Cannabis: adverse effects, and the challenge of verifying impairment

By Dr Leo Schep[1]

Part 1: It's effect on the body

Cannabis is one of the most widely used recreational drugs in the world.

The active constituent, trans-Δ9-tetrahydrocannabinol (THC), is one of approximately 64 different cannabinoids found within the cannabis plant (*Cannabis sativa*). It is the only cannabinoid that is psychoactive (affects the mind). The highest concentration is found in the flowering tops of the female plant, with lesser concentrations in the leaves and minimal amounts in the stem, seeds and roots.

Users of the drug typically smoke-dried plant matter, though ingestion has become more popular, especially in countries where cannabis and its products have been legalised. Cannabis preparations, including hash oil and hashish, are also consumed.

The percentage of THC in plant products smoked by New Zealand users has, over time, increased from 1 to 3% in the 1960s up to 6 to 25% in recent years (see table 1 below). The associated doses consumed per cigarette have proportionally increased from 10 to 60 mg per cigarette. Doses taken will be greater when users smoke cigar-like products, typically called 'cones'.

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Formulation	Source	THC (%)	Dose (mg)
Marijuana (cigarettes)	Cigarettes (1960-70s)	1-3	10
	Cigarettes (1980-2000s)	6-25	20-60
Cannabis resin	Bricks, cakes, slabs	10-20	
Hashish oil	Solvent extraction	15-65	

Table 1: *Some forms of cannabis available in New Zealand and their THC content*

Effects of cannabis use

Recreational use of cannabis produces psychoactive effects; typically, users may appear either stimulated or sedated. Other symptoms may include altered perception of mood including euphoria and relaxation, somnolence/drowsiness, increased appetite, and increased heart rate. Adverse effects can include confusion, hallucinations, ataxia, dry mouth, and time-space distortions; occasionally, fear, distrust, dysphoria (a profound state of unease or dissatisfaction that often occurs with depression, anxiety, or agitation), or panic occurs after use. Impaired short-term memory, judgment, and attention spans also occur and there is a risk of tremors, hypertension, and vomiting.

The Impaired Driver

Cannabis use can also impair the user's ability to operate machinery or drive a motor vehicle. Numerous studies have indicated that cannabis use results in impaired driving performance with an increased risk of motor vehicle crashes. Evidence suggests that driving under the influence of THC is associated with approximately double the risk of motor vehicle crashes. In the United States in 2017, for example, evidence has shown that THC was the second most frequently identified drug in drug-related incidents. Controlled studies assessing driving impairment have identified effects upon both cognitive and motor functions. Even at low doses of THC, volunteers in these studies have demonstrated impairment of their driving skills such as attention, reaction time, hand-eye coordination,

vigilance, time and distance perception, decision making and concentration. The degree of such impairment is typically dose-dependent.

Chronic Use

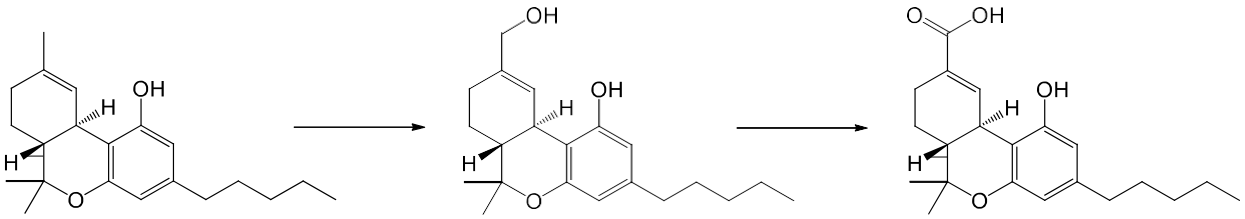
Chronic cannabis use may also be problematic, though many of the effects have not been fully established. Respiratory and cardiovascular problems can be expected and tolerance and dependence on the drug have also been noted. Chronic smoking may also lead to the development of respiratory diseases. Transient acute psychosis can occur following chronic use of cannabis and some users may display evidence of "amotivational syndrome", which is a state of withdrawal, apathetic indifference, general mental and physical deterioration, and social stagnation. Finally, long term use of high doses of cannabis can lead to a condition called hyperemesis. This is often characterized by repeated and excessive vomiting without any obvious cause; symptoms are only resolved following a long hot shower.

Part 2: Testing, forensic analysis and associated legal implications

Smoking or ingesting cannabis causes an individual to be impaired. The intensity and duration of these effects are proportional to the concentration of THC, the psychoactive component of the drug, within the bloodstream. Following the consumption of cannabis, THC levels in the blood will increase, leading to an increase in intensity of psychoactive effects. Blood levels and associated symptoms will then rapidly decrease in occasional users within 2-3 hours post-use. However, in contrast, heavy users of cannabis can have evidence of THC remaining in the bloodstream for many days after last use. One study, for example, could detect it in blood for 7 days.

Metabolism and fate of THC in the body

Once cannabis has entered into the body, the principal psychoactive constituent, THC, is metabolised predominantly in the liver to form a metabolite that is called 11-hydroxy-Δ9-tetrahydrocannabinol (11-OH-THC). This metabolite is then rapidly metabolised to form a second, more persistent, drug called 11-Nor-9-carboxy-Δ9-tetrahydrocannabinol (11-COOH-THC) (see figure 1 below). This metabolite, which is not psychoactive, lingers in the body and partitions into fat, where it can remain for weeks after consumption of the drug. The metabolite will then slowly leach from fat into the blood and be eliminated in the urine; 11-COOH-THC will be detectable in urine and will persist longer in regular drug users than for occasional users. It is this metabolite that is determined in workplace drug testing.



THC 11-OH-THC 11-COOH-THC

Figure 1: *The metabolism of THC to form 11-OH-THC before undergoing further metabolism to form the carboxylic metabolite 11-COOH-THC.*

Detecting and analysing cannabis

Cannabinoids are typically assayed in blood, urine, hair and saliva. The majority of testing in New Zealand, for evidence of recent use, is workplace urine analysis (in contrast, other countries also undertake roadside testing by analysing salivary samples which in New Zealand is only determined by subjective sobriety testing). The initial testing is a screening assay, involving point of care analysis for initial evidence of cannabinoids present in the urine sample. Screening tests have a cut off or detection limit below which the cannabinoid of interest is not detected. They also have a certain failure rate which may result in false positives (detecting the cannabinoid when none is present) and false negatives (failing to detect the cannabinoid when it is present above the cut off level). A positive test is therefore known as a 'non-negative' and requires further analysis to confirm this finding. The presumptive workplace assay therefore cannot be relied upon for proof of impairment. To demonstrate evidential recent use, cannabinoids must be detected by a reliable method that yields results that are acceptable in Court. For forensic purposes, the analysis must be specific to the cannabinoid of interest. The analysis must specifically identify THC-COOH and quantify the concentration present in the urine sample. Analytical methods that are quantitative and sufficiently specific to be accepted in Court in New Zealand include Gas Chromatography - Mass Spectrometry (GC MS) and Liquid Chromatography - Mass Spectrometry (LC MS).

Interpretation of analytical results

For forensic purposes, the toxicologist is interested in two particular analytes: THC in blood which can shed light on impairment, and 11-COOH-THC in urine, which if present indicates recent use of cannabis, typically 2-5 hours in duration.

If a urine drug test detects the presence of 11-COOH-THC at a concentration of at least more than 50 ng/mL (nanograms per millilitre of urine), then this gives a 'non-negative' result, and necessitates further investigations. For evidential purposes, verification is achieved using GC MS or LC MS. Such analysis is necessary to specifically identify and quantify 11-COOH-THC in urine. If the analysis determines the urinary concentration of 11-COOH-THC exceeded 15 ng/mL, then this evidence would support the suggestion of recent cannabis use and the subject would fail their drug test. These are the cut-off levels in the Australian/NZ standards.

It is important to note, however, these positive urine tests do not prove that the person was intoxicated or impaired at the time they took the test; rather it demonstrates the user has recently taken this drug.

Urine testing for cannabis use cannot shed light on levels of intoxication or impairment. If an employees has returned a positive test for a workplace urine test, they may want to talk to a forensic toxicologist to help you understand the significance, if any, of the result for workplace safety.

Roadside drug testing

It is possible that New Zealanders will vote for the legalisation of cannabis in the September 2020 general elections. However, present legislation for roadside drug testing only allows for police to conduct a subjective sobriety test if they suspect a driver is under the influence of a drug. If the driver fails that test, then the police can obtain a blood sample to establish whether the driver was intoxicated by a specific drug. With the short interval of time THC remains in the blood, by the

time a sample has been obtained the drug will most likely have been mostly eliminated from the blood.

Roadside drink drive testing for alcohol intoxication with a breathalyzer test provides a reliable screening method to determine the concentration of ethanol in the blood and subsequent associated impairment. This is because the blood breath concentration is directly proportional to the blood alcohol concentration. To establish cannabis-related impairment, either a blood or saliva sample should immediately be obtained from the driver (THC is not sufficiently volatile to be accurately assayed in breath). Obtaining blood requires an invasive procedure requiring an attending physician. Given saliva concentrations are directly proportional to blood concentrations, this rapid method of detection for THC-associated driving impairment has been gaining increasing use and is widely used by the Australian Police.

Relationship between impairment and THC concentrations in blood

Research on levels of impairment have determined that psychoactive effects associated with 7 to 10 ng/mL of THC in blood are equivalent to those associated with blood ethanol level of approximately 50 mg/dL of blood alcohol. Peak THC concentration in blood after smoking a cannabis cigarette often exceeds 100 ng/mL, before being rapidly eliminated from blood. During the time THC levels remain in the blood, users can be intoxicated and their ability to safely operate machinery impaired.

Post-mortem investigations

Post-mortem investigations of a deceased driver, suspected of being cannabis-impaired at the time of a crash while driving his vehicle, for example, can give one of two scenarios, depending on which site in the body from which samples were obtained. Urine analysis would indicate recent use of cannabis but cannot indicate whether the deceased was impaired at the time of the accident. However, detection of THC in blood could indicate cannabis intoxication and impairment,

depending on the concentration in the blood. THC undergoes redistribution post mortem and the significance of any evidence from samples acquired at autopsy needs to be evaluated by a forensic toxicologist.

Conclusion

In summary, the psychoactive constituent of cannabis, THC, causes mild to moderate psychoactive effects including impairment of driving, that may persist for 2-3 hours after cannabis was used. Evidence of THC in the blood at levels greater than 10 ng/mL indicates the subject was intoxicated at the time the sample was taken.

If the urine from the subject has evidence of the metabolite 11-COOH-THC, this indicates recent use of cannabis, but does not shed light on whether a person was intoxicated at the time the sample was obtained.