

IS MARIJUANA EFFECTIVE?

Based on the UNODC opinion above and other regulatory bodies such as the Institute of Medicine (IOM) and the National Institute of Health (NIH), a new open-door initiative for scientific research on the medical potential of marijuana (cannabinoids) was started back in 2002 at the University of California San Diego campus and the launch of twenty-five studies through their Cannabis Research Center. The National Institute on Drug Abuse (NIDA) website states that, currently, the quality of health research on marijuana and its components varies widely, and the whole plant is, “significantly more potent now and we now know a lot more about the potential harmful effects of marijuana on the developing brain” (NIDA, 2016). The challenge that continues to face healthcare providers, however, is that we can never condone the smoked formulation of any medication given the significant respiratory pathology patients develop. Through the act of pyrolysis followed by inhalation, the search is on for more pharmaceutically elegant formulations of marijuana in order to apply our principles of safety, quality and efficacy and the rigorous scientific testing and regulatory systems that apply to established medicines.

Although some may view the subject of marijuana as, “increasingly difficult to talk about in part because of the mixed messages being sent by the passage of medical marijuana laws and legalization of marijuana in some states” (NIDA, 2017c), health professionals can choose to become informed so that they can play a discerning role in the current dialogue about what is best for the people in their communities. In support of that role, this module presents cultural and historical context for the use of marijuana over the centuries with the evidence from the best clinical research available, including data from botanical science and clinical trials. It is the botanical background that may explain what might have attracted people to marijuana for thousands of years.

The high derived from inhaled marijuana occurs when cannabinoids in the leaf are released into the lungs, where they may in turn pass into the bloodstream. The amount of THC and other cannabinoids consumed determines the potency effects, ranging from sedating to psychoactive. The effects of smoking are rapid, whereas the effects from eating marijuana or hashish can be delayed by at least 30 to 60 minutes (Table 2). When marijuana is inhaled, either as combusted or

vaporized plant matter, THC reaches peak concentration in 2 to 5 minutes, followed by a rapid drop-off. Inhaled cannabinoids reach their peak concentration in 5 to 10 minutes, declining rapidly for a period of 30 minutes (Fasinu et al., 2016). The action of THC in inhaled oils, as one might find in electronic cigarettes, is not yet known (Abrams, 2016). Orally ingested marijuana has a lower and variable bioavailability. It may take hours for THC to reach peak plasma concentrations, which then remain elevated with a terminal half-life of 25 to 30 hours (Abrams, 2016). When THC is ingested, it is initially metabolized in the liver to a psychoactive substance called 11-hydroxy-THC, explaining why people eating marijuana-baked products or capsules may report a more significant psychoactive effect compared with those who inhale it (Abrams, 2016).

Original research leading to successful isolation of THC, led to the discovery and cloning of cannabinoid receptors in 1990 (CB1 receptors). THC acts on CB1 receptors which also receive chemicals involved in normal brain function and development, and which share a common signalling pathway with opioids, promoting each others' reinforcing properties. CB1 receptors are located at presynaptic junctions where they are involved in the regulation of ion channels and modulation of the release of dopaminergic, γ -aminobutyric acid (GABA), glutamatergic, serotonergic, adrenergic, and cholinergic neurotransmitters (Howlett, 1995).

Working backwards, if the human brain has specific cannabinoid receptors, it is unlikely that from an evolutionary standpoint humans would have developed these in response to chemicals found in plants. More likely, humans would only have evolved CB1 receptors in response to the existence of an endogenous ligand for the CB1 receptor. This research ultimately led to the discovery of arachidonic acid ethanolamide, or anandamide: naturally occurring human cannabinoid chemicals. For differentiation, the term phytocannabinoid refers to constituents that occur naturally in the marijuana plant, as opposed to endocannabinoids, which occur naturally in lipid-derived neurotransmitters found in the human body. In 1993, a second type of cannabinoid receptor was discovered and cloned and while CB1 receptors are located predominantly in the central nervous system, these other receptors are expressed in peripheral tissues and are known as CB2 receptors.

According to NIDA (2017c), science suggests that “marijuana overactivates parts of the brain that contain the highest numbers of CB1 receptors causing the ‘high’ that people feel.” (NIDA 2017c) People feel other effects from marijuana, such as changes in mood, impaired movement, altered sense of time, sensory alterations, difficulty thinking and problem solving, and

impaired memory (NIDA, 2017c). Chronic users of marijuana can generally distinguish between the highs produced by smoking *Cannabis sativa* versus the effects of *C. indica*. The *C. sativa* high is characterized as uplifting and energetic, felt in the head and described as spacey or hallucinogenic. *C. sativa* gives a feeling of optimism and well-being, along with pain relief, and it is used for daytime smoking. *Cannabis indica* provides an effect described as a “body high” that promotes relaxation, stress relief, and an overall sense of calm. *Cannabis indicas* are supposedly effective for insomnia and are therefore used in the late evening (Hazekamp & Fishedick, 2012). In higher doses of *C. sativa* or *C. indica*, people can also experience hallucinations, delusions, and psychosis (NIDA, 2017c). Conversely, it is the stimulation of CB2 receptors in the periphery which may contribute to other medicinal effects such as the less addictive, anti-inflammatory potential of cannabinoids (Thomas et al, 2007).