

THERAPEUTIC DRUG
MANAGEMENT AND TOXICOLOGY
DIVISION NEWS

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Therapeutics & Toxins News

Newsletter for the TDM and Toxicology Division of AACC

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Exploring the Emerging Trends of Delta-8 THC: The New Frontier in Cannabis Consumption

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Background

In recent years, the cannabis industry has experienced a remarkable wave of innovation and evolution. Among the notable developments is the rise of delta-8 THC, a compound derived from hemp that has garnered significant attention for its unique properties and potential benefits. As more states in the United States and countries around the world embrace cannabis legalization, delta-8 tetrahydrocannabinol (delta-8 THC or $\Delta 8$ -THC) is emerging as a new and exciting trend that is capturing the interest of consumers, businesses, and regulators alike.

In the US, the popularity of $\Delta 8$ -THC has arguably arisen because of its easy accessibility. This hemp-origin cannabinoid can be purchased at gas stations, vape shops and even online retailers across the nation. It

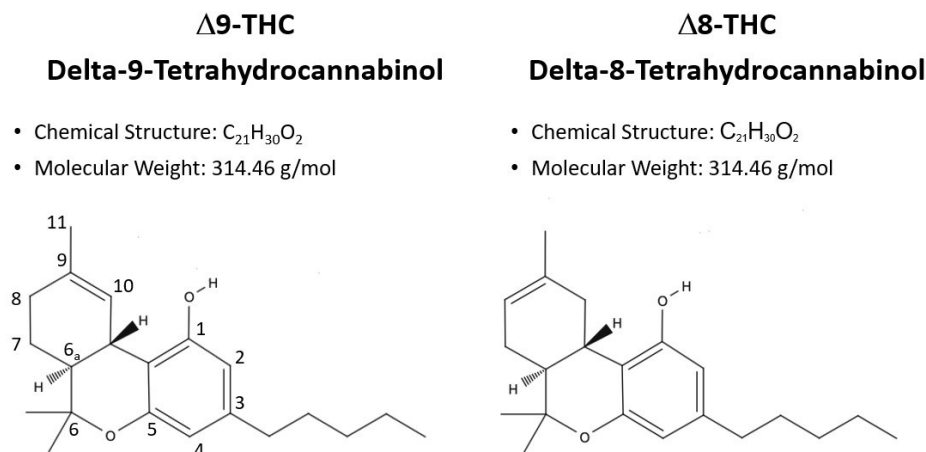
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is marketed as the legal alternative to delta-9 tetrahydrocannabinol ($\Delta 9$ -THC), which is still highly regulated and illegal on the federal level as a schedule I controlled substance. In this article, we will discuss the prevailing status of $\Delta 8$ -THC as the emerging cannabis product, including its chemistry, current legislation, and clinical impacts and testing implications.

Chemistry

Among over 100 cannabinoids discovered in the cannabis plant, $\Delta 8$ -THC only naturally occurs at trace concentration [1]. $\Delta 8$ -THC is a structural isomer to the well-known $\Delta 9$ -THC. As the name specifies, the difference is the location of the double bond. It is on the 8th carbon for $\Delta 8$ -THC, while the unsaturated bond is on the 9th carbon on $\Delta 9$.



$\Delta 8$ -THC, like $\Delta 9$ -THC, shows affinities to the common cannabinoid receptors, CB1 and CB2, in the brain and central nerve system. However, it appears to have weaker potency than $\Delta 9$ -THC. Similar psychoactive effects to $\Delta 9$ -THC are observed including euphoria, apprehension and anxiety, hunger and thirst, drowsiness etc. [2]. $\Delta 8$ -THC has been studied for its potential medical benefits, including its ability to reduce nausea and vomiting in cancer patients undergoing chemotherapy [3]. It has also been shown to have analgesic properties, making it a potential alternative to traditional painkillers [4]. Also, many $\Delta 8$ -THC users reported a “high” without the brain fog, which are commonly observed $\Delta 9$ -THC effects [5]. One of the key attractions of $\Delta 8$ -THC is its potential to offer a more mellow and balanced experience compared to $\Delta 9$ -THC. Many users describe the effects of $\Delta 8$ -THC as a smoother and clearer high, often associated with reduced anxiety and paranoia. Additionally, some consumers claim that $\Delta 8$ -

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THC provides a more functional experience, making it an appealing choice for those who want to incorporate cannabis into their daily routines without feeling overly impaired. However, these effects are reported based on subjective user experiences, and more research is needed to confirm these benefits. Currently, limited peer-reviewed scientific research is conducted to offer a systemic review or a comprehensive comparison between $\Delta 8$ -THC and $\Delta 9$ -THC. And there are still many unknowns about the long-term effects of $\Delta 8$ -THC use.

Regulations

Regulations for $\Delta 8$ -THC vary significantly by country. Some countries have strict regulations on cannabis and its derivatives, including $\Delta 8$ -THC, while others have more permissive frameworks. In the US, regulations surrounding $\Delta 8$ -THC are still evolving, and they vary by jurisdiction. The legal status of $\Delta 8$ -THC is often determined by its source, concentration, and the specific laws governing cannabis and hemp-derived products in each region. In December 2018, the Agriculture Improvement Act of 2018 was signed into law. Also known as the 2018 Farm Bill, this legislation removed hemp from Schedule I of the Drug Enforcement Administration (DEA) schedule of controlled substances and effectively legalized hemp and its derivatives, including delta-8 THC, as long as they contain less than 0.3% $\Delta 9$ -THC [6].

States have the authority to regulate $\Delta 8$ -THC within their jurisdictions. Some states have explicitly addressed $\Delta 8$ -THC in their cannabis or hemp laws, setting specific requirements for its production, sale, and consumption. Others have implemented restrictions or outright bans on $\Delta 8$ -THC due to concerns about its potency, safety, and potential for misuse. It's essential to consult state-specific laws and regulations to understand the legal status of $\Delta 8$ -THC in a particular location.

$\Delta 8$ -THC is typically synthesized from hemp-derived cannabidiol (CBD), which classifies it as a non-regulated substance. This has led to a growing market for $\Delta 8$ -THC products, including edibles, tinctures, and vaping cartridges. Many small and inexperienced manufacturers jumped on this bandwagon to share the huge $\Delta 8$ -THC market profits. Their products are made with potentially harmful chemicals and/or in uncontrolled environments. It is difficult for consumers to know exactly what they are getting when they purchase $\Delta 8$ -THC products. There have been reports of products being mislabeled or contaminated with harmful substances, such as heavy metals or pesticides [7]. Eventually, FDA published a consumer update to increase the public awareness of the severe health risks imposed by $\Delta 8$ -THC [8]. Currently, 14 states passed regulations to ban $\Delta 8$ -THC (AK, WA, ID, MT, ND, NY, IA, RI, CA, CO, DE, AD, MS, and HI). However, the legality of $\Delta 8$ -THC is still somewhat murky on a federal level, and it is unclear how long it will remain legal in countries where it is currently legal.

Clinical Impacts

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The clinical impact of $\Delta 8$ -THC consumption is an area of growing interest and exploration in the medical field. While research on $\Delta 8$ -THC is still limited, preliminary studies and anecdotal evidence suggest that it may have therapeutic potential for various conditions. $\Delta 8$ -THC has been studied for its potential anti-inflammatory properties, which could make it useful in managing conditions such as chronic pain and arthritis. Additionally, its antiemetic effects have shown promise in alleviating nausea and vomiting, particularly in cancer patients undergoing chemotherapy. However, further rigorous research, including clinical trials, is necessary to better understand the full extent of $\Delta 8$ -THC's clinical impact, its optimal dosage, and any potential side effects. Healthcare professionals and researchers are closely monitoring these developments to determine its potential as a safe and effective treatment option.

On the other hand, since $\Delta 8$ -THC shares the psychoactive and intoxicating effects as $\Delta 9$ -THC, similar clinical indicators following exposure can arise including confusion, hypotension, tachycardia and seizure-like symptoms [9]. Many $\Delta 8$ -THC infused edibles are in forms of candies, such as gummies, cookies, chocolates, etc. The appealing packaging puts children at a higher risk of $\Delta 8$ -THC exposure. Based on the reports from national poison control centers, over 30% of exposure cases involved unintentional $\Delta 8$ -THC exposure in children [8].

Testing Implications

Accurate quantification of $\Delta 8$ -THC in both the products and in biofluids is crucial to comply with legal requirements, as many jurisdictions have established limits on the allowable $\Delta 9$ -THC content in hemp-derived products, including $\Delta 8$ -THC.

In addition to cannabinoid profiling, laboratories should also test for potential contaminants and potentially toxic byproducts, such as pesticides, heavy metals, residual solvents, and microbial contaminants. These tests ensure that the $\Delta 8$ -THC products are safe for consumption and meet regulatory standards. Thorough testing protocols and stringent quality control measures are necessary to protect consumer health and establish trust in the emerging $\Delta 8$ -THC market.

However, the testing of $\Delta 8$ -THC presents unique challenges. The compound's structural similarity to $\Delta 9$ -THC can complicate the analytical process, as standard methods may not adequately differentiate between the two isomers. Laboratories must employ validated methods and calibration standards specifically tailored for $\Delta 8$ -THC to ensure accurate quantification. Thus, prevailing hospital laboratory drug screens using immunoassays can't distinguish between $\Delta 8$ -THC and $\Delta 9$ -THC. $\Delta 8$ -THC displays high cross-reactivity with currently available urine drug screens, and may also lead to false positive results for certain $\Delta 9$ -THC confirmation testing, which are assays that directly analyze $\Delta 9$ -THC and its metabolite, $\Delta 9$ -carboxy THC, without extractions [10]. There are clinically established methods to distinguish $\Delta 8$ -THC and $\Delta 9$ -THC metabolites using mass spectrometers, such as GC-MS [11] and LC-MS/MS [12]. However,

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even though this technology offers great sensitivity and high potential future growth, many hospitals are not financially capable of purchasing instruments or hiring scientists with this skillset.

Due to its legal status in the majority of US states, $\Delta 8$ -THC products are readily available, and may be used by pain management patients. In our practice, these patients tend to omit reporting $\Delta 8$ -THC use. It frequently shows up as a positive THC urine drug screening result due to the structural similarity between $\Delta 8$ -THC and $\Delta 9$ -THC. These patients may be wrongfully accused of medicine noncompliance and substance use, and even be dismissed from their treatment program. Ultimately, robust laboratory testing practices of separate and distinct measurement of $\Delta 8$ -THC and $\Delta 9$ -THC, as well as other THC compounds and metabolites, are crucial for consumer and patient safety.

Conclusion

The prevalence of products in the $\Delta 8$ -THC market highlights the pressing need for clearer regulatory guidelines to address concerns regarding product safety and quality. Extensive and well-defined research is required to fully comprehend the clinical impact of this compound. It is imperative to educate and caution the public about potential risks associated with $\Delta 8$ -THC until a safe and regulated market is established. Regulatory bodies should view the rise of $\Delta 8$ -THC as a cautionary signal within the expanding cannabis industry. Urgent action from government agencies is necessary to ensure public health and safety. Comprehensive laboratory testing of products and patient samples is pivotal in facilitating safe consumption and accurate detection of this rapidly emerging compound.

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Chair's Corner: AACC National Meeting 2023

Dear TDM/Toxicology Division Members:

The Division is off to a strong start in 2023! More than 50 abstracts were submitted for division review and our Awards Committee worked hard to select an Abstract award winner, Dr. Aja Aravamudhan, who will receive an award for her abstract titled "Aberrant lithium results after hdl assay on roche cobas c503 instrument". Dr. Aravamudhan's poster, #B-313, will be presented on Wednesday July 26th. Thanks to continued support from UTAK, the Awards Committee selected a Young Investigator award winner for 2023, Dr. Alec Saitman, from a very strong pool of nominees. Dr. Saitman will present a brief summary of his research at the Division's annual membership meeting, which will begin at noon on July 24th at the Anaheim Marriott. Not to be outdone by the Awards Committee, the Nominating Committee was instrumental in putting together a great slate of candidates to fill the 3 open positions on the Division leadership team. Elections will be open from June 19th to July 3rd and we encourage all members to vote. Look for an update on our new leaders after the elections conclude! In other news, one TDM/Toxicology Division sponsored session will be presented at the ASM (#32445, "Bridging Emergency Medicine and Public Health: Clinical Toxicology Laboratory Strategies to Characterize Local Drug Supplies and Drug Use Patterns"). In addition to these highlights, the Division will have many activities to report on at our July membership meeting in Anaheim. I hope to see many of you at there!

Jennifer Colby, Chair, TDM-TOX Division, AACC.

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AACC TDM TOX Web Resources:

<https://www.aacc.org/community/divisions/tdm-and-toxicology/>

Announcements:

We need your ideas and article contributions for this newsletter. It is a good opportunity to put authorship in resume. Please contact Dr. Pradip Datta at pradip.datta@siemens-healthineers.com.