New York City, 2016-2019. Drug Alcohol Depend. 2020;209:107889.