

# A Hemp Field Day for Psychoactive Effects: The Science of $\Delta^8$ & $\Delta^{10}$ -THC

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## Background and Objectives

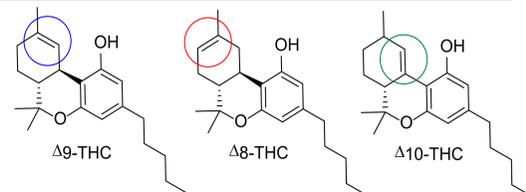
$\Delta^8$  and  $\Delta^{10}$ -THC are isomers of  $\Delta^9$ -THC trending in the cannabis and hemp industries, often marketed as “legal” substitutes for  $\Delta^9$ . While it is known that both  $\Delta^8/\Delta^{10}$  have similar pharmacology to  $\Delta^9$ , they are produced synthetically and sold outside the Medical Cannabis realm with little to no regulation through vape shops, retailers, and convenience stores throughout the country. This lack of regulation leads to concerns regarding quality, purity, and safety of these products, as many appeal to the younger population. This poster will explain the details of both  $\Delta^8$  and  $\Delta^{10}$ -THC and provide critical information for industry professionals, clinicians, students, and others as these isomers become increasingly more prevalent in the industry.

$\Delta^8$ -THC was first isolated back in 1966 (Hively et al), and its corresponding acid in 1975 (Hanus and Kerejci), proving that small amounts of  $\Delta^8$ -THC were produced by certain chemovars. Only in the past few years has interest in this “old” cannabinoid been renewed.

$\Delta^{10}$ -THC was originally discovered by Israeli Chemist Raphael Mechoulam (1984) by heating  $\Delta^9$ -THC at high temperatures under basic conditions. More recently, it was rediscovered in 2020 in California through extracted biomass and distillation process to remove fire retardant chemicals from hemp plants, through crystallization processes (Jones, 2020).

## What is $\Delta^8$ -THC and $\Delta^{10}$ -THC ?

$\Delta^8$  and  $\Delta^{10}$ -THC are isomers of  $\Delta^9$  (same formula, different structure). Because of this “shifting” of the position of the double bond, these isomers have distinct characteristics from  $\Delta^9$ .

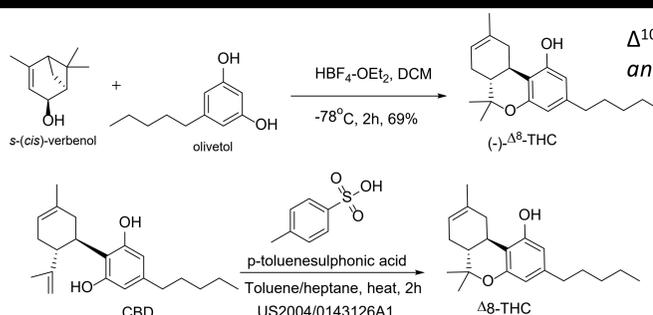


- $\Delta^8$ -THC:**
- 1) 3-4x lower binding affinity to the  $CB_1$  (78nM) and  $CB_2$  (12nM) compared to  $\Delta^9$  (8.96nM at  $CB_1$  and 3.89nM at  $CB_2$ ) [Radwan et al., 2015], likely explaining why it is called “ $\Delta^9$ -Lite” or “Diet  $\Delta^9$ ” (lower potency)
  - 2)  $\Delta^8$  has higher stability and does not oxidize to CBN upon storage.

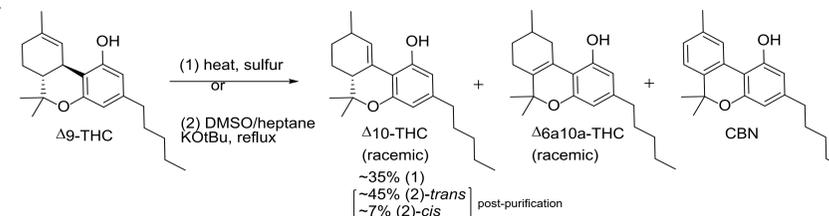
- $\Delta^{10}$ -THC:**
- 1) Lower affinity for  $CB_1$  and  $CB_2$  than  $\Delta^9$ -THC, but no binding experiments have been performed to date.
  - 2) We can infer that it likely has similar potency to  $\Delta^8$  (Mechoulam, 1988) based on drug discrimination studies in pigeons.

## How are they made?

$\Delta^8$  is made by total synthesis starting from *s*-cis-verbenol and olivetol with a Lewis acid catalyst (Mechoulam et al. 1967 and Hoffman and Studer 2018), semi-synthesis from CBD, or base catalyzed isomerization of  $\Delta^9$ . The processes result in an impure oil that **requires purification**. The most common method to make  $\Delta^8$  is by the acid catalyzed ring closing of CBD. The less common method uses less available chemicals, ultra-cold temperatures with a Lewis acid catalyst.



$\Delta^{10}$  is made by heating  $\Delta^9$  at high temperatures that produce two different stereoisomers, *cis* and *trans*.



## Regulatory Aspects

From the 2018 Farm Bill Amendments (AIA, 2018), amending the Agricultural Marketing Act of 1946: The term 'hemp' means the plant *Cannabis sativa* L. and any part of that plant, including the seeds thereof and all derivatives, extracts, cannabinoids, isomers, acids, salts, and salts of isomers, whether growing or not, with a concentration of  $\Delta^9$ -THC not more than 0.3 percent on a dry weight basis. This statement made the hemp products` producers to believe that any cannabinoid (with < 0.3  $\Delta^9$ -THC) is not controlled. It was extrapolated to include  $\Delta^8$ -THC that is manufactured and sold as hemp. Just because the starting products are legal, does it mean the product is? Are they even using hemp?

The U.S. Hemp authority has stopped certifying  $\Delta^8$ -THC products and is encouraging companies to cease producing them. (March 2021).

As of August 2022, 21 states have regulated, restricted, or banned  $\Delta^8$ -THC. Most recently,  $\Delta^8$ -THC was ruled legal in Kentucky as a court lifted an injunction prohibiting the sale and production in their state. The regulation of  $\Delta^8$ -THC was challenged in the Ninth Circuit Court (AK Futures vs. Boyd, 2022) who ruled that  $\Delta^8$ -THC products follow the guidelines of the 2018 Farm Bill for hemp products content, remain under the jurisdiction of the 2018 Farm Bill, and legal to be sold. The most recent CSA Schedule 1 includes  $\Delta^8$ -THC specifically, while  $\Delta^{10}$ -THC is currently federally legal, yet illegal in 11 states.

The USP (United States Pharmacopeia) recognizes public health concerns regarding the safety and purity of the novel substances emerging such as  $\Delta^8$ -THC,  $\Delta^{10}$ -THC,  $\Delta^8$ -THC-O-acetate, HHC (hexahydrocannabinol) and  $\Delta^9$ -THCP (tetrahydrocannbiphorol) being marketed as hemp derivatives and advises systematic preclinical investigations before releasing these substances to the market to ensure safety and to characterize and identify potential toxicities (USP, 2022).

## Methods/Results

As many students in our professional school and graduate programs were not aware of the issues surrounding isomers of  $\Delta^9$ -THC, a specific series of educational materials covering the science, pharmacology, and regulatory aspects of these isomers ( $\Delta^8/\Delta^{10}$ ) and derivatives (THC-O, THCP, HHC) were utilized in both the professional program and the MSCT program.

## Discussion

I entered this master’s program as a consultant and entrepreneur, with an academic business background, working in leadership and personal development as a coach and international yoga and mindfulness professional. I joined the program to advance my education in cannabis to support my clients and my own personal journey with cannabis, psychedelics, and PTSD. I believe cannabis is a medicine poised to advance our relationship with chronic disease and expanded consciousness. The asynchronous approach to the program allows me the flexibility to stay career oriented and focus on my studies while applying knowledge in real-time discovery and development in science and policy.

I am serving on the Executive Board for the MCSA, (Medical Cannabis Student Association) as the Director of Alumni Relations, in collaboration with the UMB School of Pharmacy’s alumni development directives. Our MCSA hosts monthly events focused on academic and career supporting experiences for students within our program. As a member of the Presidential Student Leadership Institute at UMB, the global leadership track supports my interests in science policy and social justice as I explore post-graduate work and developing career opportunities in cannabis science education and industry responsibility.

## Description of the MS in Medical Cannabis Science and Therapeutics Program

The school’s MS in Medical Cannabis Science and Therapeutics Program is a two-year Master’s degree (30 credits) that provides students with a comprehensive education in the science of medical cannabis, its therapeutic uses, and the policies that govern its use in medicine and research. Students take courses in the pharmacology, chemistry, and pharmaceuticals of cannabinoids and cannabinoid formulations and study the evidence for cannabis use in various diseases and conditions. Our cohort of students includes a variety of academic and professional backgrounds including clinicians, scientists, attorneys, public health professionals, business professionals, educators, and others. Twice a year, students come together for a symposium that includes seminars by cannabis experts and opportunities for networking with professionals in the field.

MS in Medical Cannabis Science and Therapeutics

There is a wonderful and diverse cohort that just started for Fall 2022!

