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# Cannabis Concerns: increased potency, availability and synthetic analogues

Luke A. Downey<sup>1,2</sup> , Joris C Verster<sup>2,3</sup>

1. Centre for Human Psychopharmacology, Swinburne University of Technology, Hawthorn, VIC, Australia.

2. Department of Psychology, Swansea University, Swansea, Wales, UK.

3. Utrecht Institute for Pharmaceutical Sciences, Division of Pharmacology, Utrecht University, Universiteitsweg 99, 3584 CG, Utrecht, The Netherlands.

**Corresponding author:** Luke A. Downey, PhD. E-mail: [ldowney@swin.edu.au](mailto:ldowney@swin.edu.au); Tel: +61 3 9214 5781

Over the past 10 to 15 years, the evidence concerning the consequences of cannabis smoking has detailed a number of negative health outcomes. Over the same period, a wide variety of alternative cannabis products (synthetic cannabis and cannabis extracts) have been developed and consumed for a variety of purposes. Whilst the impact of cannabis smoking on behavior in the short-term, and the psychiatric, behavioral, physiological effects of extended usage of cannabis in the longer term have been observed to produce a number of societally and individually concerning outcomes; consumption of cannabis recreationally, continues. Despite cannabis being considered a relatively innocuous recreational drug, current evidence suggests it can adversely impact mental health. Sustained use of cannabis has been shown to significantly increase the risk of developing schizophrenia and other psychiatric disorders (Szoke et al. 2014). Possibly more concerning, the legalization of cannabis in some countries, the approval of cannabis products for usage to treat symptoms associated with medical conditions, and the development of synthetic cannabinoid products provides increased avenues for people to expose themselves to cannabis and its psychoactive effects.

Cannabis is consumed for its psychoactive effects, or 'high', which include, alteration of conscious perception, feeling relaxed or reducing stress, metacognition, euphoria, and a general feeling of well-being. Cannabis consumption can also impair vision, coordination, reflexes, and induce mild anxiety and paranoia during the acute consumption phase. By reducing motor coordination and slowing reaction

time, consuming cannabis makes it very dangerous to use before driving a car. Simulated and on-road driving studies report impaired perceptual processes, such as: monitoring the speedometer and maintaining speed; response to stimuli, such as stopping and starting; and tracking ability is the most consistently reported driving skill to be impaired after cannabis consumption which presents as an increase in the sideways movements of the vehicle and an increase in the percentage of time spent out of a lane (Downey et al. 2013). Impaired driving is most pronounced if cannabis is used in combination with alcohol (Penning et al. 2010).

Recently, more potent forms of the cannabis plant have been developed which contain four to five times as much THC (delta-9-tetrahydrocannabinol) which acts on specific molecular targets on brain cells, called cannabinoid receptors. Synthetic cannabinoids have also become available, which are full agonists of the CB1 receptor. These increases in potency of cannabis and greater affinity of synthetic cannabinoids upon cannabinoid receptors translate into a greater psychotogenic effects. In acute terms, an 'increased high' may exacerbate the impairment generally associated with cannabis consumption including deficits of short-term memory; altered judgment and decision-making; and mood effects, including severe anxiety (paranoia) or even psychosis (loss of touch with reality). This increased potency may further increase the risk of endangering the lives of cannabis (synthetic or more potent plant derived cannabis) using drivers, and those they share the road with (Ashbridge et al. 2012).

More than 200 synthetic cannabis analogues of THC have been identified since 2008. Their pure agonism on the CB1 and CB2 cannabinoid receptors, illustrate a higher affinity than THC, and are responsible for their increased potency (Rosenbaum et al. 2012). The endocannabinoid system is involved in a wide variety of physiological processes including appetite, pain-sensation, mood, sleep and memory. Cannabis and its synthetic analogues over activate the endocannabinoid system, causing the "high" and other physiological and psychological effects that users experience. However, cannabis also affects brain development, and when it is used heavily by adolescents, its effects on thinking and memory may last a long time or even be permanent (Meier et al. 2012). For example, exposure-related structural abnormalities in the hippocampus and amygdala of long-term heavy cannabis users have been observed in magnetic resonance imaging studies. A number of studies have also linked chronic cannabis use and mental illness. High doses of cannabis can produce a temporary psychotic reaction (involving hallucinations and paranoia) in some users, and using cannabis when already suffering a mental illness can exacerbate the course of illness in patients with schizophrenia. As such, the development and

availability of highly potent synthetic cannabis products, cultivation of more potent cannabis plants, and increased availability of cannabis through its legalization in various communities may contribute to an increase or acceleration of the negative psychological and physiological outcomes of cannabis consumption.

The past 10 to 15 years of research focused on the effects of cannabis consumption advocate caution in consuming cannabis as a recreational drug. It has also illustrated that cannabis consumption produces short and long term dangers to users. The availability of synthetic cannabis products should therefore be treated with as much, if not more caution, when potential drug users are evaluating the possible psychological and physiological outcomes of consuming these powerful drugs. Whilst research into the acute and long-term effects of consumption of synthetic cannabis is in its infancy, anecdotal reports and case-study data indicate that its use is associated with acute psychotic episodes and longer lasting psychotic disturbances. Of more concern, is the increasing usage of synthetic cannabis products by youths across Western Society, possibly given to their perceived 'legal' status. Synthetic cannabis is also difficult to detect using regular drug screening techniques, and products containing synthetic cannabis often contain multiple cannabis analogues and do not list their ingredients. Given the great potential for harm these products hold, commonly available synthetic cannabis analogues effects on physiological, cognitive, and psychiatric indicators need to be explored in controlled administration studies. Further to this, the pharmacokinetic profile and potential abuse liability of these individual cannabis analogues also need to be documented and evaluated in order to develop a more accurate picture of their short and long term effects upon human functioning.

#### **Declaration of interest**

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