

ROSALIND FRANKLIN UNIVERSITY OF MEDICINE AND SCIENCE
SCHOOL OF PHARMACY STUDENT WRITING CLUB:

Taking the High Road to Pharmacist Knowledge of the Use of Cannabis

by Karen Caye L. Juco, BA, Amber R. Klankowski, Mphamvu T. Kalengamaliro, BS

Abstract

Medical and recreational cannabis has been a topic of controversy for many years. As its use is becoming more accepted and widespread throughout the country, pharmacists should be at the front lines to answer questions from patients. As medication experts, pharmacists need to educate themselves with the proper knowledge and understanding of its uses and interactions with medications. The objective of this article is to focus on medical and recreational use of cannabis and how it will impact pharmacists in Wisconsin.

Cannabis use has dated back to 8000 BC.¹ It was first mentioned as a medicine in China around 2900 BC. Cannabis use has developed over time from being used in medicine, religion, and agriculture. Medically, its use has served as an analgesic, antiemetic, and an appetite stimulant. However, cannabis' psychotropic effects are also used for euphoria and as a sexual stimulant. Originally cannabis use was abundant in the United States, until in 1937 when the Cannabis Tax Act criminalized it. Slowly throughout the 20th century, we have seen it becoming legalized for medical use with California being the first state to do so in 1996; it has now approved it for recreational use as well. Since its use is legal in some states, it is crucial for pharmacists to arm themselves with the proper knowledge to help educate their patients on the safest ways to use cannabis both medically and recreationally.

It is important for pharmacists to understand how cannabis works and the different parts of the plant that give

it its effects in order to educate and make informed decisions about its use when counseling patients. Cannabis is a plant with psychoactive properties. The two main components that people are familiar with are cannabidiol (CBD) and tetrahydrocannabinol (THC).² Both hemp and marijuana are considered cannabis plants, but the amount of CBD and THC differ between the two. Industrial hemp is used to extract CBD as it contains a fair amount of CBD and a little amount of psychoactive compound THC. Hemp is not a plant that can be used recreationally as a drug. On the other hand, marijuana plants contain up to 30% THC in addition to CBD. Marijuana has high levels of THC, which produces an intoxicating 'high' such as euphoria and relaxation. For this reason, marijuana has been used as a drug for centuries recreationally and medically for potential therapeutic benefits.

Cannabis has been a large topic of controversy throughout the past few years as more and more states are legalizing recreational use, medical use, and decriminalizing cannabis use. There

are currently 33 states that have legalized medical cannabis use and 11 states that have legalized recreational use.³ With recent policy changes for the state of Illinois, recreational use of cannabis has been legalized starting January 2020. This will have a large impact for pharmacists both in Illinois and Wisconsin. Here, the authors aim to give pharmacists a brief overview of the legality of recreational cannabis use in Wisconsin and neighboring states as well as medical uses and associated risks.

Legality of Cannabis Use in Wisconsin

Currently, Wisconsin's law prohibits medical and recreational cannabis use. However, the Legislature did pass Assembly Bill 726 (Lydia's Law) in 2014; this legalized CBD extract containing low levels of THC for children diagnosed with intractable epilepsy.⁴ In 2017, Senate Bill 10 was passed to expand the law to include any "medical condition." In 2018, FDA approved a prescription cannabidiol named Epidiolex[®] for treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patient 2 years and older.⁵ As these may seem like a stride in the right direction, the law in Wisconsin does not allow lawful sale or transfer of non-prescription CBD; however, a physician can write a prescription for the FDA-approved CBD, now a DEA schedule V drug. Additionally, the state has not legalized growing marijuana and the Federal law prevents transporting marijuana across state lines. However, in the Farm Bill of 2018, hemp is allowed to be grown under the restriction that it has less than 0.3% THC.⁶ Through the 2018 Farm Bill, hemp is federally legal in the United States. It allows for explicit transfer of hemp-derived products across state lines for commercial and other purposes. The bill did not put restrictions on the sale, transport, or possession of hemp-derived products as long as they are produced in accordance with the law. Ultimately, the Farm Bill does not create a completely free system in which individuals or businesses can grow hemp in any manner. There are many restrictions, including but not limited to that the cannabis plant must be less than 0.3% THC and the individual

must be cultivating with an appropriate license.

Although medical cannabis use is not legal in Wisconsin, Governor Tony Evers has made his stance on its utility clear. Soon after being elected to office, he submitted a budget proposal that included his ideas to decriminalize cannabis in the Spring of 2019. Within this plan, Gov. Evers would initiate penalties for possession of up to 25 grams of cannabis, which is more lenient than many other states that have decriminalized cannabis. Despite these efforts of Gov. Evers, this portion of the budget plan was not included in the final report.⁷ More recently, in December 2019, the first bill supported by the Wisconsin Republican party was presented at a House session. Although the bill is not anticipated to pass the State Senate, this is a huge step in the direction of decriminalization. A majority of Wisconsin residents support legalizing medical and recreational cannabis, prompting Wisconsin legislators to admit, "[p]eople are asking for medical cannabis."⁸

The Federal law currently prohibits the use of marijuana for medical or recreational purposes. Due to this, even though a person may have purchased it legally in one state, it cannot be transported between states. This is especially relevant with the new law of legalizing recreational use of marijuana in Illinois. It is inevitable that people will be transporting marijuana over the border. This is particularly important for pharmacists in Wisconsin to be aware of. As cannabis has become more accessible and use of it more widespread, pharmacists need to prepare for the questions that their patients will be asking them about cannabis use, interactions with their medications, as well as legal concerns. Pharmacists have to stay current with the clinical information as more studies are conducted and results are released for the use of marijuana.

In the bordering states Minnesota, Michigan, and Illinois, the medical use of cannabis is legal. Interestingly enough, Minnesota with strict medical marijuana laws, allows pharmacists to play a huge role in the Medical Cannabis Program overseen by the Department of Health.⁹ It is mandated that Minnesota licensed Pharmacists meet with patients to develop a plan of care. They are able to provide

counseling on product selection and dosing of THC and CBD components with the patient. Pharmacists in Minnesota are the only individuals in the state that are legally allowed to dispense medical marijuana. In Michigan and Illinois, recreational use is permitted for individuals 21 years and older only.¹⁰ As of 2019, residents in Michigan are able to possess as well as cultivate cannabis. This puts healthcare providers in Wisconsin in somewhat of a predicament. Regardless of the legal status of recreational or medical use of cannabis in Wisconsin, it is advantageous for pharmacists to be just as knowledgeable in the potential impact the implementation of these laws has on the individuals living in Wisconsin and surrounding states.

Medical Uses of Cannabis

According to a report on the medical effects of cannabis from the National Academies of Sciences, Engineering, and Medicine (NASEM), the medical conditions with the most data supporting improvement with cannabis use were chemotherapy-induced nausea and vomiting (CINV) and pain, with symptomatic management in multiple sclerosis.² Notable disease states without enough evidence to comment on cannabis effectiveness include glaucoma and anxiety.

Nabilone and dronabinol, two cannabinoids, are thought to act on cannabinoid receptor, CB1, is found in the vomiting center and the chemoreceptor trigger zone, areas of the medulla oblongata which control nausea and vomiting.^{11,12} Findings show that these cannabinoid medications were just as useful as traditional antiemetic medications for CINV, like ondansetron or metoclopramide.^{13,14} Cannabinoids may be beneficial adjunctive therapy in patients with severely emetogenic chemotherapy regimens or those who are refractory to other antiemetic classes. Despite these promising findings, inadequate literature exists for use of ingested or inhaled plant-derived cannabis products.

Pain has been listed as one of the most common reasons for patients to seek medical cannabis.² According to this NASEM report, cannabinoids are thought to improve many types of pain, such as neuropathic pain or fibromyalgia,

chronic pain, post-operative pain, cancer pain, and rheumatoid arthritis. Several randomized control trials cited in the NASEM review provide evidence to support the use of cannabinoids to treat pain, but more research should be done to evaluate different doses and routes of administration. Most research focuses on the effects of vaporized cannabis flowers. NASEM concluded that there was substantial evidence that cannabinoids would be effective for pain treatment in adults.

Cannabis also has proven efficacy in the treatment of spasticity in multiple sclerosis (MS) due to CB1 receptor activity in the brain's motor areas and pain pathways, and CB2 receptor activity in immunomodulation.⁸ In a systematic review, Whiting and colleagues found that most cannabinoids have statistically improved short-term MS-related spasticity, but the clinical significance of that difference is likely minimal.¹⁵ One study presented evidence that oral cannabis extract and oral THC are possibly effective in the long-term (about 1 year).¹⁶ Although cannabis efficacy for spasticity due to MS is controversial, cannabis may also be helpful for sleep and pain concerns in patients with MS.

Risks of Cannabis Use

While cannabis use seems to be helpful in some patients, there are inevitable risks that come with its use. Acute THC administration has been shown to cause increased sympathetic tone, leading to an increase in blood pressure.¹⁷ However, with repeated doses, this switched to a decrease in sympathetic tone and increased parasympathetic tone, indicating a possible development of tolerance. The acute increase in sympathetic tone leads to increased blood pressure and heart rate, potentially putting the individual at an increased risk of myocardial infarction. However, there is little data to support a statistical association between THC use and cardiovascular outcomes.¹⁸

There is a lack of quality evidence in cannabis effects of respiratory functions.² Many of the studies reviewed in the NASEM report depended on self-reporting of smoked cannabis use and failed to adjust for confounders such as use of inhaled

tobacco or environmental exposures.^{19,20} As such, no conclusive evidence exists to link smoking cannabis to specific lung diseases or pulmonary function tests.² It is worth noting that in September 2019, cases of e-cigarette, or vaping, product use-associated lung injury (EVALI) spiked.²¹ These e-cigarettes often contain nicotine and THC, and both drugs have been implicated in EVALI. Therefore, CDC is currently encouraging all clinicians to continue to report possible cases of such lung injuries to their local or state health department so further investigation can be implemented. Cases have since declined due to increased public awareness, but it is still important for clinicians to ask patients the type of substances used in their e-cigarette or vaping products such as THC or nicotine.

Research has shown that the clinically advantageous pharmacologic interventions within the endocannabinoid system are becoming well established. Cannabinoid receptors (CB1 and CB2) are capable of being activated by either endogenous cannabinoids (endocannabinoids) or exogenous agonists such as THC and CBD.²² The CB1 receptors are found primarily in the brain, with a small degree of expression also seen in the periphery, whereas the CB2 receptor is expressed mainly in immune cells. As researchers continue to discover the utility of the endocannabinoid systems, new drugs will enter the market and pharmacists will be required to be knowledgeable on how to properly counsel patients on their cannabis derived therapies.

As states continue to legalize medical and recreational use of cannabis, the need for well-trained pharmacists becomes apparent for several reasons. Pharmacists are able to combat clinical issues that arise with the use of medical cannabis; this includes understanding of benefits when used in certain disease states and evaluation of potential drug-drug interactions.²³ Both THC and CBD are metabolized via CYP450 enzymes.²⁴ More specifically THC is metabolized by CYP3A4 and CYP2C9.²⁵ Whereas CBD is primarily metabolized by CYP3A4 and CYP2C19. Therefore CYP2C9 inhibitors such as amiodarone, and voriconazole would be expected to increase the plasma concentration of THC.

Conversely, strong CYP3A4 inhibitors and inducers, such as ketoconazole and rifampin respectively, can alter serum concentrations of both CBD and THC and may lead to potential adverse effects. Currently, there is limited data available to strongly support drug-drug interactions involving the effect of cannabis on other drugs as they have not been well-studied. The current body of literature includes in vitro studies and case reports. However this does not mean that interactions do not exist. Therefore, monitoring the responses of patients who use cannabis with certain medications may be prudent. As drug experts, pharmacists should be the most qualified health professionals to take on this role.

Conclusion

Legalizing recreational use of cannabis will have a large impact on pharmacists and patient's relationship with their pharmacist. Patients need to be able to consult their pharmacist openly about questions they may have regarding the use of cannabis and interactions that it may have with their current medication therapies. As the role of cannabis is still fairly new, there is not a lot of scientific literature for pharmacists to utilize. It would be in their best interest to stay current with the scientific updates of cannabis use as well as laws that are specific to the states and its pharmacy practice. Pharmacists in Wisconsin and other states should start asking patients specifically about cannabis use when obtaining medication histories.

Karen Caye Juco, Amber Klankowski, and Mphamvu Kalengamaliro are Doctor of Pharmacy Candidates at Rosalind Franklin University of Medicine and Science College of Pharmacy in North Chicago, IL.

PR

This article has been peer-reviewed. The contribution in reviewing is greatly appreciated!

Acknowledgements: The authors thank Dr. Gary Oltmans, of Rosalind Franklin University of Medicine and Science, for his expertise on the subject. We also thank Dr. Khyati Patel for meaningful suggestions throughout construction of the manuscript.

Disclosure: The authors declare no real or potential

conflicts or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts, and honoraria.

References

1. Hill, K. Marijuana: The Unbiased Truth about the World's Most Popular Weed. Hazelden Publishing, Center City, MN. Published 2015. Accessed December 15, 2019.
2. The National Academies of Science, Engineering, and Medicine. The health effects of cannabis and cannabinoids: the current state of evidence and recommendations for research. <https://www.nap.edu/read/24625/chapter/1>. Accessed December 11, 2019.
3. Legal Medical Marijuana States and DC. ProCon.org. <https://medicalmarijuana.procon.org/legal-medical-marijuana-states-and-dc/>. Accessed December 15, 2019.
4. Nunley K. Wisconsin marijuana laws: recreational vs. medical legalization. <https://www.medicalmarijuanainc.com/wisconsin-marijuana-laws/>. Published September 1, 2019. Accessed December 15, 2019.
5. Epidiolex (cannabidiol) [prescribing information]. Carlsbad, CA: Greenwich Biosciences, Inc.;2020.
6. Hudak J. The farm bill, hemp legalization and the status of CBD: an explainer. <https://www.brookings.edu/blog/fixgov/2018/12/14/the-farm-bill-hemp-and-cbd-explainer/>. Published December 14, 2018. Accessed March 18, 2020.
7. White L. Report: Gov. Tony Evers' marijuana proposal goes further than other states. Wpr.org. <https://www.wpr.org/report-gov-tony-evers-marijuana-proposal-goes-further-other-states>. Published April 30, 2019. Accessed December 16, 2019.
8. Dupont A. 'People are asking for medical marijuana:' GOP support grows with unveiling of 1st bill by Republicans. Fox6now.com <https://fox6now.com/2019/12/11/gop-support-grows-to-legalize-medical-marijuana-in-wisconsin/>. Published December 11, 2019. Accessed December 16, 2019.
9. Bonner L. Pharmacists take on medical cannabis dispensing roles in 3 states. Pharmacy Today. [www.pharmacytoday.org/article/S1042-0991\(15\)00021-3/fulltext](http://www.pharmacytoday.org/article/S1042-0991(15)00021-3/fulltext). Published January 13, 2016. Accessed March 20, 2020.
10. Project, Marijuana Policy. "Gov. Evers Proposing Decrim, Medical Cannabis as Part of His Budget; Legislature Blocks the Proposals." MPP.org, <https://www.mpp.org/states/wisconsin/>. Published October 1, 2019. Accessed December 16, 2019.
11. Cesamet (nabilone) [package insert]. Bridgewater, NJ: Bausch Health US, LLC; 2020.
12. Dronabinol [package insert]. Lake Forest, IL: Akorn; 2017.
13. Meiri E, Jhangiani H, Vredenburg JJ, et al. Efficacy of dronabinol alone and in combination with ondansetron versus ondansetron alone for delayed chemotherapy-induced nausea and vomiting. *Curr Med Res Opin.* 2007;23(3):533-543.
14. Heim ME, Queisser W, Altenburg HP. Randomized crossover study of the antiemetic activity of levonantradol and metoclopramide in cancer patients receiving chemotherapy. *Cancer*

- Chemother Pharmacol.* 1984;13(2):123-125.
15. Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for medical use: a systematic review and meta-analysis. *JAMA.* 2015;313(24):2456-2473.
 16. Zajicek JP, Sanders HP, Wright DE, et al. Cannabinoids in multiple sclerosis (CAMS) study: safety and efficacy data for 12 months follow up. *J Neurol Neurosurg Psychiatry.* 2005;76(12):1664-1669.
 17. Benowitz NL, Jones RT. Cardiovascular and metabolic considerations in prolonged cannabinoid administration in man. *J Clin Pharmacol.* 1981;21(suppl 8-9):214S-23S.
 18. Sidney S. Cardiovascular consequences of marijuana use. *J Clin Pharmacol.* 2002;42(suppl 11):64S-70S.
 19. Papatheodorou SI, Buettner H, Rice MB, Mittleman MA. Recent marijuana use and associations with exhaled nitric oxide and pulmonary function in adults in the United States. *Chest.* 2016;149(6):1428-1435.
 20. Pletcher MJ, Vittinghoff E, Kalhan R, et al. Association between marijuana exposure and pulmonary function over 20 years. *JAMA.* 2012;307(2):173-181.
 21. Centers for Disease Control and Prevention.

- For healthcare providers: electronic cigarettes. https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease/healthcare-providers/index.html. Accessed February 14, 2020.
22. Pacher P, Batkai S, Kunos G. The endocannabinoid system as an emerging target of pharmacotherapy. *Pharmacol Rev.* 2006;58(3):389-462.
 23. Marijuana Policy Project. Medical cannabis: a new frontier for pharmacists. Pharmacy Today. [https://www.pharmacytoday.org/article/S10420991\(19\)31155-7/fulltext#back-bib1](https://www.pharmacytoday.org/article/S10420991(19)31155-7/fulltext#back-bib1). Published June 9, 2019. Accessed December 16, 2019.
 24. Alsherbiny MA, Li CG. Medicinal cannabis-potential drug interactions. *Medicines (Basel).* 2018;6(1):3.
 25. Horn JR, Hansten PD. Drug interactions with marijuana. Pharmacy Times. www.pharmacytimes.com/publications/issue/2014/December2014/Drug-Interactions-with-Marijuana. Published December 9, 2014. Accessed March 20, 2020.

"I'M ALWAYS WATCHING OUT FOR MY PATIENTS, BUT WHO'S WATCHING OUT FOR ME?"



WE ARE.

We are the Alliance for Patient Medication Safety (APMS), a federally listed Patient Safety Organization.

Our Pharmacy Quality Commitment (PQC) program:

- Helps you implement and maintain a continuous quality improvement program
- Offers federal protection for your patient safety data and your quality improvement work
- Assists with quality assurance requirements found in network contracts, Medicare Part D, and state regulations
- Provides tools, training and support to keep your pharmacy running efficiently and your patients safe

Pharmacy Quality[™]
COMMITMENT
A program designed to reduce medication errors.

Call toll free (866) 365-7472 or visit www.pqc.net

PQC IS BROUGHT TO YOU BY YOUR STATE PHARMACY ASSOCIATION