



Drug detection *on the road*

BY **DAVE SAMMUT**

Despite numerous studies, our standards of evidence for drugs in relation to driver impairment still fall behind those for alcohol and fatigue.

Road safety is a significant issue worldwide. In Australia, we have been slowly reducing our road fatality statistics since the 1960s, but over recent years the pace of improvement has decreased. While education and enforcement have been relatively successful in changing behaviours in relation to alcohol and fatigue, the issue of the effect of drug impairment on driving has proved substantially more complex.

A problem of substance

NSW Government data indicates that from 2010 to 2013, alcohol (17%), fatigue (17%) and illicit drugs (13%) were all contributing factors in analysed road fatalities (bit.ly/2iSqSVa). Internationally, certain classes of licit drugs have also been identified as contributing to crashes, and evidence is growing that the risk of a crash increases significantly when mixing drugs and/or alcohol.

amphetamines, methamphetamines, opiates, cocaine and methadone) and licit drugs (such as benzodiazepines) have all been found to contribute to driver impairment, singly and, most particularly, in combination.

Drug detection

The detection of alcohol is relatively easy. Ethanol is a simple molecule, soluble in both aqueous and organic systems, and is volatile. It transfers easily from the blood to expired air, and is detectable in primary form rather than as metabolites.

Drug detection is significantly more complex. Most drugs do not transfer to expired air, requiring the analysis of fluid samples – blood, urine or oral fluid. Drugs are comparatively complex molecules, with multiple forms across multiple classes, and with a considerable spectrum of behaviour both between and within individuals over time.

The collection of blood or urine is impractical for random roadside screening, leaving only oral fluid, which is itself a complex combination of saliva, cells, blood and even food debris. It varies in pH between acid and alkaline (generally 6.0–7.9), viscosity and volume, and can vary with time of day, age of person, and other factors such as drug interactions. Several classes of drugs inhibit saliva production, making sampling more difficult, and samples can also be affected by extraneous factors. Inhaled cannabis smoke can transfer the active ingredient, tetrahydrocannabinol, directly to saliva.

So it is little wonder that it has taken nearly three decades of development to produce field screening methods that are practical, reliable and economic. In 2004, Victoria was the first jurisdiction worldwide to introduce mobile drug testing (MDT). Most other Australian states have since followed.

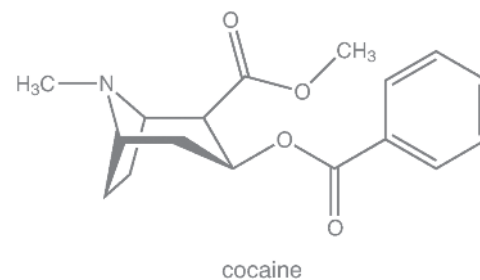
MDT methods use an immunochromatographic process. A sample (typically 10–1000 μL) is

collected on an absorbent collection pad, and transferred via capillary action or lateral diffusion. A buffer containing antibodies is used, where those antibodies are designed to be specific for the shape of the target molecule and/or structurally related class of molecules. An opiate immunoassay, for example, will detect morphine, codeine, heroin and related compounds. The methods indicate concentration, with different test manufacturers citing various accuracies.

If drugs are absent (or below detection limits), the unbound antibodies travel down the strip and bind to immobilised lines of the drug in the test region. If drugs are detected, the already-bound antibodies travel down the strip and pass by the immobilised lines. In the case of the instrument used in NSW, the test strip is then measured in a portable instrument for greater reproducibility and data storage.

These methods test directly for the target drug/drug class, as compared to other assay methods (most commonly LCMS on a blood and/or urine sample), which test for both the drug and the metabolites. Hence, the immunochromatographic approach gives less information about the timing of the drug use.

For drugs to pass from the bloodstream to saliva, the molecules must be lipid soluble, non-ionised and unbound to proteins. The pH of the saliva can significantly affect the drug transfer. An example from the road safety study in Ireland showed that the saliva to plasma ratio for cocaine varies from 273 to 0.44 between pH 5



A study by the Medical Bureau of Road Safety in Ireland found that in 2011 more than 75% of blood and urine samples taken from drivers suspected of intoxication contained at least one drug. Cannabis (>52%) and benzodiazepines (>40%) were the most common, but cocaine and opiates (including morphine, heroin and/or codeine) were each also encountered in more than 10% of samples (bit.ly/2jmJLvu). Nearly 50% of samples contained at least two drugs, and 9% contained four or more.

Illicit drugs (cannabis,



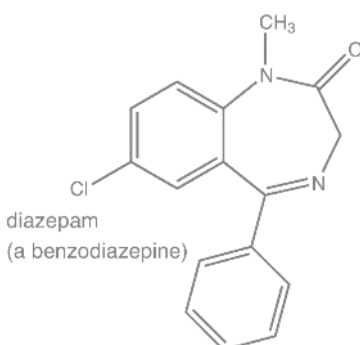
A multi-drug test strip.

and 7.8. Conversely, the ratios for benzodiazepines and cannabis are generally low.

This pH and volume of saliva varies with multiple factors. It has been observed that the sampling devices used in MDT can induce salivation, but the higher flow rate causes the pH to rise. Conversely, cannabis and ecstasy can reduce salivation, making it difficult to obtain sufficient sample from drug-affected drivers.

The MDT methods accommodate much of these variations.

The various test manufacturers then apply different threshold limits to alert the user to the presence or absence of the target drugs. The aim is to maximise sensitivity (the limit of detection, and ability to return a positive result when it should),



accuracy (agreement to other assay methods) and specificity (limitation of false negatives).

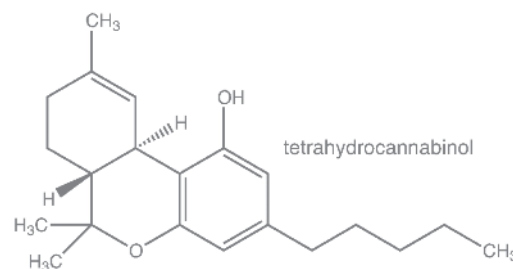
Perceptions of validity and risk

The development of fast, reliable and transportable (roadside) detection methods has been relatively slow. As late as 2006, Rosita-2, an extensive international field trial of nine commercially available MDT units found that all of them failed (to a greater or lesser extent) to meet the full set of criteria set down for the trial. However, with another ten years of development, subsequent studies, such as the DRUID project by the Federal Highway Research Institute in Germany (bit.ly/2k5MUR4), have concluded that the testing technologies are now becoming mature enough for field use.

Scientific data linking the timing of drug use and both the persistence of impairment and the ability to subsequently detect the drugs in certain samples remains relatively 'thin'.

In the absence of definitive science encompassing the whole field of MDT, there has been a lot of argument over the validity and 'fairness' of efforts to apply the technique in the field. Given that, by definition, illicit drug use is illegal, the most common approach in

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many jurisdictions has been 'zero tolerance'. By contrast, less government attention has been paid to the even more complex issue of legal drugs, particularly benzodiazepines.

Opponents such as MP David Shoebridge of the Australian Greens have argued that this approach represents an 'ideological war' on illicit drugs, and that drug takers are being prosecuted for their use, rather than for any direct correlation to the users' actual impairment. Relying on anecdote rather than science, Shoebridge has emphasised cases where users *claim* to have taken the drugs up to four days before driving and still returned positive results. However, this is a clear example of where the precautionary principle must apply. There is enough evidence to demonstrate that driving under the influence of drugs is potentially unsafe, particularly when linking blood levels to driver impairment.

This points to a substantial dichotomy in the perception of risk for driving under the influence of drugs. A

Weary workers: urine test for fatigue could help prevent accidents

Doctors, pilots, air traffic controllers and bus drivers have at least one thing in common – if they're exhausted at work, they could be putting lives at risk. But the development of a new urine test, reported in *Analytical Chemistry* (doi: 10.1021/acs.analchem.6b03421), could help monitor just how weary they are. The results could potentially reduce fatigue-related mistakes by allowing workers to recognise when they should take a break.

The effects of fatigue have long been recognised and studied as a problem in the transportation and healthcare industries. In the early 2000s, studies published in scientific journals reported that fatigue-related mistakes were linked to thousands of vehicular crashes every year, and were a major concern in patient safety. Weariness can cause anyone on or off the job to lose motivation and focus, and become drowsy. Although very common, these symptoms come with biochemical changes that are not well understood. Zhenling Chen, Xianfa Xu and colleagues set out to determine whether a urine test could detect these changes.

The researchers analysed urine samples from dozens of air traffic controllers working in civil aviation before and after an eight-hour shift on the job. Out of the thousands of metabolites detected, the study identified three that could serve as indicators of fatigue. Further work is needed to validate what they found, the researchers say, but their initial results represent a new way to investigate and monitor fatigue – and help prevent worn-out workers from making potentially dangerous errors.

American Chemical Society

survey by the Australian Drug Foundation (bit.ly/2jea5Kx) found that non-users and users had very similar perceptions that driving under the influence of alcohol was 'very risky' (94% vs 90%), but radically different perceptions for driving under the influence of cannabis (79% vs 30%) and even cocaine (83% vs 26%).

Arguments against the accuracy of MDT have to be acknowledged. However, there have been considerable improvements in the last decade. And just as a roadside breath test for alcohol is not directly used in prosecution, but is followed by more accurate confirmatory testing, then by exactly the same principles MDT is followed by more accurate blood and/or urine testing for those drivers identified as suspected of having threshold levels of key drugs in their system.

Most mine sites and many industrial facilities routinely use random drug

and alcohol testing, correctly arguing that this is a critical consideration to workplace safety when using heavy machinery. Yet we also know that even a relatively light vehicle is potentially hazardous, even before the potentially erratic and unpredictable behaviour of drug takers is taken to account.

A combined approach

Given that illicit drugs are already illegal, then until safe limits can be scientifically linked to impairment, zero tolerance is the logical precautionary approach.

At its current level of technical development, MDT appears to be suitable as a convenient roadside screening method when linked to subsequent confirmatory testing. Used in this way, the emphasis should be on accuracy and selectivity in the initial screening. Given the evidence of the substantive increase in risk through mixing drugs and alcohol, then a

combined approach to enforcement would also be a logical approach.

In the meantime, Victorian survey data cited in the Rosita-2 study is already showing that MDT has a substantive deterrent effect on driving under the influence of drugs (bit.ly/2je9dWk). Combined with education and other supporting initiatives, roadside drug enforcement can only improve the safety of our roads.

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