Importance of a standard unit dose for cannabis research

A standardized measure for 9-tetrahydrocannabinol (THC) content in cannabis products is necessary to advance research both on the adverse effects of cannabis (e.g. risks for brain development, mental illness and addiction) and on the drug's potential medical uses

Recognizing the increasing diversity of cannabis products and their expanded use, Freeman & Lorenzetti propose a standard unit dose of 5 mg 9-tetrahydrocannabinol (THC) to be used for all cannabis products, regardless of method of administration [1]. They argue that a standard dose would help to guide consumers towards safer patterns of cannabis use. The National Institute on Drug Abuse (NIDA) strongly supports the need for a standardized measure to facilitate research, and this was a key recommendation from NIDA's Cannabis Policy Research Council Workgroup [2].

However, as discussed by Freeman & Lorenzetti, the development of such a measure has been challenging, due to concerns that the effects of any standardized dose would differ on the basis of mode of consumption or, possibly, how it is combined with other cannabinoids such as cannabidiol (CBD) [3].

These complexities hardly negate the value of having a standardized measure of THC, irrespective of product type. In fact, having and using such a standard is a prerequisite for comparing the effects of various cannabis products on THC bioavailability, pharmacokinetics and pharmacological effects [3], which is knowledge fundamental to studies pertaining to medical use of cannabis.

A standardized measure will also be essential for advancing our understanding of some of the major concerns related to cannabis use, especially its influence on brain development, and the risk for cannabis use disorders and psychoses [4,5]. Current and past studies evaluating the effects of cannabis on brain development and cognition, whether focused prenatally or during childhood or adolescence, are limited to rough estimates on the basis of reported frequency of use (life-time, past year, past month or regular use) and there is no information on the THC content of the product(s) consumed [6].

This lack of information on THC content probably contributes to discrepancies among investigators, with some reporting adverse effects even after single cannabis exposure [7] and others showing no differences with regular exposures during adolescence [8]. The Adolescent Brain and Cognitive Development (ABCD) study will prospectively investigate close to 12 000 children as they transition from childhood into adulthood with a variety of measures, including brain imaging, neurocognitive and behavioral tests, educational achievement and patterns of drug use [9]. This study and others like it would benefit enormously from a standardized measure of THC, as would pre-clinical studies aiming to mimic clinical exposures.

It is widely believed that the increase in THC content of cannabis (which almost tripled in the past 2 decades) [10,11] is responsible for greater adverse effects associated with cannabis consumption [12]. Evidence already points to a higher risk for cannabis use disorder and for psychoses with consumption of cannabis with high vs. low THC content, but these associations have been based on estimates of the THC content of cannabis in the region studied [13,14], and research on the influence of THC content on adverse outcomes is very limited. One of the main challenges for conducting such research has been the multiplicity of issues that influence the dose of THC a user is exposed to, e.g. the ability to titrate the dose of an inhaled product. A standard dose will not, by itself, be able to address all of the various complexities noted, but it will move us towards greater precision in our measures.

Although cannabis remains an illicit substance in the United States, the expanded legalization by states requires us to develop the knowledge base that can help states develop policies to minimize risk from cannabis exposures, such as limits on the THC content of cannabis products.

Regarding what a standard THC dose should be, Freeman & Lorenzetti propose a unit dose of 5 mg THC for all cannabis products and methods of administration. Their rationale is that this dose has psychoactive effects regardless of route of administration, but is mostly devoid of adverse effects. This is a reasonable justification based on our current knowledge, although future research will help to determine its usefulness and whether there is a need to further refine the measure. Further research will also be necessary to develop a concomitant standard dose for CBD. Despite the multiple caveats and complexities, the use of a standard unit dose of THC in research is an important step for improving our ability to understand the effects of cannabis in the population.

Declaration of interests

None.

Keywords Brain development, cannabidiol, cannabis use disorders, marijuana, psychotic disorders, tetrahydrocannabinol.

NORA D. VOLKOW & SUSAN R.B. WEISS
National Institute on Drug Abuse, Bethesda, MD, USA
E-mail: nvolkow@nida.nih.gov

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