



# Medical Marijuana: An Update for the Podiatric Physician

The author explores treatment strategies, pharmacology, cannabis use disorder, and the ever-changing medical marijuana laws.

BY ROBERT G. SMITH, DPM MSC, R.PH

## Learning Objectives

Participants completing this course will be able to

- 1) Identify, acknowledge, and comprehend the pharmacology, actions, and adverse effects of the pharmacological product marijuana tetrahydrocannabinol (THC) within the context of potency;
- 2) Appreciate and understand the recently published investigation of the role of marijuana (cannabis) in treating peripheral neuropathy and the implications for the podiatric physician; and
- 3) Be able to provide practical strategies to offer patients within the context of marijuana use, guarding against drug misadventure within the construct of the rapidly changing federal and state opinions and laws.

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Following this article, an answer sheet and full set of instructions are provided (pg. 134).—**Editor**

### Introduction

In July 2020, the International Association for the Study of Pain (IASP) revised its definition of pain for the first time in 40 years.<sup>1</sup> This new definition describes the experience of pain as “an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential

tissue damage.”<sup>1</sup> The previous definition, published in 1979, defined pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.” The updated definition offers a more nuanced, systemic view of pain and aims to change how pain is understood, communicated, and treated.<sup>1</sup>

This allows for treatment interference, where providers may explore expanded use of existing treatments while discovering treatment options that involve agents or substances deemed illicit and dangerous.

The Drug Enforcement Agency classifies such substances as Schedule I pharmaceuticals, defined as drugs

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with no currently accepted medical use and a high potential for abuse, such as marijuana, 3,4-methylenedioxymethamphetamine (MDMA), and lysergic acid diethylamide (LSD). In the U.S., marijuana laws are changing at a rapid pace across all 50 states, making legality questions confusing at times. To keep up with the ever-changing laws, podiatric physicians need to perform their due diligence and continue to familiarize themselves with their local jurisdiction statutes and laws governing marijuana, particularly those related to prescribing or recommending medical marijuana for their patients. In the era of legalized marijuana, cannabis can hardly be called marijuana at all because its refinement produces an end product in the form of concentrated oil that is as much as 95% or even 99% tetrahydrocannabinol (THC).

At present, 48 of the 50 states allow for the use of some form of medical marijuana.<sup>2</sup> This means that every US state except for Nebraska and Idaho has passed at least some legislation allowing legal medical

for health when used for medicinal purposes due to the false notion of its being non-hazardous.<sup>3</sup> Thus, the debate surrounding the medicinal use of cannabinoids has recently gained importance, pointing to scientific concerns that must be brought forward to facilitate a scientifically grounded discussion that brings patient care and

physicians to enhance the care of these patients.

**Marijuana Legislation**

On April 30, 2024, the *Washington Post* reported that Attorney General Merrick Garland recommended loosening restrictions on marijuana, marking a historic shift in federal

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### A prescription Drug Monitoring Program dates back to as early as 1918 in New York.

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patient well-being to the foreground. It has been noted that the article “US adult illicit cannabis use, cannabis use disorder, and medical marijuana laws,” published in *JAMA Psychiatry* in 2017, resurrected the controversy of marijuana legalization.<sup>4,5</sup>

The present article is focused on the podiatric physician’s role in treating patients who are using either medical marijuana products or self-prescribed marijuana and THC products. First, this white paper provides a brief update on current legislative initiatives centered on mari-

drug policy that could broaden access to the drug for medicinal use and boost cannabis industries in states where it is legal.<sup>6</sup> The Justice Department submitted this formal recommendation to the White House, and it was made the task of the Drug Enforcement Administration to approve the Federal Health Agency recommendation that marijuana be reclassified from a Schedule I to a Schedule III drug. Schedule III drugs refer to drugs with a moderate-to-low potential for physical and psychological dependence,<sup>7</sup> whereas Schedule I pharmaceuticals are drugs with no currently accepted medical use and a high potential for abuse.

Marinol® is a synthetic version of tetrahydrocannabinol THC available in a capsule form called dronabinol. It is a cannabinoid-type antiemetic-appetite stimulant residing in Schedule III drugs that is used to treat nausea and vomiting caused by cancer chemotherapy.<sup>8</sup> Further, dronabinol is also used to treat loss of appetite and weight loss in patients with HIV infection.<sup>8</sup> Notably, Epidiolex®, the medication approved by the Food and Drug Administration (FDA) for the treatment of seizures associated with two rare and severe forms of epilepsy (i.e., Lennox-Gastaut syndrome and Dravet syndrome), is no longer considered a controlled substance.<sup>9</sup> In April 2020, the US Drug Enforcement Administration (DEA) removed cannabidiol (CBD), the active ingredient in Epidiolex®, from Schedule V of the Controlled Substances Act.<sup>9</sup>

In the *Washington Post* arti-

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cannabis use, although many of these laws may be very restrictive.<sup>2</sup> Lower extremity providers need to acknowledge this fact so they can fully appreciate the balance of the risk-to-benefit-outcome ratio posed by the use of medical marijuana among their patient population when evaluating strategies to treat lower extremity ailments and systemic disease.

The term “medicinal marijuana” can be understood as a marketing strategy to reduce the risk perception of drug use.<sup>3</sup> In this perspective, marijuana has acquired the status in the collective unconscious of being good

juana; differences in marijuana’s potency; and differences in marijuana’s routes of administration to include bioavailability and pharmacokinetics, drug-drug interactions, and possible marijuana adverse effects. Then, it provides the podiatric physician with a deeper understanding of how the full weight and breadth of medical marijuana may pose a threat to patient care by both comparative and contrasting evidence-based clinical observations. Finally, it provides treatment strategies and suggestions for podiatric patients who engage in marijuana use to empower podiatric

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cle titled, “Attorney general moves to reclassify marijuana as lower-risk drug,” the authors provided an excellent overview of the history, possible political motivations, and economic tax benefits of medicinal marijuana in a fair and balanced fashion;<sup>6</sup> however, they overlooked a salient point. Although the authors asserted that “once medical marijuana is reclassified,” it “could persuade more doctors to recommend marijuana, despite the lack of FDA approval for marijuana plant products as prescription,” they did not explore the possibility that as a Schedule III marijuana product used for pain indication, it would now be a mandatory pharmaceutical that must be entered into the respective state’s prescription drug monitoring program (PDMP).

## PDMPs

PDMPs have become a widely embraced policy to address the US opioid crisis as well as substance use disorder. Despite mixed scientific evidence on their effectiveness at improving health and reducing overdose deaths, they have received strong bipartisan legislative support. The District of Columbia, Puerto Rico, Northern Mariana Islands, and Guam have all operational prescription drug monitoring programs. In New York, PDMP dates back to as early as 1918, while California has been maintaining the oldest continuously operating PDMP program since 1939.<sup>10</sup> Several other states implemented PDMPs modeled after the California program in subsequent decades, including Hawaii (1943), Illinois (1961), Idaho (1967), New York (1973), Rhode Island (1978), Texas (1981), and Michigan (1988), among others.<sup>10</sup> In 1991, Oklahoma became the first state to establish a technologically modern PDMP that collected and distributed prescription data electronically.<sup>10</sup>

A PDMP is a tool that can be used to address prescription drug diversion and abuse. PDMPs serve multiple functions, being patient care tools, drug epidemic early warning systems, and drug diversion and insurance fraud investigative tools. They also help prescribers avoid drug interac-

tions and identify drug-seeking behaviors or “doctor shopping.” Moreover, PDMPs can be used by professional licensing boards to identify clinicians with patterns of inappropriate prescribing and dispensing, as well as assist law enforcement in cases of controlled substance diversion.

Simultaneously, protecting patient privacy is of the utmost importance, which is why PDMPs ensure the protection of patient information just as well as, if not better than, any other medical record. Law enforcement may not access patient-specific PDMP data unless they have an active investigation, and healthcare providers can access only the PDMP data relevant to their patients.<sup>10</sup> A total of 41 states, as well as the District of Columbia and Puerto Rico, have medical marijuana programs,

as a part of their overall plan of treatment. Only physicians who are licensed and certified can recommend medical marijuana. To become authorized to recommend medical cannabis, doctors must follow specific legal and medical protocols, which involve obtaining a special certification in many jurisdictions. Patient eligibility is often determined based on conditions and state regulations.

Thus, navigating the process of obtaining medical marijuana can be complex, which is why it is essential to consult with a certified professional who can provide guidance tailored to one’s patients’ health needs. In the present case, personal email correspondence with Dr. Cicchinelli, Chief Medical Director of the PICA Group, reassured this author that podiatric physicians maintain their parity with

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whereas only two states (Connecticut and New York) require that providers of medical marijuana enter such “prescriptions” into their prescription drug monitoring programs.<sup>10</sup>

It must be acknowledged that PDMPs, emerging as an early form of narcotics enforcement in the early 20th century, have been transformed from tools of law enforcement surveillance to systems of public health monitoring, even as modern PDMPs continue to serve both purposes. PDMPs are certainly useful tools for addressing some aspects of the opioid epidemic, such as improving opioid-prescribing practices and preventing opioid diversion through doctor shopping. Today, they serve the same purpose for medical marijuana, moving the recommending and dispensing forward in the form of drug therapy.

Since marijuana remains illegal under federal law, doctors do not write prescriptions for medical marijuana as they would for other types of medicine; rather, they write recommendations stating that a patient will benefit from medical marijuana

their drug-ordering counterparts by stating, “In short, there is no specific action a DPM needs to perform to be insured by PICA as long as their prescribing habits align 100% with their state specific requirements, scopes, laws, and licenses and accepted best practices [sic].”

After reviewing several doctor registrations for the medical marijuana certification programs, a salient point that can be observed is that many use the descriptor “Doctor.”<sup>11</sup> Medical associations or a state health department often oversees training. Moreover, doctors must stay updated with the latest research and guidelines to ensure that they can effectively assess whether a patient should use medical marijuana based on their medical conditions.<sup>12</sup> Physicians may also need to pass exams to demonstrate proficiency in this area.<sup>12</sup> For instance, Oklahoma physicians licensed by and in good standing with the Board of Podiatric Medical Examiners are authorized to recommend medical marijuana.<sup>13</sup>

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**Employee Drug Testing**

Another interesting observation is that employers are generally allowed to test employees for the presence of drugs, although in most cases they are not required to administer tests at all. Most states impose some restrictions on testing, such as allowing it only when there is suspicion of substance use or following a workplace accident. The testing of employees in safety-sensitive jobs is commonly authorized as well. As these laws are subjective, employers need to clearly explain in their handbooks what they will and will not tolerate when it comes to marijuana use at work. While practicing for podiatry residency interviews, I used to ask myself, “What would I do if a director, mentor, or peer was visually impaired by alcohol or drugs?” My answer was grounded in my belief on the topic of substance use disorder before the unveiling of the opioid crisis. Today, I am posing the same question to the readers as both medical and recreational marijuana become commonplace. Another question that I want to pose is, “What defines a sensitive job?”

Perhaps the dispenser of medical marijuana is a “sensitive job”

given that not all states are required to employ registered pharmacists to dispense medical marijuana as a “budtender” does the job. The cannabis card holders are allowed to enter the dispensary where an employee referred to as a “budtender” discusses the various available products. An interesting caveat is that most budtenders have little to no medical training. In September 2023, LoParco, et al. examined the requirements for budtenders working in non-medical dispensaries in the 20 states with ac-

training was also required in seven states, while five states required employee training.<sup>14</sup> Here, two noticeable facts present themselves: (1) training is needed for healthcare professionals and budtenders to assist with patient/customer discussions about perinatal cannabis use<sup>15</sup> and (2) a registered pharmacist or dispensing provider is the most obvious choice to select a cannabis product and protect the patient from both pharmacokinetic and pharmacodynamic drug-drug interactions by performing a drug reconcilia-

**In 1964, Cannabis Sativa contained 1% tetrahydrocannabinol (THC).<sup>17</sup>**

tive non-medical cannabis markets.<sup>14</sup> They discovered that the age requirement for budtenders was ≥ 21 years old (n = 17) or ≥ 18 (n = 3).

Moreover, 16 states required background checks, 10 states specified felony convictions preventing employment, five states allowed the department to determine eligibility, and two states allowed petitions upon denial. Further, 12 states required fingerprinting, whereas there were application fees (\$25–300) in 13 states. Structured

tion on every patient or customer who has been assigned or desires medical marijuana. Major cannabinoids and their metabolites found in the plasma of cannabis users inhibit several P450 enzymes, including CYP2B6, CYP2C9, and CYP2D6.<sup>16</sup>

**Marijuana Potency**

In 1964, Cannabis Sativa contained 1% THC.<sup>17</sup> In 1969, Lerner asserted that a THC content of 0.5% would be the threshold level of a “normal” marijuana cigarette weighing 325 mg.<sup>17</sup> According to Nahas, a psychoactive dose of THC is approximately 10 mg present in a 1 g cigarette.<sup>18</sup> It is a fact that the potency of cannabis is different today compared to the 1970s when weed became quite popular around the world. The 1980s and 1990s made way for new methods of cannabis cultivation, one of which is the hydroponic system. This method enabled growers to create stronger and more potent products by growing weed in solutions that are richer in nutrients.<sup>18</sup>

Moreover, during this period, growers started experimenting with hybrid strains and combining Sativa and Indica strains, which led to the cultivation of marijuana with higher levels of THC.<sup>19</sup> According to a 2016 study by the National Center for Natural Products Research at the University of Mississippi, cannabis strains today are much more potent compared to those

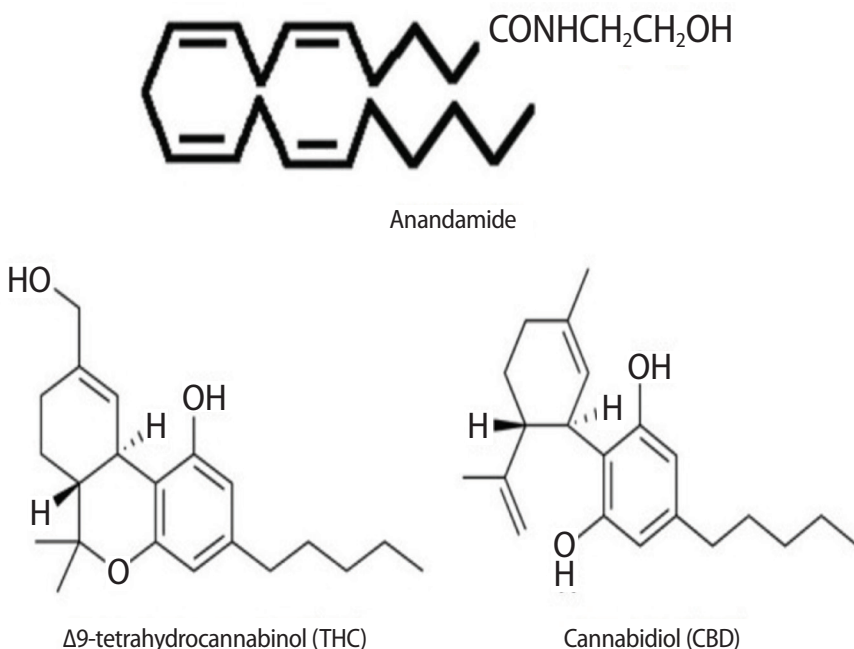


Figure 1: Comparison of Anandamide, Cannabidiol (CBD), delta-9-tetrahydrocannabinol (THC)

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20 years ago.<sup>19</sup> Moreover, according to studies conducted in 2016 and 2020, the potency of cannabis strains today is much higher compared to cannabis strains in the 1970s.<sup>19,20</sup>

In the 1970s, marijuana contained roughly 1–3% THC, while today the average potency is 18–23%.<sup>20–23</sup> Modern strains often possess THC levels well above 15%, some even reaching 30% or higher.<sup>21</sup> This increase in potency is a direct result of sophisticated breeding practices that have been refined over decades.<sup>20–23</sup> The data shows a clear trend: over the last 50 years, the average amount of THC in cannabis—the plant’s main psychoactive component—has increased more than tenfold.<sup>19–23</sup> Lastly, a Washington state cannabis potency and price study demonstrated that flowers with THC > 15% accounted for over 90% of sales while flowers with THC 10% accounted for about 2% of expenditures between 2014 and 2016.<sup>24</sup>

Pleasant experiences with marijuana are by no means universal. Instead of relaxation and euphoria, some people experience anxiety, fear, distrust, or panic because of it. These effects are more common when a person takes too much marijuana, the marijuana has an unexpectedly high potency, or the person is inexperienced. People who have taken large doses of marijuana may experience acute psychosis, which includes hallucinations, delusions, and a loss of the sense of personal identity. These unpleasant but temporary reactions are distinct from longer-lasting psychotic disorders, such as schizophrenia, that may be associated with the use of marijuana in vulnerable individuals.

The THC chemical structure is like the brain chemical anandamide<sup>25</sup> (Figure 1). Endogenous cannabinoids such as anandamide function as neurotransmitters because they send chemical messages between nerve cells (neurons) throughout the ner-

vate Cannabinoid receptor 1 (CB1).<sup>25</sup> THC increases the likelihood that the presynaptic neurons it affects will temporarily stop sending neurotransmitters. Getting high is a simple phenomenon. THC floods the endocannabinoid system with signals the postsynaptic neurons did not send. When presynaptic neurons across the brain get the message to stop sending neurotransmitters, this alters the normal flow of information among neurons, resulting in a high.<sup>26</sup>

Cannabidiol (CBD) is a negative allosteric modulator of CB1. CBD effectively alters the shape of the CB1 receptor,<sup>25–29</sup> a change that makes it more difficult for CB1 agonists like THC to stimulate the receptor. Because CBD does not bind to, or stimulate, CB1, it is also the reason it does not produce the psychotropic effects associated with THC. The mechanisms of action of CBD are not well-defined and are very complex.<sup>25–29</sup> Cannabinoid receptors (CBs) are highly prevalent in the human nervous system (CB1) and immune cells (CB2).<sup>27</sup> Unlike THC, CBD has a relatively small affinity to bind CB1 and CB2 receptors and inhibits THC binding at CB1 receptors.<sup>28</sup> At low concentrations, CBD has weak CB1 and CB2 antagonistic effects.<sup>27–29</sup>

Cannabinoids exert various effects through the activation of G-protein-coupled cannabinoid receptors in the brain and peripheral tissues.<sup>25–29</sup> Additionally, there is evidence for non-receptor-dependent mechanisms. Natural cannabis products and single cannabinoids are usually inhaled or taken orally. Other ways of taking them such as through the rectal route, sublingual administration, transdermal delivery, eye drops, and aerosols have only been used in a few studies and are of little relevance in practice today.<sup>29</sup>

The pharmacokinetics of THC vary as a function of its route of administration. Pulmonary assimilation of inhaled THC causes a maximum plasma concentration within minutes, and the psychotropic effects start within seconds to a few minutes, reaching a maximum after 15–30 minutes and tapering off with-

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## Tetrahydrocannabinol (THC) chemical structure is like the brain chemical anandamide.<sup>25</sup>

### Marijuana Biopharmaceutics

The CB1 receptor is located primarily in the central and peripheral nervous system with a particularly high abundance in the brain.<sup>25–29</sup> As a potent agonist of CB1, THC stimulates the CB1 receptor, leading to the psychotropic effects experienced when consuming cannabis. When marijuana is smoked, THC and other chemicals in the plant pass from the lungs into the bloodstream, which rapidly carries them throughout the body to the brain. If marijuana is consumed in foods or beverages, these effects are somewhat delayed—usually appearing after 30 minutes to 1 hour—because the drug must first pass through the digestive system.<sup>25–29</sup>

Eating or drinking marijuana delivers significantly less THC into the bloodstream than smoking an equivalent amount of the plant.<sup>25–29</sup> Thus, because of the delayed effects, people may inadvertently consume more THC than they intended.

vous system. The similarity in structure allows the body to recognize THC and alter normal brain communication. Because of this similarity, THC can attach to molecules called cannabinoid receptors on neurons in these brain areas and activate them, disrupting various mental and physical functions and causing the effects described earlier.

The neural communication network that uses THC’s chemical structure is like the brain chemical anandamide,<sup>25</sup> and this similarity in structure allows the drugs to be recognized by the body, allowing them to alter normal brain communication. These cannabinoid neurotransmitters, known as the endocannabinoid system, play a critical role in the nervous system’s normal functioning; therefore, interfering with it can have profound effects.

When THC enters the brain, the THC molecules diffuse into the synapses between neurons and “acti-

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in 2–3 hours.<sup>29</sup> Following oral ingestion, psychotropic effects set in with a delay of 30–90 minutes, reaching their maximum after 2–3 hours and lasting for about 4–12 hours, depending on dose and specific effect.<sup>29</sup>

At doses exceeding the psychotropic threshold, ingestion of cannabis usually causes enhanced well-being and relaxation with an intensification of ordinary sensory experiences. The most important acute adverse effects caused by overdosing are anxiety and panic attacks, with somatic effects including increased heart rate and changes in blood pressure. Regular use of cannabis may lead to dependency and mild withdrawal syndrome. The existence and the intensity of possible long-term adverse effects on psyche and cognition, immune system, fertility and pregnancy remain controversial.<sup>29</sup>

**Marijuana May Be Too Strong for Seniors and Pediatrics**

While most of the conversation around legalizing cannabis centers around the health risks to teens, seniors are also at risk. In a new study, researchers found that the number of people who are 65 or older and going to the hospital for cannabis poisoning doubled after Canada legalized marijuana in 2018 and tripled when the sale of edibles was legalized 15 months later.<sup>30,31</sup> Some of these cases resulted from accidental ingestion such as when people mistook their adult children's THC-laced gummy bears for sweets. In some cases, the seniors intended to take the drug but simply did not realize how much stronger the modern products are than the joints they rolled in their youth (up to 10 times more potent). Overall, there were more than 2,300 visits to emergency departments for cannabis poisonings among older adults—i.e., people averaging 69.5 years of age—over the study period.<sup>31</sup>

Keyhani, et al. conducted a cohort study among individuals aged 18 years and older who had urine drug screening from 2014 to 2019 and received any prescription opioid in the prior 90 days or long-term opioid therapy, defined as more than 84 days of the prior 90 days, through the Veter-

ans Affairs health system.<sup>32</sup> The resulting data were analyzed from November 2020 through March 2022.<sup>32</sup> This study found that cannabis use among adults receiving opioid analgesic medications was not associated with any change in mortality risk but was associated with a small increased risk of adverse outcomes and that short-term risks were higher among older adults receiving long-term opioid therapy.<sup>32</sup>

are inconspicuous, palatable, and easily accessible, they are increasingly popular among adolescents.<sup>36</sup> Additionally, the packaging of edible baked goods, candies, and drinks is often purposefully very similar to that of mainstream foods, increasing the risk of accidental ingestion by children.<sup>36</sup> Additionally, Hjorthøj, et al.'s recent cohort study discovered that young males might be particularly suscep-

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**One of the most consistent effects of cannabis smoking on the heart is a 20–100% increase in heart rate, which can last up to 2–3 hours, often accompanied by a slight increase in supine blood pressure.<sup>38</sup>**

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The change in legal status of cannabis (the botanical species *Cannabis sativa*, commonly known as marijuana) in the US has had significant impact on pediatric drug exposures. In states with decriminalization of recreational and medicinal use of cannabis, emergency department visits and poison control center calls for unintentional pediatric cannabis intoxication have been on the rise in the last few decades.<sup>33</sup> In 2017, use of marijuana among Black or African American (42.8%) and Hispanic (42.2%) students was higher than among White (32.0%) students. The prevalence of current marijuana use was also higher among gay, lesbian, and bisexual (30.6%) students compared with heterosexual (19.1%) and “not sure” (18.9%) students.

Older students had a higher prevalence of current marijuana use, with 13.1% of ninth-grade students, 18.7% of 10th-grade students, 22.6% of 11th-grade students, and 25.7% of 12th-grade students reporting current use. With legalization, marijuana use during pregnancy has become more common, with 7.1% of pregnant women reporting marijuana use in the past month and 3.1% reporting daily use.<sup>34–35</sup>

Edible marijuana products are often indistinguishable in appearance from normal food items and lack the smell and visible smoke associated with inhaled marijuana. Because they

tible to the effects of cannabis on schizophrenia. At a population level, assuming causality, one-fifth of cases of schizophrenia among young males might be prevented by averting cannabis use disorder (CUD).<sup>37</sup> Results from this investigation highlight the importance of early detection and treatment of CUD and policy decisions regarding cannabis use and access, particularly for 16–25-year-olds.<sup>37</sup>

**Cardiac Effects of Cannabis**

In 1977, Kanakis and Rosen reported cardiovascular effects of marijuana in men, which included sinus tachycardia, improvement in function of the sinus node, and facilitation of atrioventricular nodal conduction.<sup>38</sup> Bradycardia has also been reported with intoxication with marijuana.<sup>38</sup> The effects of blood pressure have varied from no significant change to small but significant increases in both systolic and diastolic pressures.<sup>38</sup> A decrease in systemic vascular resistance, as well as an increase in the flow of blood in the forearm, has also been observed. Further, an increase in cardiac output without an increase in stroke volume has been reported.<sup>38</sup>

One of the most consistent effects of cannabis smoking on the heart is a 20–100% increase in heart rate, which can last up to 2–3 hours, often accompanied by a slight increase in supine blood pressure.<sup>38</sup> This effect of can-

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nabis on heart rate is thought to be due to cannabis-induced vasodilation causing reflex tachycardia. The use of propranolol before marijuana will attenuate tachycardia, further supporting the idea that cannabis-induced tachycardia is attributable to sympathetic nervous system activation.<sup>38</sup>

Theerasuwipakorn, et al. performed a systematic search for publications describing the adverse CV events of cannabis use, including acute myocardial infarction (MI) and stroke. The search was performed via *PubMed*, *Scopus*, and *Cochrane Library* databases,<sup>39</sup> and 20 studies with a total of 183,410,651 patients were included. It was found that the risk of adverse CV events including acute MI and stroke does not exhibit a significant increase with cannabis exposure;<sup>39</sup> however, caution should be exercised when interpreting the

findings due to the heterogeneity of the studies.<sup>39</sup> A summary of cannabis' adverse effects is provided in Figure 2.

**Cannabis and Peripheral Neuropathic Pain**

It has been suggested that cannabis-based medicines (CbMs) and medical cannabis (MC) may be treatment options for those with chronic neuropathic pain. CbMs and MC are available in different forms, such as licensed medications or medical products (plant-derived and/or synthetic products such as tetrahydrocannabinol or cannabidiol); magistral preparations of cannabis plant derivatives with defined molecular content such as dronabinol (tetrahydrocannabinol); and herbal cannabis with a defined content of tetrahydrocannabinol and/or cannabidiol, together with other active ingredients (phytocannabinoids other than cannabidiol/tetrahydrocannabinol, terpenes, and flavonoids).<sup>40</sup>

Depending on the studies included in the various quantitative syntheses, different authors have reached divergent conclusions on the efficacy of CbMs and MC for chronic neuropathic pain, from them being ineffective to having a clinically meaningful benefit.<sup>40</sup> Cannabinoids are often prescribed for neuropathic pain, but the evidence-based recommendation is "weak against."<sup>40,41</sup>

Zubcevic, et al. conducted a randomized, double-blind trial with treatment arms for cannabidiol (CBD), tetra-hydro-cannabinol (THC), CBD and THC combination (CBD/THC), and placebo in a 1:1:1:1 ratio and flexible drug doses (CBD 5-50 mg, THC 2.5-25 mg, and CBD/THC 5 mg/2.5 mg-50 mg/25 mg). The treatment periods of 8-week duration were preceded by one week for baseline observations. Patients with painful polyneuropathy,

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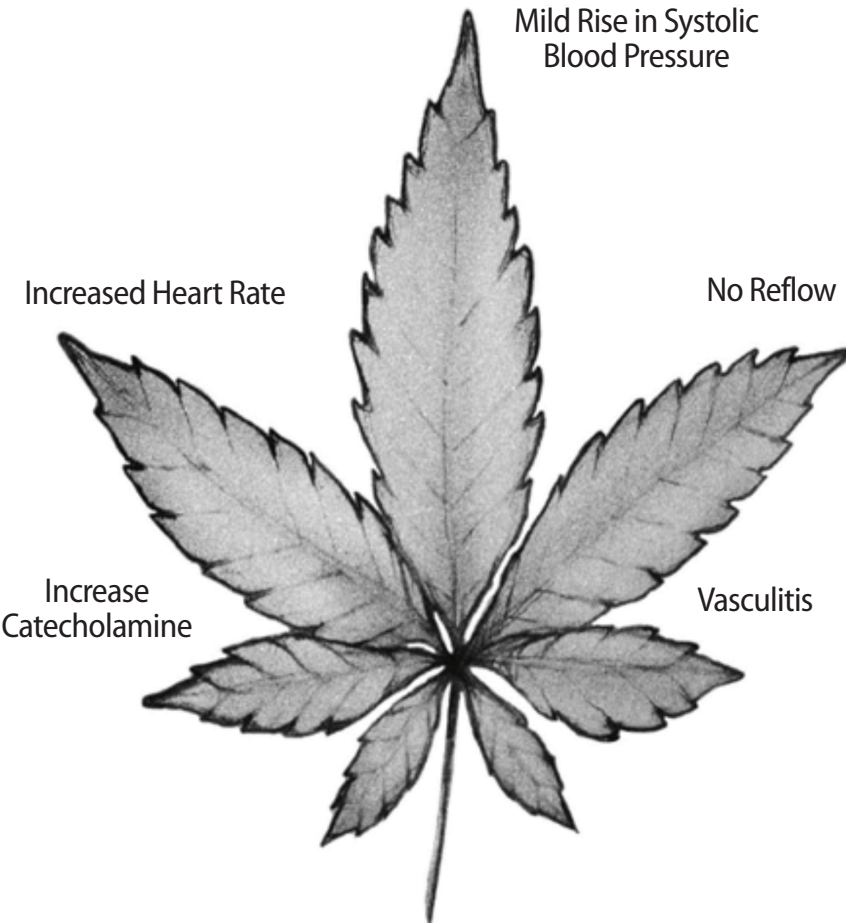


Figure 2: Adverse Effects Related to Cannabis Consumption

**CARDIOVASCULAR**

- increased angina frequency
- myocardial infarction
- cardiac death
- cardiomyopathy
- arrhythmia

**CEREBROVASCULAR**

- transient ischemic attack
- strokes

**PERIPHERAL**

- thromboangitis obliterans
- Raynaud's Phenomenon
- ischemic ulcer
- digital necrosis

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post-herpetic neuralgia, and peripheral nerve injury (traumatic or surgical) failing at least one previous evidence-based pharmacological treatment were eligible for inclusion. None of the treatments reduced pain compared to placebo.<sup>41</sup>

Thus, Zubcevic, et al. concluded that CBD, THC, and their combination did not relieve peripheral neuropathic pain in patients failing at least one previous evidence-based treatment for neuropathic pain.<sup>41</sup>

**Conclusion**

Podiatric providers need to be aware of policies and laws around marijuana in their states to provide appropriate and evidenced-based recommendations and counsel appropriately to prevent exposure and, thus, harm to developing brains. The health and well-being of seniors, children, and adolescents should be prioritized when providing this information on medical and recreational marijuana. Podiatric physicians are encouraged to participate as members of the interdisciplinary team during the reconciliation of a patient's prescribed medications, over-the-counter products, social product consumption, or herbal products, either medicinal or recreational, to enhance patient outcomes and prevent patient harm. More research is needed on the long-term effects of marijuana and should also be focused on prevention of use in adolescents. **PM**

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*Continued on page 133*



*Marijuana (from page 132)*

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**Dr. Smith** is in private practice in Ormond Beach, FL.

## CME EXAMINATION

SEE ANSWER SHEET ON PAGE 135.

- 1) Zubcevic, et al. concluded that CBD, THC, and their combination did not relieve pain in patients, failing at least one previous evidence-based treatment for \_\_\_\_\_.
  - A) somatic pain
  - B) visceral pain
  - C) traumatic pain
  - D) peripheral neuropathic pain
- 2) Major cannabinoids and their metabolites found in the plasma of cannabis users inhibit several P450 enzymes, including all EXCEPT
  - A) CYP2B6
  - B) CYP3Z13
  - C) CYP2C9
  - D) CYP2D
- 3) The use of \_\_\_\_\_ before marijuana will attenuate tachycardia, further supporting the idea that cannabis-induced tachycardia is attributable to sympathetic nervous system activation.
  - A) hydrochlorothiazide
  - B) ephedrine
  - C) naltrexone/bupropion
  - D) propranolol
- 4) Pulmonary assimilation of inhaled THC causes a maximum plasma concentration within \_\_\_\_\_.
  - A) years
  - B) hours
  - C) minutes
  - D) days
- 5) A total of 41 states, as well as the District of Columbia and Puerto Rico, have medical marijuana programs, while only two states, \_\_\_\_\_, require that providers of medical marijuana enter such “prescriptions” into their prescription drug monitoring programs.
  - A) Florida and Connecticut
  - B) New York and North Carolina
  - C) Nevada and Idaho
  - D) Connecticut and New York
- 6) In 1964, Cannabis Sativa contained \_\_\_\_\_ tetrahydrocannabinol (THC)
  - A) 50%
  - B) 1%
  - C) 33%
  - D) 24%

Continued on page 134

(Continued from page 133)

- 7) A prescription Drug Monitoring Program dates back to as early as \_\_\_\_\_ in New York.
- A) 1970
  - B) 1776
  - C) 1864
  - D) 1918
- 8) Tetrahydrocannabinol (THC) chemical structure is like the brain chemical\_\_\_\_\_.
- A) anandamide
  - B) cortisol
  - C) insulin
  - D) thyroid
- 9) One of the most consistent effects of cannabis smoking on the heart is a 20–100% increase in heart rate, which can last up to \_\_\_\_\_.
- A) 12–72 hours
  - B) 6–7 hours
  - C) 2–3 hours
  - D) 36–48 hours
- 10) Marinol® is a synthetic version of tetrahydrocannabinol THC in a capsule form called dronabinol that aims to be a cannabinoid-type antiemetic-appetite stimulant residing in \_\_\_\_\_and is used to treat nausea and vomiting caused by cancer chemotherapy.
- A) Schedule VIII
  - B) Schedule V
  - C) Schedule VII
  - D) Schedule III

**SEE ANSWER SHEET ON PAGE 135.**

The author(s) certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest), or non-financial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

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**EXAM #10/24**  
**Medical Marijuana: An Update for**  
**the Podiatric Physician**  
**(Smith)**

Circle:

- |            |             |
|------------|-------------|
| 1. A B C D | 6. A B C D  |
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Strongly agree [5]	Agree [4]	Neutral [3]	Disagree [2]	Strongly disagree [1]
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- 1) This CME lesson was helpful to my practice \_\_\_\_
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- 5) This lesson presented quality information with adequate current references \_\_\_\_
- 6) What overall grade would you assign this lesson?  
A B C D
- 7) This activity was balanced and free of commercial bias.  
Yes \_\_\_\_ No \_\_\_\_
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\_\_\_\_hour \_\_\_\_minutes

What topics would you like to see in future CME lessons ?  
Please list :

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