The role of the laboratory in dealing with cannabis in the workplace

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INTRODUCTION

Cannabis is a mixture of plant alkaloids (phytocannabis) also known as marijuana, dagga or tetrahydrocannabinol (THC). Three constituents, delta-9-tetrahydrocannabinol (Δ^9-THC), cannabidiol (CBD) and cannabinol (CBN), are the most abundant principle constituents. Whilst most of the phytocannabinoids are not psychoactive, Δ^9-THC, and 11-hydroxy-THC are the most psychoactive of all the constituents of marijuana.

The two major cannabis plants, *Cannabis sativa* and *Cannabis indica*, grow wild and are illegally harvested or commercially cultivated. *Cannabis sativa* has the highest concentration of the active component, Δ^9-THC. However, this varies in percentage (by ±12%), depending on the demographics and climate. *Cannabis indica* has a higher ratio of Δ^9-THC:CBD whilst *Cannabis sativa* has a lower Δ^9-THC:CBD ratio. *Cannabis sativa* has more of a sedative effect,[1] whereas cannabis strains with CBD:THC ratios > 5:2 are more likely to have a relaxing and anxiolytic effect.

The recent legalisation of dagga has placed it in the spotlight. While many articles highlight the beneficial and positive effects of cannabis, including treating cancer, providing relief from chronic pain and insomnia, and stimulating appetite, we still don't fully understand the impact of chronic use on health. The question remains as to whether the effect experienced by the patient is psychological or whether there is a true clinical benefit. Figure 1 demonstrates some of the medical benefits associated with cannabis use.

While there are differences in the effects of cannabis for chronic and recreational users, both may pose a risk in the workplace. A chronic user of marijuana requires increasing doses to achieve a response, whereas recreational users consume smaller quantities of THC and experience a state of euphoria, alteration of time and space perceptions, and a different/confused awareness of their surroundings in ways that can impair driving.[3] With the recent legalisation of cannabis for recreational use in South Africa, many questions have been raised, regarding the impact it will have on the workforce. Some of these include:

- How do we approach the monitoring of workers and the general driving population?
- How do we determine the concentration of THC at which employees are considered to be under the influence and a risk to themselves and their co-workers?

It is estimated that workers who recently used cannabis (t½ = 3-13 days for a frequent user) are 1.5-2 times less coherent and a risk to their co-workers),[4] whilst a blood alcohol concentration (BAC) of 0.08-0.12% (t½ = 3-14 hours) increases the risk of an accident 5-30 fold.

Laboratory challenges in testing for cannabis

Whilst point-of-care (POC) strips and laboratory immunoassay-based methods are useful (quick with acceptable turnaround times), metabolites of cannabis can remain in the urine for days to weeks after use, making it difficult to distinguish between recent and prolonged use or exposure. With technological advancements and the development of mass spectrometry-based methods, we are now able to quantify 15 of the most common phytocannabinoids and their metabolites in urine, oral fluid and whole blood. These can be analysed at very low levels with a high degree of certainty.[5-7]

Some of the common phytocannabinoids screened for and analysed

Table 1. Analytical summary of THC testing in the different matrices

Sample matrix	Active THC compounds	Analytical calibration range (ng/ml)	Analytical Technique	Comment
Urine	Δ^9-THC	20.0-50.0	LC-MS/MS or GC/MS immunoassay antibody testing	Clinical routine screening
Oral fluid	Carboxy-delta-9-THC,	2.0-10.0	LC-MS/MS or GC/MS	Early detection – most recent usage of cannabis
Whole blood	11-nor-9-carboxy-delta9-THC, Δ^9-THC, cannabidiol	2.0-10.0	LC-MS/MS or GC/MS	Routine confirmation of positive screening on whole blood required for positive oral fluid and urine samples

Table 2. Legal cut-off limits for THC levels in blood and/or oral fluid in different countries

Country	Legal cut-off limit (ng/ml)*	Comment	Reference
Belgium, Denmark, Ireland, Luxembourg, The Netherlands	1.0-2.0	Penalties with increasing blood concentration	Hughes, 2017[11] Ramaekers, 2017[12] Vindenes, 2017[13]
Norway	1.3-9.0	The severity of penalties increases with increasing blood concentration	Hughes, 2007[11]
United Kingdom	2.0	Zero-tolerance approach	Wolff et al., 2013[14] Ramaekers et al., 2017[15]
United States of America	5.0	No significant evidence of impairment below 5.0 ng/ml	Compton, 2017[16]

*a high degree of impairment might be expected above the legal cut-off limit

include: 11-OH-THC, 11-COOH-THC, 11-nor-9-carboxy-delta-9-THC-glucuronide, THC, cannabichromene, cannabidiol, cannabidiolic acid, cannabidivarin, cannabidivarinic acid, cannabigerol, cannabigerolic acid, cannabinol, cannabinolic acid, tetrahydrocannabinolic acid, and tetrahydrocannabivarin.

Delta-9-tetrahydrocannabinol is metabolised to the active metabolite, 11-hydroxy-THC (11-OH-THC), and to the inactive metabolite, 11-nor-9-carboxy-THC (THCCOOH). The analysis and quantification of these species, together with a few minor species, in oral fluids, urine and whole blood, are now possible, utilising liquid chromatory-tandem mass spectrometry (LC-MS/MS) (Table 2). Oral fluid is the least invasive and the preferred matrix for measurement. LC MS/MS techniques are superior to other methods (immunoassay-based), as they can accurately quantify and distinguish the different THC-metabolites, allowing one to estimate the time of exposure, based on the pharmacokinetics. To put this into perspective, we are now able to distinguish between an individual who smoked more than eight hours ago and one who smoked on shift at work, using THC analytes in oral fluid and whole blood. A positive oral fluid test is usually followed by a confirmatory blood sample to determine whether the person is a regular or a recreational user.

It must be noted that, in 32% of cases, a positive oral fluid result does not correlate with the blood result. It is believed that this finding is made when the THC analyte is below the detection limit.[8] In this case, a negative blood result following a positive oral fluid result indicates a once-off exposure in an individual. High levels of THC in blood and oral fluid is proof that an individual has used, or been exposed, to cannabis.

Table 1 summarises the analytical methods used to determine the important THC metabolites and cut-offs in different matrices.

It must be noted that the amount of THC in oral fluid or blood does not strongly correlate to driver impairment in the same way that BAC does for alcohol-impaired driving.[3] The first indication of impairment has been demonstrated at THC blood levels of 2.0-5.0 ng/ml.[9] A blood THC concentration of 3.7 ng/ml is comparable to a BAC of 0.05%.[10]

It is for this reason that there is no defined concentration that correlates THC levels in the blood with impairment. Impairment levels are also difficult to define in a recreational user compared to a chronic user. Table 2 summarises THC legal limit concentrations in some countries.

CONCLUSION

Alcohol-induced impairment remains a much larger safety and public health problem than current cannabis-induced impairment. The legalisation of dagga has changed this dynamic and will require the employment of stricter monitoring policies to safeguard against misuse. The analysis of THC metabolites in oral fluid, urine and whole blood by mass spectrometry will assist occupational health practitioners to make appropriate decisions regarding the health and safety of employees and their co-workers.

Please contact PathCare Laboratories for more information on THC and THC metabolite testing on whole blood and oral fluid.

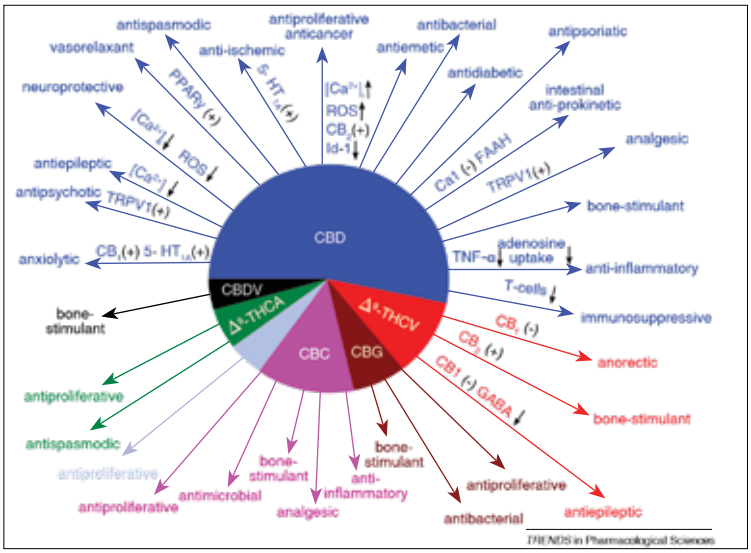

Fig 1. Proposed pharmacological actions of the many non-psychotropic cannabinoids[2]

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