

LETTER TO THE EDITOR

CBD products and their impact on urine toxicology analyses: Evidence from a six-case series

Productos con CBD y su impacto en los análisis toxicológicos de orina: Evidencia de una serie de 6 casos

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In Spain, daily or almost daily cannabis use has a prevalence of around 3.7%, making Spain one of the three countries in the European Union with the highest use in this risk pattern (Manthey et al., 2021). The plant from which cannabis consumer products are derived has around 500 components, of which more than 40 are cannabinoids. The main cannabinoids are delta-9-tetrahydrocannabinol (THC) - the psychoactive component in the highest quantity - and cannabidiol (CBD) (Casajuana Kögel et al., 2018). Recently, the use of cannabis derivatives with low THC content (<0.2%) and high CBD content (at times higher than 10%) has become popular, since they are sold within an ambiguous legal framework and offered as a less harmful, sometimes even healthy alternative, despite the lack of scientific evidence. Researchers and healthcare professionals are wondering whether the use of these products can lead to positive

results in routine urine THC tests, given that they contain a minimal dose of THC (<0.2%, according to the labels).

We conducted a clinical and analytical study of the THC metabolite (11-nor-9-carboxy-delta-9-THC) with six healthy volunteers. These six researchers smoked a standard joint (Casajuana Kögel et al., 2017) with high CBD and low THC content, according to the label (<0.2% THC); three of them had the “weed” equivalent format (“Remedy” variety, CBD <13%) and the other three the “hashish” equivalent (“Ketama” variety, CBD<15%). Per protocol, it was ensured that no participant had a history of substance use disorder, a personal or family history of serious mental disorder, or any medical illness. All participants were of legal age (age range: 27 – 39), two were women (non-lactating and non-pregnant) and four were men, and all freely gave their consent. The product was purchased from a specialized CBD store. None of

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the participants presented psychoactive effects. The only adverse effect detected was one user's self-limiting irritating cough and mild dizziness, probably related to the route of administration, the user not being a regular smoker. Twelve hours after smoking, each participant provided a urine sample that was sent to the laboratory for routine analysis of the THC metabolite by immunoassay screening (Atellica Solutions, Siemens Healthineers) followed by confirmatory analysis performed by gas chromatography-mass spectrometry (GC-MS) (Agilent Technologies). The results in all six cases and for both types of analysis were negative.

Cannabis use is contraindicated in certain pathologies (such as schizophrenia, COPD, etc.), conditions (pregnancy, breastfeeding, driving, etc.) or circumstances (alternative penal measures, transplant evaluation processes, prisons, etc.) (Kriss et al., 2024; Petrilli et al., 2022; Solmi et al., 2023). This may lead some regular cannabis users to look for alternatives they consider less harmful and which, at the same time, do not prove positive in urine tests; for example, anxiolytic or hypnotic effects without other psychoactive effects are sought after, beyond the limited scientific evidence available regarding such effects. Given the lack of knowledge about the effects of the low THC content of these products and their detectability by routine cannabis analysis, which may have implications for certain populations (pregnancy, breastfeeding, driving or other legally regulated circumstances), studies are needed to clarify the safety and adverse effects of cannabidiol use, as well as its impact on toxicological studies.

To our knowledge, this is the first study of its kind. However, other groups have already warned of CBD products being accidentally contaminated with THC and even heavy metals or pesticides. Some CBD samples could thus have higher THC concentrations than stated on the label. Of particular concern is the online purchase of such products due to the risk of fraud (Bonn-Miller et al., 2017; Gidal et al., 2024; Johnson et al., 2022; Liebling et al., 2022). A helpful simile in understanding the knowledge gap would be the differentiation between non-alcoholic beers (up to 1.2% alcohol) and 0.0 beers (up to 0.04% alcohol) where the limits are clear. While the former has clinical and toxicological implications, the second type of beer is less relevant at these levels. Currently, we do not know if the CBD products on the market are more like "0.0" or "non-alcoholic" beers, or even if, in some cases, they could be beers with the usual amount of alcohol and labelling errors.

Our study has some limitations. Firstly, the detectability of the THC metabolite was only analysed in a reduced intake. Furthermore, we have only used two types of samples from a single supplier. Our sample size is small. Finally, we have not analysed other psychoactive cannabinoids such as delta-8-tetrahydrocannabinol (La Maida et al., 2022).

We can conclude that, for this specific batch from this specific producer, the use of CBD with a low percentage of THC is not detectable in urine with screening laboratory analyses nor confirmatory for cannabis. There is a need for studies which investigate different suppliers and batches, as well as different sales environments (cannabis user associations, black market, specific CBD stores, online products, etc.) so that users can be correctly informed about the risks associated with the use of available products with CBD and low THC content, including those related to forensic studies or medical evaluations.

Conflict of interests

MJM has received medical education and training courses support from Rovi, Janssen-Cilag and Casen Recordati and travel support from Rovi.

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