

Synthetic cannabinoids: The Australian experience

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Please note that the information on cannabis and the law given in this bulletin does not constitute legal advice and should not be relied upon in this way. The information is correct at the time of publication. People wanting legal advice should consult a lawyer. Correct as of March 2012.

Introduction

A wide range of legal ‘herbal’ products, claiming to have similar effects to cannabis, have been available in Australia for many years. Australian ‘head shops’ (retail outlets specialising in drug paraphernalia used for consumption of a range of licit and illicit substances, including cannabis), the first being established in 1976 (Inn of Sixth Happiness, 2011), have continued to sell a range of so-called ‘legal highs’ through their stores, and more recently via their websites. The names of the products have changed regularly, with more recent ones including *Marijuanilla*, *Happy Clappy Mix*, *California Dreaming* and *Pink Lotus*.

Little, if any, information is available on these products and whether they actually contain the ingredients they list on the promotional material and accompanying packaging. An example of one such ingredient is *Leonurus sibiricus*, a herbaceous plant native to central and southwest Asia. A respiratory stimulant, its leaves have been used in traditional medicine to treat chronic rheumatism, and the juice from the plant is used in the treatment of psoriasis, scabies and chronic skin eruptions (An et al, 2008). Although it is acknowledged in the literature that alkaloids contained in such herbs, such as leonurine, could in general produce ‘cannabis-like effects’ (Auwarter, 2009), drug user forums provide a variety of accounts on the effects of the product, ranging from “more stoned than I ever imagined I would be” (Bluelight, 2009) through to “absolutely worthless to smoke” (Erowid, 2003).

Taimapedia lists 41 head shops currently operating in Australia, with stores open in most capital cities (Taimapedia, 2011). In recent years many of these businesses have come under greater public scrutiny due to a range of legislative changes that have been introduced, particularly regarding the sale of drug paraphernalia such as ‘bongs’, hookahs and glass pipes. But it has been the introduction of synthetic cannabinoid products (often referred to as ‘synthetic cannabis’) onto the Australian market that has garnered the most attention, leading governments across the country to respond by banning a range of compounds due to concerns regarding public health and safety.

This Bulletin aims to provide a brief background of what we currently know about synthetic cannabinoids. What are they, who uses them and why, and what harms have been identified in their use? An examination of the history of their use in Australia, along with a summary of the current state of play, in terms of legal status, will also be provided.

What are ‘synthetic cannabinoids’?

‘Cannabinoids’ are a structurally diverse family of compounds with a large number of biological targets and can be classified into three groups: phytocannabinoids, endocannabinoids and synthetic cannabinoids (Sun & Bennett, 2007). The effects of all three groups of cannabinoids reflect the areas of the brain with which they interact.

Phytocannabinoids are only found in significant quantity in the cannabis plant. The most prevalent natural cannabinoids that have been isolated are delta-9-tetrahydrocannabinol ($\Delta 9$ -THC), cannabidiol (CBD) and cannabinol (CBN). Endocannabinoids are produced within the body and it is believed that these are synthesized “on-demand” rather than made and stored for later use (Vardakou et al, 2010).

The final group of cannabinoids are a large family of chemically unrelated structures which act like THC but are more effective (Geller, 2007). Synthetic cannabinoids are functionally similar to THC and, as with THC, they bind to the same cannabinoid receptors in the brain.

Since the 1960s, many analogues of THC have been developed, including HU-210, which is reported to have 100 times the potency of THC (Vardakou et al, 2010). In 1994, J.W. Huffman and colleagues synthesized a large series of synthetic exogenous cannabinoid receptor agonists including a number of what are now known as JWH compounds, after the name of their inventor. These included JWH-015, JWH-018, JWH-073, and JWH-398 (EMCDDA, 2009).

In Australia, some synthetic cannabinoids have been used for medicinal purposes and have been scheduled as such by the appropriate authorities. These include the following:

- Rimonabant (Schedule 4): once used to treat obesity, but has since been withdrawn from the market due to severe side effects.
- Nabilone (Schedule 8): used for the treatment of anorexia and for its antiemetic effects (e.g., for cancer patients undergoing chemotherapy).
- Dronabinol (Schedule 8): used to treat multiple sclerosis and chronic pain patients.

The use of synthetic cannabinoids in products: ‘Spice’

Since approximately 2004, herbal mixtures marketed as incense or air freshener became widely available across the world via the Internet or head shops and began to be used as a substitute for cannabis (Dresen et al, 2010). Warnings on the products stated that they were not intended for human consumption, but these messages were a dramatic contrast to the accompanying marketing which promoted the products as a cannabis alternative which was undetectable by conventional drug testing.

The wide range of products typically contained between 1-3 g of dried plant matter and their labeling declared the contents to be a variety of ‘herbal blends’ which were completely legal. Based on these accounts the products were not banned by European authorities. Instead their popularity as ‘legal drugs’ dramatically increased based on their reputation of being “potent herbal intoxicants” and legal alternatives to cannabis (Lindigkeit et al, 2009).

In Europe, amongst the first, and certainly the most well-known of these herbal mixtures, was a brand known as ‘Spice’, with a range of products being available, e.g. Spice Silver and Spice Diamond. Since the Spice brand first appeared in 2004, a large number of competing products made by other manufacturers also became available.

As the products became increasingly popular, there was growing suspicion that the labeling of these products was not accurate and that synthetic compounds were responsible for the effects that users were reporting. In December 2008 the German company THC Pharma reported JWH-018 as an active ingredient in *Spice* products and as a result, German health authorities prohibited the synthetic cannabinoids identified in the product (JWH-018 and CP 47,497-C8) (Lindigkeit et al, 2009). The herbal ingredients cited on *Spice*'s packaging did not appear to contribute to its psychoactivity, and in fact they were not even present in most of the samples tested (Piggee, 2009).

Further studies have discovered that there is also variability in the combinations and concentrations of the synthetic cannabinoids within *Spice* products such that using different brands, or even different batches of the same brand, can produce dramatically different effects (Dresen et al, 2010).

It is now believed that “the synthetic cannabinoids receptor agonists are sprayed in a liquid solution onto a mixture of “smokable herbs””, which once dried is packaged and made available for sale to users (Dargan et al, 2011).

Who uses synthetic cannabinoid products and why?

There are limited epidemiological data regarding the use of synthetic cannabinoids and little is known about the effects users of these products experience, apart from those mentioned in case reports where they have presented to emergency departments.

Vandrey and colleagues (2011) used a web-based study targeting adults reporting at least one lifetime use of a *Spice* product and concluded that the respondents exhibited a diverse profile of use patterns as is typical for other drugs. Primarily male with more than 12 years of education, just over one in five (21%) of the study recruits identified *Spice* products as their preferred drug. The primary reasons for use were curiosity, positive drug effect, relaxation and to get high without having a positive drug test.

Fattore and Fratta (2011) suggested five possible reasons why these products are popular amongst user groups. These were that they induce psychoactive effects; they are legal (even though many products have been controlled in some countries, they are still legal in many, and this leads to heavy global marketing); they are readily available and highly attractive; they are perceived as safe; and they are not easily detectable in urine and blood samples.

In Australia, the Ecstasy and Related Drugs Reporting System (EDRS) provides a national monitoring system that annually interviews regular ecstasy users (REUs). One of its aims is to identify emerging trends and in 2011 questions were asked about the use of synthetic cannabinoid products. Overall numbers amongst the national sample were small with only four people reporting using K2/*Spice*, with 32 (6% of our national sample) reporting the use of some other cannabinoid in the previous 12 months. The WA sample were the most likely to report use of these products (Sindicich & Burns, in press).

Harms associated with use of synthetic cannabinoids

Synthetic cannabinoids are often classified as ‘research chemicals’. Research chemicals are experimental chemicals that are not approved for human consumption. The vast majority of these chemicals have only been recently synthesized and up until very recently, little, if any data have been available regarding their effects, adverse reactions, long-term damage, or dependence potential with regards to humans.

Almost all of the available published data on the harms relating to the use of synthetic cannabinoids by humans deal exclusively with the range of ‘*Spice*’ products and one particular compound – JWH-018.

The first case report related to a *Spice* product was published in 2009 after two of the authors smoked 0.3g of ‘*Spice Diamond*’ (Auwarter, 2009). The effects reported included reddened conjunctivae, increased pulse rates, xerostomia (dry mouth), and an alteration of mood and perception. Since that time there have been reports from across the world, in countries where these products have been available, of emergency presentations for a range of adverse effects, including tachycardia, agitation, excess sedation and a loss of consciousness as a result of their use (Pierre, 2011).

These case studies report such severe reactions as a 17 year old girl who became “violent” and “crazy” after inhaling the drug (Vearrier & Osterhoudt, 2010), a 21 year old man who presented with vomiting and a “reported seizure activity” (Simmons et al, 2011), and three 16 year old boys who presented separately to an emergency department due to chest pain after smoking a synthetic cannabinoid product (K2), who were lately diagnosed with myocardial infarction (MI) (Mir et al, 2011).

Recent published reports, examining primarily the “chronic abuse” of *Spice*, “clearly demonstrate signs of addiction and withdrawal symptoms”, similar to those observed with cannabis use (Vardakou et al, 2010). Zimmermann and colleagues first presented a case study identifying a withdrawal syndrome after discontinuation from smoking *Spice* in 2009. A 20 year old patient reported smoking the product for 8 months and when he ceased use he developed “inner unrest, drug craving, nocturnal nightmares, profuse sweating, nausea, tremor and headache”, resembling that seen in cannabis dependence. The authors suggested that this is consistent with the dependence syndrome described for other psychoactive drugs in the two major mental health disorder classification systems of ICD-10 and DSM-IV.

Pierre and colleagues (2011) provide eight case reports of psychosis associated with synthetic cannabinoids and conclude that collectively, these suggest that use of these products is associated with acute psychosis, as well as exacerbations of previously stable psychotic disorders. They may also have a propensity to trigger a chronic psychotic disorder among vulnerable individuals.

As has been stated, more evidence is available on the synthetic cannabinoid JWH-018 than any other, with recently published papers discussing case reports of emergency department presentations (Schneir et al, 2011) and a study exploring the relationship between the cannabinoid and psychotic symptoms (Every-Palmer, 2011) providing increasing evidence of the potential harms of this particular analogue.

Of course, almost all synthetic cannabinoid products are smoked, with use as a tea (a route of administration favoured by some cannabis users) uncommon due to the lipophilic compounds’ low solubility in water (AGDHA, 2011). The carcinogenic potential caused by smoking products containing synthetic cannabinoids has not yet been evaluated (EMCDDA, 2009), nevertheless, all the harms associated with smoking any substance need to be considered by potential users.

Synthetic cannabinoids in Australia

It would appear that synthetic cannabinoid products have been available in Australia for some time via the Internet as well as through specialist adult stores (e.g., ‘sex shops’ or ‘head shops’) or tobacconists. Although *Spice* is certainly the most well-known product in Europe and the United States, other products including *Kalma*, *Voodoo*, *Kaos* and *Mango Kush* are also believed to contain synthetic cannabinoids. There is no reason to believe that these products, as well as many others, have not been brought into Australia by users and distributors via the Internet since 2004.



The Australian Crime Commission's Illicit Drug Data Report (IDDR) 2008-09 commented on the appearance of JWH-018 in Germany and Austria stating that “the emergence of synthetic cannabinoids ... will continue to pose challenges for health and law enforcement authorities”, however, there was no mention of these compounds in the 2009-10 report (ACC, 2009).

It was not until early 2011, however, following the growing media interest in the product '*Kronic*', that Australian authorities began to focus their attention on this rapidly emerging class of drugs.

It is difficult to establish when the brand name *Kronic* first became available in Australia. One Australian website that has sold *Kronic* products claims to have been doing so since 2009 (BillyBong, 2011), and media reports in 2011 claimed that the product had been available in Australia for “about four years” (Spriggs, 2011). *Kronic* products are produced and distributed by a New Zealand company. Available evidence suggests that the company imports the synthetic cannabinoids, possibly from China. These are then dissolved in acetone and sprayed onto a range of herbal products, potentially leading to widely varying potency due to uneven spraying, and then distributed throughout New Zealand, Australia and worldwide via the Internet.

In April 2011, media outlets in Western Australia began reporting that “mineworkers” were “getting high on a synthetic cannabis that impairs their ability to operate machinery but cannot be detected by drug and alcohol tests used at the sites” (Macdonald, 2011). The reports also stated that the product was “five to 10 times stronger” than THC and had been banned in 16 countries after being linked to deaths. Mineworkers were interviewed and claimed that they had used the product and were randomly drug tested afterwards and had escaped detection.

A test to detect these compounds was requested by mining companies and the Western Australian testing facility ChemCentre had very soon implemented processes, arranged a methodology for testing and purchased standards from a US pharmaceutical company (Hastie, 2011). Even so, the Centre stated that “there is a challenging task ahead of them” with regards to identification of these compounds, as there were “many more synthetic cannabinoids widely available in bulk over the internet, and very little literature or standards for the pharmacological metabolites available.”

According to an article written by the *Australian Journal of Mining (AJM)* in June of that year, ChemCentre claimed to have found 10% of workers on mine sites returning positive readings in a recent sweep of testing across the state, with 30% failing the drug test in one instance (AJM, 2011).

Representatives of the mining industry urged authorities to “closely scrutinise the legality of the substance” and in May 2011, the Chamber of Minerals and Energy WA wrote to the Minister for Health requesting that synthetic marijuana products be added to the Poisons Act, following Rio Tinto and BHPB which had already banned synthetic cannabinoids on their sites (AJM, 2011).

On 17 June, 2011, WA implemented a ban via state-specific legislation on seven synthetic cannabinoids. Within several days of the release of the intent to ban these substances, however, an alternative synthetic cannabinoid formulation was being marketed claiming to circumvent these controls (AGDHA, 2011). On August 5, the WA Government banned 14 more synthetic cannabinoids hours after a 38 year old Perth man died after “suffering a heart attack” reportedly after smoking *Kronic Black Label*, a product that distributors had claimed was not covered under the previous legislation (Trenwith, 2011).

The production of *Kronic* products was significantly affected in July, 2011, when New Zealand authorities identified the anti-anxiety medication phenazepam in *Kronic Pineapple Express*. Importers of the product claimed that the product had been ‘sabotaged’, later even stating that analysis they had conducted independently actually showed no contamination at all (3 News, 2011). Nevertheless, the NZ Ministry of Health issued an immediate recall of the product, ordering retailers to stop selling it (SMH, 2011).



On August 4, 2011 legislation was introduced in New Zealand Parliament allowing the country's Associate Health Minister, Mr Peter Dunne, to class synthetic cannabinoids products as "temporary controlled drugs" and withdrew them from sale for 12 months. During that time, products will be assessed by a committee, appointed by the Minister, which would judge whether it is safe to be sold.

Since that time the Minister has issued two more Temporary Class Drug Notices. The first in October 2011 targeted three other synthetic cannabinomimetic substances ("substances that have been incorporated into products traded as legal alternatives to cannabis") and the other in December temporarily banning the supply and sale of AM-2233 (New Zealand Ministry of Health, 2011). Interestingly, these legislative changes specifically target the manufacturers of these products and not the consumers, as it is not illegal "to use or to possess a quantity of less than 56 grams of these products".

Government response in Australia

Shortly after the WA Government announced their decision to ban seven synthetic cannabinoids, the Commonwealth Government, in considering prohibitions on synthetic cannabinoid analogues, classified eight synthetic cannabis-like substances as prohibited substances throughout Australia. These restrictions, effective from 8 July 2011, still allowed access to these substances for use in strictly-controlled medical and clinical studies to allow for appropriate investigation of any potential future therapeutic uses (Australian Government Department of Health and Ageing, 2011).

It is important to note that enforcement of Commonwealth scheduling decisions are implemented within the states and territories under local drugs and poisons legislation. Commonwealth controls are automatically adopted through reference in Victoria, the Northern Territory and the ACT.

Ahead of the Commonwealth's decision on national scheduling of synthetic cannabinoid analogues, jurisdictions across the country took action to place bans on the possession and sale of products containing these substances within their own jurisdictions. In addition to the Western Australian Government's response already discussed, the following legislative changes have been made, or plan on being made, at the time of publication:

| Jurisdiction | Date | Amendment to legislation |
|------------------------------|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Australian Capital Territory | July 8, 2011 | In response to the Commonwealth announcement, ACT Government Health issued a media release stating that they would "automatically adopt this ban under local medicines law, and as such, it will be illegal to manufacture, obtain, possess, sell, supply or use products containing synthetic cannabis compounds in the ACT" (ACT Government Health, 2011). The ACT Government also arranged to have an amnesty until 1 August 2011 when people would not be prosecuted for offences related to these products. |
| New South Wales | July 1, 2011 | The NSW Government banned the sale of synthetic cannabinoids. The products were banned through regulations under the NSW Drug Misuse and Trafficking Act, meaning that "the psychoactive ingredients will be prohibited drugs in the same category as cannabis, heroin and cocaine" (NSW Government, 2011). |
| | July 8, 2011 | The possession of synthetic cannabinoids made illegal. |
| Northern Territory | August 12, 2011 | The Northern Territory's Chief Minister announced amendments to their Misuse of Drugs Act, making "a new range of drugs similar to cannabis" illegal for sale or use. Penalties in that jurisdiction include up to \$2329 for personal use at home and \$5480 or 2 years imprisonment for those found possessing the substance in public (NT Government, 2011). |



| Jurisdiction | Date | Amendment to legislation |
|------------------------|------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Queensland | June 16, 2011 | The Queensland Government announced that it was moving to ban synthetic cannabinoids under the (Qld) Drugs Misuse Act (Queensland Government, 2011). |
| | October 14, 2011 | Amendments were made to the Drugs Misuse Act allowing “authorities to charge someone with selling a banned substance even if key ingredients had changed to circumvent laws” (Queensland Government, 2011a). At that time, the Attorney General also stated that the Government was continuing to investigate another 19 cannabinoids to see if they should be added to the banned list. |
| South Australia | June 17, 2011 | South Australia’s Attorney General announced the banning of “the active ingredients of synthetic cannabis”, stating that there had been reports of users experiencing paranoia, anxiety, racing thoughts and irritability, ... vomiting and chest pain” (AAP, 2011). |
| Tasmania | August 3, 2011 | The Tasmanian Government made an amendment to the Misuse of Drugs Act 2001 which they stated would “assist Tasmanian Police in dealing with a range of emerging drug issues including the synthetic cannabinoid <i>Kronic</i> ” (Tasmania Police, 2011). This change, together with recent amendments to Tasmania’s Poison Act 1971 which resulted in a number of synthetic cannabinoids scheduled as prohibited drugs, ensured consistent legislation that prohibited the use of these drugs. |
| Victoria | June 29, 2011 | Victoria announced the introduction of new regulation making legislation to allow quick action to ban emerging dangerous drugs, including <i>Kronic</i> (Premier of Victoria, 2011). |

These changes, introduced quickly in response to concern over risks to public health and safety fuelled by a rapid increase in popularity and use, largely driven by intense media attention, caused a great deal of confusion regarding the legal status of the range of products available. Changes to the law also caused significant problems for those who sold them as they were often under the belief that they were legally able to do so. The Australian Sex Party issued a media release in response to the changes to the law in NSW stating that the government must “compensate businesses that are having a legal part of their business outlawed with less than a week’s notice” (Australian Sex Party, 2011). The release went on to say that businesses had paid GST on the products and that the NSW Government would have to pay this back. It also discussed reports coming from the USA suggesting that in haste to ban synthetic cannabinoids, authorities from that country may have inadvertently banned a number of other products that contain cannabinoids or “indirect cannabinoid receptor stimulants” including analgesics, chocolate sauce and some motor additives. These claims from the Retail Compliance Association (RCA), a trade association for sellers of synthetic cannabis, have yet to be confirmed.

In addition to the consideration of domestic controls within each state and territory, the Commonwealth is currently pursuing broader regulatory options in relation to controlling existing and emerging synthetic analogue drugs.

Conclusion

Cannabis continues to be the most widely used illicit drug in Australia and around the world. It should not be surprising therefore that when a ‘legal’ alternative for the drug becomes available there is a great deal of interest in the product. Add to this packaging which utilises established ‘drug culture’ references, as well as marketing that focuses on the product being undetectable in standard drug testing regimes, and the manufacturers of this product can be hopeful of strong sales.



There can be little doubt that we are going to continue to see new synthetic cannabinoids on the market. Even though many jurisdictions have legislated to ban a variety of these compounds, many products claiming to contain other synthetic cannabinoids continue to be sold. Whether these compounds are more or less harmful than those already banned is not known.

In a statement issued by the NZ Associate Health Minister at the time of the banning of the 43 products containing synthetic cannabinoids, Mr Dunne was quoted as saying that it was “clearly unacceptable that psychoactive substances can be sold without regulatory controls or any assessment of their potential harm.” He also stated that his government would “reverse the onus of proof so anyone wishing to sell these products would need to prove they are safe” (Dunne, 2011).

If companies wish to produce ‘legal alternatives’ to illicit drugs, under the notion that it is important to regulate the market, thus removing the need for a black market, then it is reasonable to expect that all safety aspects need to be considered. Pharmaceutical companies have to follow rigorous testing procedures and safety regulations, as well as comply with labeling laws in order to have their product reach the shelves. We should expect no less from the companies producing this new range of synthetic compounds. We have recently seen the industry seek some form of self-regulation by the establishment of the Association of Independent Research Chemical Retailers (AIRCR), however this move should be treated with caution due to it being run by the main importer for the major online retailers in the UK (Blackwell Research, 2011).

Synthetic products being sold as ‘legal highs’ are very similar to drugs available on the illicit market – little is known about what is in them or what the effects will be for individuals. Governments will continue to ban synthetic compounds that may present a risk to public health and safety but there is little doubt that the companies producing these products will continue to remain one step ahead, potentially developing compounds that may possibly be even more harmful than the originals. Individuals need to be educated about the risk if they choose to use these unregulated products and proactive legislation should be enacted that places the onus of proof about the safety of these products on the manufacturers.

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