



### In brief

**Chemists are alarmed about impurities formed** during the synthesis of the cannabinoid  $\Delta^8$ -tetrahydrocannabinol (delta-8-THC), sold in gummies, vape products, and other items. Delta-8-THC is a mildly euphoric isomer of psychoactive delta-9-THC. Delta-8-THC is typically synthesized from cannabidiol (CBD) extracted from hemp. The reaction often yields a high percentage of delta-8-THC, as well as small amounts of other cannabinoids and reaction by-products. Little is known about the health effects of these impurities, and chemists have not identified all of them.



# Delta-8-THC craze concerns chemists

Unidentified by-products and lack of regulatory oversight spell trouble for cannabis products synthesized from CBD

BRITT E. ERICKSON, C&EN STAFF

**M**ove over cannabidiol (CBD). The popularity of another cannabinoid,  $\Delta^8$ -tetrahydrocannabinol (delta-8-THC), is on the rise. Found in gummies, vape cartridges, tinctures, and other products, delta-8-THC is popping up in gas stations, convenience stores, tobacco shops, and cannabis dispensaries throughout the US and beyond—often with no age restrictions.

Unlike CBD, delta-8-THC produces euphoric effects that are similar to but milder than those of delta-9-THC, the well-known psychoactive compound in cannabis. Delta-8-THC is an isomer of delta-9-THC. The only difference between the two molecules is the location of a double bond between two carbons.

The delta-8-THC craze began when an oversupply of CBD extracted from US-grown hemp caused the price of CBD to plummet. Producers began looking for ways to turn the glut of CBD into something profitable. Using simple chemistry reported in the 1960s, the industry got creative and started experimenting with ways to convert CBD into delta-8-THC. The resulting products target consumers who are looking to relieve stress and anxiety, especially those who don't want to use traditional cannabis products or those who live in places where cannabis products are not legally available.

But with no regulatory oversight and limited laboratory testing, most products sold as delta-8-THC are not actually pure delta-8-THC. Such products typically contain a high percentage of delta-8-THC and small amounts of other cannabinoids, including delta-9-THC, and reaction by-products. Some of the cannabinoids are not naturally found in cannabis. In most cases, nothing is known about the health effects of these impurities.

Several states are starting to crack down on sales of delta-8-THC products. But as long as they are derived from hemp and contain no more than 0.3% of delta-9-THC on a dry-weight basis—the limit under federal law—many lawyers and hemp industry officials consider them legal. Regardless of whether delta-8-THC is legal, chemists are sounding the alarm after finding several

CREDIT: SHUTTERSTOCK (BACKGROUND); MICHAEL COFFIN (PRODUCT PHOTOS)

unidentified compounds in products labeled as delta-8-THC.

## Safety concerns skyrocket

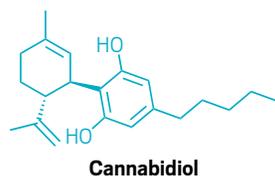
“My concern is that we have no idea what these products are,” says Christopher Hudalla, president and chief scientific officer of ProVerde Laboratories, an analytical testing firm with facilities in Massachusetts and Maine. “Consumers are being used as guinea pigs. To me, that’s horrific,” he says.

Using chromatographic methods with ultraviolet or mass spectrometry detection, scientists at ProVerde have tested thousands of products labeled delta-8-THC. “So far, I have not seen one that I would consider a legitimate delta-8-THC product,” Hudalla says. “There’s some delta-8 in there, but there’s very frequently up to 30 [chromatographic] peaks that I can’t identify.” There are often also peaks that correlate with delta-9-THC as well as another isomer, delta-10-THC, he notes. Little is known about the effects of delta-10-THC, but users have anecdotally reported feeling euphoric and more focused after consuming it.

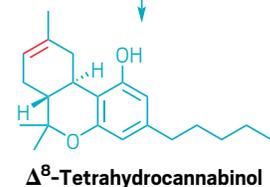
“I’m less concerned with traditional THC isomers than I am of the ubiquitous unknowns,” says Michael Coffin, chief scientist at Elevation Distro, a California-based cannabis manufacturing and distribution firm. “Delta-8, delta-9, and even delta-10 don’t seem to have any ill effects on people that we know of at this point,” he says. But a lot of people are doing a poor job of cleaning up their reaction products, he adds, which results in “quite a soup” of by-products and other unwanted compounds.

The conversion of CBD to delta-8-THC involves refluxing CBD in an organic solvent, such as toluene or heptane, with *p*-toluenesulfonic acid or another acid that serves as a catalyst. The reaction is typically run for 60–90 min. “You basically close the ring on the CBD molecule,” Coffin says.

“These are pretty aggressive synthetic



Acid catalyst,  
solvent, heat



**The conversion of cannabidiol into delta-8-tetrahydrocannabinol (delta-8-THC) also produces small amounts of delta-9-THC and delta-10-THC.**

conditions that use strong acids,” Hudalla says. “They might be using strong bases to neutralize. They can use metal catalysts. I hear different people doing it different ways.” In a pharmaceutical environment, PhD chemists ensure that products don’t include harmful unconsumed reactants, he says. But nobody is measuring the pH of delta-8 products or testing for strong acids and residual metals that are left behind, he says.

It is possible to separate delta-8-THC from unwanted reaction leftovers or by-products, but “most people are not actually taking the time to distill it or use chromatography” to do so, says Kyle Boyar, a staff research associate at the University of California San Diego’s Center for Medicinal Cannabis Research.

One by-product commonly found in delta-8-THC products is olivetol, a precursor of THC, Boyar says. “There’s a patent for olivetol oral compositions” that inhibit cannabis intoxication from delta-9-THC, he says. If olivetol also inhibits intoxication from delta-8, it may contribute to

the perceived milder effects of that isomer. The patent applies to an oral dose of olivetol. “I don’t think anybody really knows the safe inhalation dose of olivetol,” he adds.

“A lot of irresponsible production is

going on in the sense that most of these people are getting their information from online forums, and many of them aren’t necessarily trained chemists,” Boyar says.

Like many other scientists, Greg Gerdeman, acting CEO and president of Nashville Commodities Exchange (NASHCX), which is devoted to hemp and its derivative products, is concerned about the lack of oversight for delta-8-THC products. “It really needs to be cleaned up,” he says. “I just know there’s a great deal of experimentation” by producers. And despite claims of delta-8-THC being less potent than delta-9-THC, “it can make you really high,” Gerdeman says. “It’s just a matter of dose. Another issue is, How many of these products have way more delta-9 in them than they say?”

Gerdeman has met both very experienced cannabis users and naive cannabis users who thought delta-8 wouldn’t make them anxious. But it did when they took too much, he says. “The beauty of cannabis is you don’t get fatal overdoses, but it can make you feel absolutely horrible.”

Tiffany Coleman, director of quality and processing at Carbidex, a cannabis firm in Michigan, experiments with making small-scale batches of delta-8-THC from CBD as a hobby. The state doesn’t allow such activity in commercial cannabis facilities. “I am trying to make sure the science is good,” Coleman says. “I’m working with peers all over the country and looking at different purification methods.”

Product toxicity aside, Coleman worries that people are making delta-8-THC without proper reaction safety controls. The conversion of CBD to delta-8 is an exothermic reaction, so it creates a lot of heat,

**Signs for delta-8-THC products are increasingly showing up on street corners and in windows of retail stores.**



# “A lot of irresponsible production is going on.”

—**Kyle Boyar**, research associate, University of California San Diego, Center for Medicinal Cannabis Research

Coleman says. “This needs to be done in a controlled environment,” such as under dry ice and acetone, they add. Coleman uses glycol chillers to cool down the reaction. An ice bath isn’t cold enough, Coleman warns, saying they know of people who tried that approach and “blew stuff up.”

Coleman also has concerns about some of the solvents people are using. One popular method uses dichloromethane, also known as methylene chloride. Dichloromethane should not be used “without appropriate ventilation and controls because it’s a silent killer,” Coleman says. “A lot of these shops, even the shops in the legal markets, are not ready for this kind of activity.”

## The case for regulation

Regulators aren’t ready for it either. Many states are scrambling to control sales of delta-8-THC, which is now the fastest-growing product in the hemp industry. More than a dozen states have banned delta-8-THC, and others are developing rules. And it’s not just an issue in the US.

Although the surge of delta-8 products started because of an oversupply of CBD in the US, delta-8-THC is also becoming popular in Europe, Coffin says. The US allows export of CBD isolate, and people in other countries can do whatever they want with it, he says. All the materials needed to make delta-8-THC are easy to get, he adds.

“This problem will not go away,” says Jeffrey Raber, cofounder and CEO of the Werc Shop, a California-based cannabis contract manufacturing and testing firm. “It might actually morph and change into bigger problems” if regulators don’t get a handle on it, he says.

Raber saw delta-8-THC’s market potential in 2018, when Congress legalized hemp in the US. “It’s a very interesting molecule, one that has very different physiological activity depending upon the entourage” and how it is administered, he says.

The Werc Shop published a white paper in 2018 that pointed out the limited availability of high-purity delta-8-THC due to uncontrolled processing steps. Raber is urging regulators to address those purity concerns and deal with delta-8-THC “in a sensible fashion” that enables its use in safe, protected ways. To accomplish that, he says, “make sure it’s tested.”

But existing independent analytical labs can’t handle the burden of exhaustive

testing on all delta-8-THC products, according to Amber Wise, scientific director at Medicine Creek Analytics, a cannabis testing firm in Washington State. There are a handful of methods being discussed on online forums that use chemicals “that I would not want to have as residuals” in delta-8-THC products, such as dichloro-

methane and trichloroacetic acid, Wise says. Her lab hasn’t developed methods to test for those chemicals, she says, adding that it’s not practical to develop methods for every possible reagent people are using to make delta-8-THC. Instead, Wise says, regulators should require manufacturers to reveal what chemicals they use to make



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delta-8-THC and what compounds are in their final products.

It's possible that one day there will be cannabis plants that contain sufficient delta-8-THC to extract in pure form. But for now, cannabis plants typically contain 0.1% delta-8-THC or less. "We have seen reports of plants containing as much as 1%," but those are exceptions, Raber says. Economical extraction of delta-8-THC from cannabis requires levels of about 15–20%. "Genetics folks are going after that now," he says, but synthetic products will dominate for a while.

Raber also worries that if regulators simply ban delta-8-THC as they did with delta-9-THC, "folks will make delta-10-THC or other types of ring isomers or alkyl chain analogs" such as tetrahydrocannabinavarin. Some of these analogs could be toxic or "wildly psychoactive," Raber says. The regulatory language needs to be broad, or "you'll be stuck in this multiyear cycle of legislative fix." This is in contrast to the 2018 farm bill, which limited the amount of delta-9-THC in hemp and hemp-derived products, such as CBD.

Gerdeman is particularly concerned about another cannabinoid called THC-O-acetate, the acetate ester of THC, which he's seeing popping up in gummies

**"Like making methamphetamine from cold medicine, just because the starting materials are legal does not make the resulting product legal (or safe)."**

—**Christopher Hudalla**, president and chief scientific officer, ProVerde Laboratories

and vapes. It is basically acetylated THC, which does not occur naturally in cannabis plants, he says. Heroin was created by acetylating morphine over 100 years ago, resulting in a drug that is much more potent than morphine because of pharmacokinetics, Gerdeman points out. "Do we have human studies on the effects of acetylated THC? No, not at all," he says. And, as is the case with delta-8-THC, there's no information on what else is in those products.

Without better regulation, consumers will continue to be duped by unscrupulous producers, according to Hudalla. For delta-8-THC, he says, "we need to get the truth out to the public" that it is a synthetic compound made from an ingredient extracted from hemp. "Like making methamphetamine from cold medicine, just because the starting materials are legal

does not make the resulting product legal (or safe)," Hudalla warns. He, like many chemists, believes delta-8-THC is a synthetic cannabinoid that is not legal.

"Many participants in the hemp industry see delta-8-THC as the salvation, providing a financial bridge until the [US Food and Drug Administration] approves CBD as a dietary ingredient," Hudalla says. "But I do not believe that it should be at the expense of unsuspecting consumers, who are being misled about what products they are being sold, to bail out the producers and investors who gambled on the CBD market," he says.

"I believe that delta-8 has a legitimate place in therapeutics and potentially adult use," Hudalla adds. "But I just don't see anybody doing it appropriately. It's all bathtub gin." ■



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