The implications of the use of cannabidiol-related products in a safety-sensitive drug testing environment: A medical-legal perspective

J Jooste,1 BSc, BSc Hons; J B Laurens,2 BSc (Ed), BSc Hons, MSc (Chem), MSc (Appl Tox), MPhil (Med Law), PhD (Chem), PhD (Med Law); M Jordaan,3 BSc Hons, MSc (Chem Path); A A S Marais,4 BSc, BSc Hons, MSc (Chem Path); L G Curlewis,2 BLC, LLB, LLM (Proc Law), LLM (Lab Law), LLM (Comm Law), LLD

1 Department of Chemistry, Faculty of Agriculture and Natural Sciences, University of Pretoria, South Africa
2 Expert Laboratory Services, Pretoria, South Africa
3 Forensic Science Laboratory, South African Police Service, Pretoria, South Africa
4 Department of Procedural Law, Faculty of Law, University of Pretoria, South Africa

Corresponding author: J B Laurens (tim@expertlabservices.co.za)

Cannabis access laws allow for the use of cannabis in private and the trade, purchase and use of hemp-related products as a complementary medicine and for other benefits. Cannabidiol (CBD) has the treatment potential for several conditions but, with the lack of resources in South Africa to maintain the legislation, products contaminated with delta-9-tetrahydrocannabinol (Δ9-THC) are sold by some suppliers who do not comply with the legislative provisions in terms of the threshold concentrations for Δ9-THC. This dilemma complicates a medical review officer’s decision regarding intentional use of Δ9-THC or otherwise, since a CBD user may have purchased the product legally and in good faith. Hemp- and CBD-containing products were analysed by gas chromatography-mass spectrometry and compliance was assessed for CBD and Δ9-THC purity against the legislative thresholds. A strategy based on metabolite ratios is suggested to distinguish between intentional or irresponsible cannabis use and legitimate CBD use.


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Cannabis sativa L. was brought to Africa by Arab traders, and has been cultivated for at least 5 000 years for many established medical and historical purposes.[1-3] Marijuana and hemp are colloquial names for cannabis strains of the same plant genus. Hemp is characterised by a low concentration of delta-9-tetrahydrocannabinol (Δ9-THC), the primary psychactive compound in C. sativa, popularising hemp cannabidiol (CBD) oils, as the medical benefits can be obtained without the psychoactive effect of marijuana, the latter characterised by high concentrations of Δ9-THC.

CBD demonstrates a decreased agonism of the CB-1 receptor compared with Δ9-THC, explaining the absence of psychoactive effects.[5] It is claimed that CBD can reduce the use of opioids owing to its antinociceptive effects in inflammation models, reducing heroin-seeking behaviour.[5-8]

After numerous calls for legalisation from the South African (SA) public and activists, despite some caution raised by academics,[8,9] C. sativa access laws were passed, first by legalising the private use of cannabis,[11-14] and secondly, by amendments to the schedules of the Medicines and Related Substances Act No. 101 of 1965 (Medicines Act),[15] applying a threshold concentration approach for CBD and Δ9-THC.

As with all crucial decisions, unforeseen consequences have created dilemmas. One of these is that hemp products and CBD oils are contaminated with Δ9-THC owing to unregulated cannabis plant strains, ineffective enrichment and purification procedures, inadequate analytical quality control and testing and known law enforcement constraints to ensure product compliance in SA. These factors were legitimate concerns before legalisation, and have remained, since SA is a developing country that lacks resources to manage the broad social impact of legalisation.[16-19]

Medical practitioners who function as medical review officers (MROs) in the occupational health setting are confronted with the difficulty of distinguishing between intentional or negligent use of Δ9-THC where it is prohibited, as opposed to non-intentional administration using complementary medicine. Delta-9-THC contamination of CBD oils is also critical in other areas where medical practitioners advise on test results: for school drug-testing programmes where CBD oils are sometimes administered to learners by their parents as complementary medicine; parents in custody cases being tested for substance abuse and adjudicated in SA family courts; sports doping tests where such substances are prohibited; and driving under the influence of intoxicating substances.

The results of incorrect interpretation regarding cannabis testing results have two aspects. First, there is the possibility of cross-reactivity of the screening due to non-specific interference from other cannabinoids, leading to false positives, most common in immunoassays.[17] Second, there are difficulties in discriminating the source of Δ9-THC in the case of true positives.

The legitimate use of CBD-enriched oil as complementary medicine has gained a tremendous amount of traction recently. Its use as complementary medicine, or as edible and drinkable products, is legal if compliant with the schedules of the Medicines Act.[15,18] There is a danger of compromising safety in the workplace and triggering positive drug tests if the products are contaminated with Δ9-THC.[19-22]

The use of CBD-related products may also become the first line of defence for individuals who smoke cannabis and fail threshold drug
tests in the workplace. An uninformed MRO decision may also result in injustice if an individual uses a hemp product not knowing that it is contaminated with Δ^2-THC.

Relevant legislation
The fundamental human rights related to the legal use of cannabis and its refined products must be balanced against the health and safety of others.[20] The relevant human rights of privacy, freedom, autonomy, freedom of religion and the equal enjoyment of rights and privileges are indicated in the Bill of Rights of the Constitution of the Republic of SA.[21] The legalisation in effect confirmed that cannabis and hemp product users should enjoy equal protection and benefit of the law, including the enjoyment of rights and freedom.[22]

The legalisation of the private use of cannabis also did not preclude the health and safety legislation and regulations applicable to workplaces and risk-sensitive environments.[23,24] Screening and confirmation threshold testing, followed by validation by a MRO, are mainly utilised to detect individuals with prohibited substances in their bodies.[25]

The schedules of the Medicines Act classify CBD-containing products for human consumption as follows[26]:
- All products intended for human ingestion with a Δ^2-THC purity greater than 0.001 mass percentage are classified as schedule 6.
- All CBD-containing products are classified in schedule 4, unless the products are indicated as complementary medicine, with a total mass of less than 600 mg CBD per package, intended to be administered in a regimen of less than 20 mg CBD per dose.
A product that complies with this specification is classified in schedule 0.

Pharmacodynamics and pharmacokinetics of CBD and Δ^2-THC
CBD and Δ^2-THC have similar pharmacokinetics. The shared highly lipophilic character of Δ^2-THC and CBD results in rapid distribution throughout the body, with both compounds metabolised in the liver by cytochrome P450 enzymes.[48]

These compounds are mainly excreted in the faeces as un-metabolised compounds,[49] and in the urine as metabolites THC-COOH[50] and CBD-glucuronide.[51] The elimination half-life of these compounds is similar, ranging from 3 to 4 days for THC-COOH[51] and 2 to 5 days for CBD.[52] Therefore, a similar detection window is expected.

Synthesis: Legislation, science and ethics
The cannabis access laws in the form of amendments to the Drugs and Drug Trafficking Act No. 140 of 1992,[53] the Medicines Act[54] and their respective schedules should, in principle, not affect drug test results performed as part of a health and safety programme in workplaces and other areas where drug tests are performed. The national health and safety legislation did not change, and it is still the responsibility of employers to ensure a safe workplace, which includes drug testing. However, Δ^2-THC-contaminated hemp and CBD products can affect cannabis drug test results in unforeseen ways.
First, CBD product (primarily oils and tinctures) use may trigger positive drug tests since Δ⁹-THC can accumulate in the human body owing to its lipophilic character and extensive half-life, exceeding administrative thresholds or cut-off concentration values. Second, it may become a first-line defence for non-negative screening tests and positively confirmed Δ⁹-THC test results. The integrity of such a defence must be interrogated if a transgression by the employee of workplace policy or contract has indeed occurred, where a delictual liability exists or where criminal sanctions may apply.

The absence of intent must be kept in mind when the MRO assesses the organisation’s risk due to the possible use of cannabis by the individual. A strict liability approach is not justified in a workplace drug testing programme, but decisive action must follow for users with no legitimate excuse for intentional or negligent use. It will be a complex task for the MRO to investigate whether Δ⁹-THC ingestion is due to the ingestion of a contaminated CBD oil product. The MRO may consider analysing the product to verify the Δ⁹-THC purity, since a non-compliant CBD product is already suspicious. Doubt will, however, not be eliminated even if the product does comply with the legislative requirements. Dosage frequency, dose amounts, and the continuous homoeostatic process related to the body’s hydration status, which may concentrate drug metabolites in the urine, are all bioaccumulation factors that must be considered.

It will also be problematic for a company to prohibit and enlist the use of hemp- and CBD-containing complementary medicine, purchased legally, in good faith and used correctly according to the prescribed dose regimen in schedule 0. For this reason, legitimate use of CBD products should be considered carefully to exclude the possibility of a confirmed positive test result due to the use of such products that may be contaminated with Δ⁹-THC.

The prohibition of cannabis use and possession in a workplace could justify invoking the Constitutional limitation-of-rights clause within reasonable boundaries.[27] However, in the authors’ opinion, it is doubtful that this can be justified for a schedule 0 substance such as CBD when used within all legal bounds.

The issue of contaminated hemp and CBD products may be attributed to the fact that SA does not have adequate resources to maintain the Medicines Act and related regulations’ legislative provisions. Also, advertising the products by stating that the product ‘contains no THC’ is a qualitative statement that should be supported with a definitive value. If the purities are not reported accurately, it amounts to false advertising, which has far-reaching consequences. The authors believe that all cannabis test results must be cautiously assessed by the organisation’s risk due to the possible use of cannabis. It will not take long for some cannabis users to understand that a ‘normal’ CBD:Δ⁹-THC ratio can be skewed by CBD co-administration. Therefore, more research is required to discover unique and selective markers that will enable more accurate discrimination between Δ⁹-THC and CBD users.

Conclusions

The recent changes in the schedules of the Medicines Act related to CBD necessitate proper quality control of CBD products from a compliance drug-testing perspective. The analysis of commercial products containing CBD highlighted quality-control shortcomings. Products commonly did not match the CBD values listed on their packaging, and one of the products was contaminated with Δ⁹-THC, showing levels far above the SA legislative threshold of 0.001 mass percent. CBD users risk administering unknown amounts of cannabinoids, including Δ⁹-THC, and are at risk of positive cannabis drug test results.

It is recommended that medical practitioners consider CBD:Δ⁹-THC metabolite ratios in urine or oral fluid to distinguish between an intentional or irresponsible cannabis user and a legitimate CBD user.

Declaration. None.

Acknowledgements. None.

Author contributions. The authors contributed equally to the initial concept and preparation of the manuscript.

Funding. None.

Conflicts of interest. None.

25. Constitution of the Republic of South Africa, Chapter 2, section 9(1) and 9(2).


Accepted 15 June 2021.