


Delta-8 tetrahydrocannabinol: a scoping review and commentary

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Abstract

Background and Aims: Delta-8 tetrahydrocannabinol (THC) is a psychoactive substance from the *Cannabis* plant that has been rising in popularity in the United States since the 2018 US Farm Bill implicitly legalized it. This study reviewed research from peer-reviewed and non-peer-reviewed (e.g. anecdotal and news) reports related to delta-8 THC to summarize current knowledge and implications for public health and safety.

Methods: A scoping review was conducted using PubMed, Scopus, Google Scholar and Google as search engines, leading to the identification of 103 documents that were summarized. The themes that emerged were (1) legality, (2) use (popularity, motives, psychoactivity/potency, benefits/consequences), (3) synthesis (byproducts, laboratory testing) and (4) retail (availability, price, packaging, youth-oriented marketing). A second author independently coded 20% of the documents, which verified the categorization of articles by these emergent themes.

Results: Most research used animal/cell models or focused upon ways to identify the chemical structure of delta-8 THC in various products. Findings suggest that people often use delta-8 THC as a substitute for other substances. Anecdotally, delta-8 THC is a less potent psychoactive than delta-9 THC; however, several negative consequences have been reported. There is no federal age restriction for purchase/possession of delta-8 THC products. Delta-8 THC is readily accessible on-line, is typically less expensive than delta-9 THC and is often marketed in ways that would seemingly appeal to children. There are no regulations on synthesis, resulting in products being contaminated and/or yielding inconsistent effects. There have been thousands of calls to US poison control centers due to accidental delta-8 THC exposure among minors.

Conclusions: Most research on delta-8 THC is largely anecdotal, not peer-reviewed and does not involve human subjects. Future research should examine delta-8 THC use using nationally representative samples to more clearly understand the prevalence and consequences of use. Laws are needed to mitigate the risks of using delta-8 THC, particularly quality control of synthesis and minimum purchase age.

KEYWORDS

2018 US Farm Bill, Delta-8 THC, Federal Agriculture Improvement Act, harm reduction, hemp-derived cannabinoids, novel psychoactive substance

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INTRODUCTION

The sale and use of delta-8 tetrahydrocannabinol (THC) has increased in the United States since the passing of the Farm Bill in 2018 [1–3]. Delta-8 THC is a psychoactive substance from *Cannabis* plants [4]. However, the levels of delta-8 THC that exist in the plant naturally are very low [1, 5–7]. Most delta-8 THC in the market-place is produced from cannabidiol (CBD), the latter of which is typically derived from hemp. Although prima facie delta-8 THC is legal at the federal level because of the Farm Bill, the Drug Enforcement Agency (DEA) has placed delta-8 THC on the list of controlled substances, further adding to the confusion regarding its legal status federally [8, 9]. Moreover, due to litigation, existing cannabis laws and creation of new laws there is much confusion regarding its legality in various states [10].

Given the rising popularity of delta-8 THC and the prevalence of negative consequences associated with its use (e.g. calls to poison control, emergency department visits, driving while under the influence) [11, 12], it is important to more clearly understand what is known about delta-8 THC and to identify important gaps in the literature where future research is needed. The existing body of literature on delta-8 THC is largely anecdotal, with scientific and peer-reviewed sources lacking. Therefore, it is important to supplement peer-reviewed literature with additional sources, including news articles, laws and governmental guidance documents. This study provides, in a single source, a current and succinct summary of what is known about delta-8 THC and the implications for public health and safety.

METHODS

Data sources and searches

This scoping review followed the Arksey & O'Malley framework [13] and the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines for scoping reviews [14]. Table 1 provides specific information about the literature search, including search terms and the number of articles identified. PubMed and Scopus were used to identify peer-reviewed research articles related to delta-8 THC. Google Scholar was used to supplement findings and include 'gray literature' (e.g. unpublished or non-peer-reviewed works). To provide more information from non-peer-reviewed resources, Google searches were used to identify related news articles, anecdotal reports and governmental fact sheets. Searches to identify all articles were performed on 26 August 2022. While the screening of articles took place over several days, all articles were collected on a single day. This analysis plan was not pre-registered; thus, results should be considered exploratory.

Study selection

The identification and review of documents as well as classification by topics were performed by the lead author (C.R.L.). The inclusion

TABLE 1 Search terms.

Database (articles identified)	Search terms
PubMed (<i>n</i> = 335)	('marijuana'[Title/Abstract] OR 'cannab*'[Title/Abstract] OR 'thc'[Title/Abstract]) AND ('delta-8'[Title/Abstract] OR 'delta 8'[Title/Abstract] OR 'Δ-8'[Title/Abstract] OR 'Δ 8'[Title/Abstract])
Scopus (<i>n</i> = 485)	('marijuana' OR 'cannab*' OR 'thc') AND ('delta-8' OR 'delta 8' OR 'Δ-8' OR 'Δ 8')
Google Scholar (<i>n</i> = 26)	marijuana delta-8; marijuana delta 8; marijuana Δ-8; marijuana Δ 8; cannabis delta-8; cannabis delta 8; cannabis Δ-8; cannabis Δ 8; delta-8 thc; delta 8 thc; Δ-8 thc; Δ 8 thc
Google searches (<i>n</i> = 42)	marijuana delta-8; marijuana delta 8; marijuana Δ-8; marijuana Δ 8; cannabis delta-8; cannabis delta 8; cannabis Δ-8; cannabis Δ 8; delta-8 thc; delta 8 thc; Δ-8 thc; Δ 8 thc

criterion was that one of the main themes of the document had to be delta-8 THC (i.e. the article's predictor or outcome variables and other information presented were focused upon delta-8 THC). Manuscripts from all disciplines were included. In total, 888 documents were identified; 79 duplicates were removed. Reference lists for these manuscripts were also examined for potential inclusion. Subsequently, 710 documents were removed through title and abstract screening, as they did not relate to delta-8 THC (e.g. most related to delta-9 THC only). Four unpublished manuscripts by co-authors of the current study were included to supplement findings. In total, 103 documents were included in this review. Figure 1 depicts a flow-chart for visualization of study selection using the PRISMA framework.

Extraction and topics

Information extracted included, as appropriate, the design, sample size, findings, limitations, conclusions and a summary. Themes were developed using an inductive and grounded theory approach. After reviewing all articles, four overarching topics were identified and used to organize the presentation of findings: legality (federal and state), use (popularity, motives, psychoactivity/potency and benefits/consequences), synthesis (byproducts and laboratory testing) and retail (availability, price, packaging and youth-oriented marketing). Each document could contain information falling under multiple themes. Two authors coded information from a random sample of 20 articles (19%) to determine the presence of themes in each document, the study design and the sample size (where applicable). There was 88% agreement on themes ($\kappa = 0.75$), indicating a high level of agreement for the inclusion of information into the same thematic category. In a second round, codes were compared and consensus was reached before assigning a theme. There was 100% agreement on the study design and the sample size, given that this was low-inference coding. Table 2 provides a full list of the articles included as well as

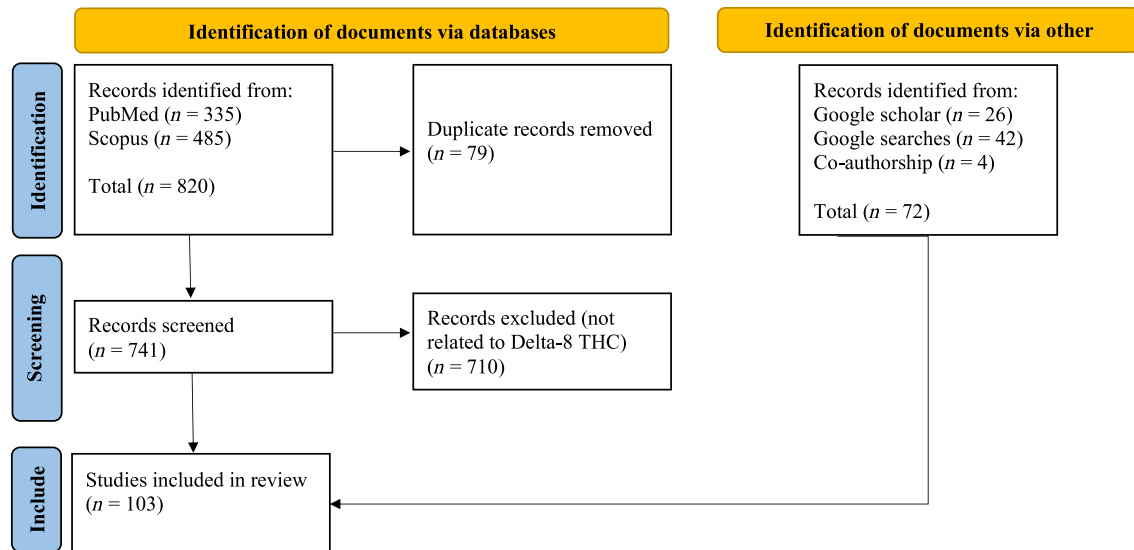


FIGURE 1 Flow-chart of document inclusion. All articles identified through Google Scholar and all co-authored articles were peer-reviewed; all Google searches were not.

information about the study designs and sample size. This review summarizes information on delta-8 THC, contextualizes study findings, identifies important gaps in the research literature and provides recommendations pertaining to legal interventions that can help to prevent and reduce related harms.

RESULTS

Legal overview

Federal laws

There is some ambiguity regarding the legal status of delta-8 THC due to the numerous seemingly contradictory laws [11,15,16]. There are currently no federal laws that explicitly address delta-8 THC legality, nor a governing body to regulate it [2, 10, 17, 18]. Delta-8 THC began rising in popularity after the Agriculture Improvement Act (aka the Farm Bill) was passed by US legislators in 2018 [18]. To allow for commercial production of hemp products, this Act provided legal definitions of the substances found in and/or synthesized from the *Cannabis* plant: cannabis (> 0.3% delta-9 THC by dry weight) and hemp (< 0.3% delta-9 THC by dry weight) [19]. Because the 2018 Farm Bill does not explicitly mention delta-8 THC, it is widely assumed by retailers, consumers and legal experts to be legal due to this 'loophole' defining it as hemp rather than cannabis, despite it being a cannabinoid [2, 20].

In contrast, the Federal Analogue Act (aka the Controlled Substance Act) bans any substance that has a chemical structure or effects similar to a controlled substance [15]. However, this Act does not specify what constitutes a similar chemical structure nor similar

effect [15]. Because delta-8 THC is widely considered to have fewer potent psychoactive properties than delta-9 THC [2, 21–23], some legal experts believe that delta-8 THC is therefore not addressed under this Act [24]. It appears to be the general consensus by cannabis legal experts that, federally, delta-8 THC products are legal as long as they contain less than 0.3% delta-9 THC by dry weight [20, 24].

The DEA specified in August 2020 that all synthetically derived THC's should be considered schedule 1 substances [8]. However, there was no formal definition of what should be considered 'synthetic', leaving some ambiguity [8, 20, 25]. Importantly, the DEA has placed delta-8 THC on the list of controlled substances [8, 9]. Nevertheless, it is unclear whether this ruling is legally binding and if the DEA will take any related actions [3, 8, 10, 25].

State laws

In addition to these federal laws, each state can create laws that explicitly address delta-8 THC. It is important to note that state laws surrounding delta-8 THC are constantly changing, and legal status differs between states [26, 27]. Some states have banned delta-8 THC [28, 29], some have decisions tied up in jurisdictional politics and litigation [30–32] and others have regulated the sale of delta-8 THC in the same way as delta-9 THC [18]. However, in most states, there are no governing bodies in place to assess compliance with and enforce laws related to the sale of delta-8 THC. These changing and often contradictory laws at the federal, state and local level have led to misinformation and misunderstanding among retailers and consumers [16, 26, 27, 33–35]. One qualitative study among delta-8 THC retailers found that some retailers conduct daily research on the legality of delta-8 THC and create contingency plans if it is ever made illegal.

TABLE 2 Articles included.

Title	Study design	n
Peer-reviewed		
Human studies		
Abrahamov, A., Abrahamov, A., & Mechoulam, R. (1995). An efficient new cannabinoid antiemetic in pediatric oncology. <i>Life Sciences</i> , 56(23–24), 2097–2102	Experimental (human)	8 children aged 3–13 with hematological cancer
Akpunonu, P., Baum, R. A., Reckers, A., Davidson, B., Ellison, R., Riley, M., ... & Geron, R. (2021). Sedation and acute encephalopathy in a pediatric patient following ingestion of delta-8-tetrahydrocannabinol gummies. <i>The American Journal of Case Reports</i> , 22, e933488-1	Case study (human)	1
Badawy, Z. S., Chohan, K. R., Whyte, D. A., Penefsky, H. S., Brown, O. M., & Souid, A. K. (2009). Cannabinoids inhibit the respiration of human sperm. <i>Fertility and Sterility</i> , 91(6), 2471–2476	Fertility evaluation (human)	41 men
Bergeria, C. L., Strickland, J. C., Spindle, T. R., Kalaba, M., Satyavolu, P. U., Feldner, M., ... & Weerts, E. (2022). A crowdsourcing survey study on the subjective effects of delta-8-tetrahydrocannabinol relative to delta-9-tetrahydrocannabinol and cannabidiol. <i>Experimental and Clinical Psychopharmacology</i>	On-line survey (human)	252 past-year delta-8 THC users
Bozman, M. E., Manoharan, S. V. R. R., & Vasavada, T. (2022). Marijuana variant of concern: delta 8-tetrahydrocannabinol (delta-8-THC, Δ8-THC). <i>Psychiatry Research Case Reports</i> , 1(2), 100028	Case study (human)	2
Gong Jr, H., Tashkin, D. P., Simmons, M. S., Calvarese, B., & Shapiro, B. J. (1984). Acute and subacute bronchial effects of oral cannabinoids. <i>Clinical Pharmacology & Therapeutics</i> , 35(1), 26–32	Experimental (human)	59 men who were chronic marijuana users
Hollister, L. E., & Gillespie, H. K. (1973). Delta-8-and delta-9-tetrahydrocannabinol; comparison in man by oral and intravenous administration. <i>Clinical Pharmacology & Therapeutics</i> , 14(3), 353–357	Experimental (human)	6 men oral, 4 men i.v.
Jo, N. Y., Chu, C. C., & Ramsey, B. C. (2021). Brugada electrocardiogram pattern induced by recreational delta-8-tetrahydrocannabinol (THC): A case report. <i>Cureus</i> , 13(10)	Case study (human)	1
Kruger, D. J., & Kruger, J. S. (2021). Consumer experiences with delta-8-THC: medical use, pharmaceutical substitution, and comparisons with delta-9-THC. <i>Cannabis and Cannabinoid Research</i>	On-line survey (human)	521; 90% in states where non-medical use of delta-9 THC was not legal
Kruger, J. S., & Kruger, D. J. (2022). Delta-8-THC: delta-9-THC's nicer younger sibling? <i>Journal of Cannabis Research</i> , 4(1), 1–8	On-line survey (human)	521; 90% in states where non-medical use of delta-9 THC was not legal
Livne, O., Budney, A., Borodovsky, J., Walsh, C., Shmulewitz, D., Fink, D. S., ... & Hasin, D. S. (2022). Delta-8 THC use in US adults: sociodemographic characteristics and correlates. <i>Addictive Behaviors</i> , 107374	On-line survey (human)	4348 cannabis users
Rosenthal, J., Howell, M., Earl, V., & Malik, M. (2021). Cannabinoid hyperemesis syndrome secondary to Delta-8 THC use. <i>The American Journal of Medicine</i> , 134(12), e582–e583	Case study (human)	1
Wurz, G. T., Montoya, E., & DeGregorio, M. W. (2022). Examining impairment and kinetic patterns associated with recent use of hemp-derived Δ8-tetrahydrocannabinol: Case studies. <i>Journal of Cannabis Research</i> , 4(1), 1–12	Experimental (human)	3 males
On-line trends		
Leas, E. C., Nobles, A. L., Shi, Y., & Hendrickson, E. (2022). Public interest in Δ 8-Tetrahydrocannabinol (delta-8-THC) increased in US states that restricted Δ 9-Tetrahydrocannabinol (delta-9-THC) use. <i>International Journal of Drug Policy</i> , 101, 103 557	Google trends	-

(Continues)

TABLE 2 (Continued)

Title	Study design	n
Livingston, M. D., Walker, A., Cannell, M. B., & Rossheim, M. E. (2022). Popularity of delta-8 THC on the internet across US states, 2021. <i>American Journal of Public Health</i> , 112(2), 296–299	Google trends	–
Szczyпка, G., Pepper, J. K., & Kim, A. (2022). Weed Light: An exploratory study of delta-8 THC conversations on Reddit. RTI Press	Reddit posts	47 556 Reddit posts
Animal or cell (in vitro/in vivo) studies		
Adams, M. D., Earnhardt, J. T., Dewey, W. L., & Harris, L. S. (1976). Vasoconstrictor actions of $\Delta 8$ and $\Delta 9$ tetrahydrocannabinol in the rat. <i>Journal of Pharmacology and Experimental Therapeutics</i> , 196(3), 649–656	Experimental (rats)	48
Avraham, Y., Ben-Shushan, D., Breuer, A., Zolotarev, O., Okon, A., Fink, N., ... & Berry, E. M. (2004). Very low doses of $\Delta 8$ -THC increase food consumption and alter neurotransmitter levels following weight loss. <i>Pharmacology Biochemistry and Behavior</i> , 77(4), 675–684	Experimental (mice)	102
Bátkai, S., Mukhopadhyay, P., Horváth, B., Rajesh, M., Gao, R. Y., Mahadevan, A., ... & Pacher, P. (2012). $\Delta 8$ -Tetrahydrocannabinol prevents hepatic ischaemia/reperfusion injury by decreasing oxidative stress and inflammatory responses through cannabinoid CB2 receptors. <i>British Journal of Pharmacology</i> , 165(8), 2450–2461	Experimental (in vitro and in vivo cells)	–
Colasanti, B. K., Lindamood III, C., & Craig, C. R. (1982). Effects of marijuana cannabinoids on seizure activity in cobalt-epileptic rats. <i>Pharmacology Biochemistry and Behavior</i> , 16(4), 573–578	Experimental (rats)	25
Doty, P., Dykstra, L. A., & Picker, M. J. (1994). Discriminative stimulus effects of phencyclidine: pharmacologically specific interactions with $\Delta 9$ - and $\Delta 8$ -tetrahydrocannabinol. <i>Drug and Alcohol Dependence</i> , 35(2), 151–158	Experimental (rats)	8
Dwivedi, C., & Harbison, R. D. (1975). Anticonvulsant activities of $\Delta 8$ - and $\Delta 9$ -tetrahydrocannabinol and uridine. <i>Toxicology and Applied Pharmacology</i> , 31(3), 452–458	Experimental (mice)	–
El-Alfy, A. T., Ivey, K., Robinson, K., Ahmed, S., Radwan, M., Slade, D., ... & Ross, S. (2010). Antidepressant-like effect of $\Delta 9$ -tetrahydrocannabinol and other cannabinoids isolated from <i>Cannabis sativa</i> L. <i>Pharmacology Biochemistry and Behavior</i> , 95(4), 434–442	Experimental (mice)	7–10 mice/group
Elsohly, M. A., Harland, E. C., Benigni, D. A., & Waller, C. W. (1984). Cannabinoids in glaucoma II: the effect of different cannabinoids on intraocular pressure of the rabbit. <i>Current Eye Research</i> , 3(6), 841–850	Experimental (rabbit)	–
Gupta, D., & Elbracht, C. (1983). Effect of tetrahydrocannabinols on pubertal body weight spurt and sex hormones in developing male rats. <i>Research in Experimental Medicine</i> , 182(2), 95–104	Experimental (rats)	20
Muchtar, S. F. S. M. T. S., Almog, S., Torracca, M. T., Saettone, M. F., & Benita, S. (1992). A submicron emulsion as ocular vehicle for delta-8-tetrahydrocannabinol: effect on intraocular pressure in rabbits. <i>Ophthalmic Research</i> , 24(3), 142–149	Experimental (rabbit)	–
Semlali, A., Beji, S., Ajala, I., & Rouabhia, M. (2021). Effects of tetrahydrocannabinols on human oral cancer cell proliferation, apoptosis, autophagy, oxidative stress, and DNA damage. <i>Archives of Oral Biology</i> , 129, 105200	Experimental (oral cancer cells)	–
Watanabe, K., Kijima, T., Narimatsu, S., Nishikami, J., Yamamoto, I., & Yoshimura, H. (1990). Comparison of pharmacological effects of tetrahydrocannabinols and their 11-hydroxy-metabolites in mice. <i>Chemical and Pharmaceutical Bulletin</i> , 38(8), 2317–2319	Experimental (mice)	–

(Continues)

TABLE 2 (Continued)

Title	Study design	n
Whyte, D. A., Al-Hammadi, S., Balhaj, G., Brown, O. M., Penefsky, H. S., & Souid, A. K. (2010). Cannabinoids inhibit cellular respiration of human oral cancer cells. <i>Pharmacology</i> , 85(6), 328–335	Experimental (human oral cancer cells)	–
Xi, Z. X., Muldoon, P., Wang, X. F., Bi, G. H., Damaj, M. I., Lichtman, A. H., ... & Gardner, E. L. (2019). Δ 8-Tetrahydrocannabinol has potent anti-nicotine effects in several rodent models of nicotine dependence. <i>British Journal of Pharmacology</i> , 176(24), 4773–4784	Experimental (rats and mice)	(~30, 6–12/group)
Reviews/summaries		
Babalonis, S., Raup-Konsavage, W. M., Akpunonu, P. D., Balla, A., & Vrana, K. E. (2021). Δ 8-THC: legal status, widespread availability, and safety concerns. <i>Cannabis and Cannabinoid Research</i> , 6(5), 362–365	Review	–
Bernhard, W., Heeb, T., & Tytgat, J. (2022). Delta-8-tetrahydrocannabinol, an emerging NPS and other structurally related cannabinoids. <i>Toxicologie Analytique et Clinique</i> , 34(3), S174	Review	–
Dotson, S., Johnson-Arbor, K., Schuster, R. M., Tervo-Clemmens, B., & Evins, A. E. (2022). Unknown risks of psychosis and addiction with delta-8-THC: a call for research, regulation, and clinical caution. <i>Addiction</i>	Review	–
Gussow, L. (2021). Toxicology rounds: your ED patients are likely using delta-8-THC. <i>Emergency Medicine News</i> , 43(8), 18	Review	–
Johnson-Arbor, K., & Smolinske, S. (2022). The current state of delta-8 THC. <i>The American Journal of Emergency Medicine</i> , 56, 259–261.	Review	–
Knopf, A. (2021). CDC and FDA warn of delta-8 THC harms. <i>Alcoholism & Drug Abuse Weekly</i> , 33(36), 7–7	Review	–
Leas, E. C. (2021). The hemp loophole: a need to clarify the legality of delta-8-THC and other hemp-derived tetrahydrocannabinol compounds. <i>American Journal of Public Health</i> , 111(11), 1927–1931	Review	–
Love, C. A., Schichlein, K. D., Clapp, P. W., & Jaspers, I. (2022). Cannabinoid vaping products present novel challenges for assessment of respiratory health effects. <i>Toxicological Sciences</i> , 188(1), 1–3	Review	–
Meehan-Atrash, J., & Rahman, I. (2021). Cannabis vaping: existing and emerging modalities, chemistry, and pulmonary toxicology. <i>Chemical Research in Toxicology</i> , 34(10), 2169–2179	Review	–
Tagen, M., & Klumpers, L. E. (2022). Review of delta-8-tetrahydrocannabinol (Δ 8-THC): comparative pharmacology with Δ 9-THC. <i>British Journal of Pharmacology</i> , 179(15), 3915–3933	Review	–
White, R. M. & Cone, E. J. (2022). Δ 8-Tetrahydrocannabinol: another cannabinoid of rising interest and concern. <i>Forensic Science Review</i> , 34(1), 2–4	Review	–
Wilson, N. (2021). New market entrants and uncertain drug policy in the United States. <i>Ohio State Legal Studies Research Paper</i> (611)	Review	–
Chromatography/mass spectrometry studies		
Chan-Hosokawa, A., Nguyen, L., Lattanzio, N., & Adams, W. R. (2022). Emergence of delta-8 tetrahydrocannabinol in DUI investigation casework: method development, validation and application. <i>Journal of Analytical Toxicology</i> , 46(1), 1–9	Chromatography and mass spectrometry	–
Ciolino, L. A., Ranieri, T. L., Brueggemeyer, J. L., Taylor, A. M., & Mohrhaus, A. S. (2021). EVALI vaping liquids part 1: GC-MS	Chromatography and mass spectrometry	300 cannabis-based vaping liquids

(Continues)

TABLE 2 (Continued)

Title	Study design	n
cannabinoids profiles and identification of unnatural THC isomers. <i>Frontiers in Chemistry</i> , 9		
Czégény, Z., Nagy, G., Babinszki, B., Bajtel, Á., Sebestyén, Z., Kiss, T., ... & Csupor, D. (2021). CBD, a precursor of THC in e-cigarettes. <i>Scientific Reports</i> , 11(1), 1–6	Chromatography and mass spectrometry	–
Duffy, B., Li, L., Lu, S., Durocher, L., Dittmar, M., Delaney-Baldwin, E., ... & Spink, D. (2020). Analysis of cannabinoid-containing fluids in illicit vaping cartridges recovered from pulmonary injury patients: identification of vitamin E acetate as a major diluent. <i>Toxics</i> , 8(1), 8	Chromatography and mass spectrometry	38 e-liquid cartridges
Duffy, B. C., Li, L., Lu, S., Dittmar, M. A., Delaney-Baldwin, E., Durocher, L. A., & Spink, D. C. (2022). Chemotyping of Δ 8-THC-containing e-liquids analyzed during the 2019–2020 New York state EVALI investigation. <i>Journal of Analytical Toxicology</i> , 46(7), 743–749	Chromatography and mass spectrometry	175 e-liquid cartridges
Evans, T., Seither, J., Knittel, J., Karschner, E., & Walterscheid, J. (2022). The rise of the ‘cannabisomers’. <i>Paper presented at the American Academy of Forensic Sciences</i>	Chromatography and mass spectrometry	–
Fernando, M., & Strongin, R. (2021). Examining Δ 8-THC vaping degradant toxicant formation	Chromatography and mass spectrometry	–
Guo, W., Vrdoljak, G., Liao, V. C., & Moezzi, B. (2021). Major constituents of cannabis vape oil liquid, vapor and aerosol in California vape oil cartridge samples. <i>Frontiers in Chemistry</i> , 9	Chromatography and mass spectrometry	12 cannabis vape oil cartridges
Helander, A., Johansson, M., Andersson, A., & Villén, T. (2022). Analytical and medico-legal problems linked to the presence of delta-8-tetrahydrocannabinol (delta-8-THC): results from urine drug testing in Sweden. <i>Drug Testing and Analysis</i> , 14(2), 371–376	Chromatography and mass spectrometry	–
Krämer, M., Schäper, M., Dücker, K., Philipsen, A., Losacker, M., Dreimüller, N., ... & Hess, C. (2021). Detectability of cannabinoids in the serum samples of cannabis users: Indicators of recent cannabis use? A follow-up study. <i>Drug Testing and Analysis</i> , 13(9), 1614–1626	Chromatography and mass spectrometry	117 serum samples
Leite, J. D. A., de Oliveira, M. V., Conti, R., Borges, W. D. S., Rosa, T. R., Filgueiras, P. R., ... & Neto, Á. C. (2018). Extraction and isolation of cannabinoids from marijuana seizures and characterization by ^1H NMR allied to chemometric tools. <i>Science & Justice</i> , 58(5), 355–365	Proton nuclear magnetic resonance	156 marijuana samples
Lin, L., Amaratunga, P., Reed, J., Huang, P., Lemberg, B. L., & Lemberg, D. (2022). Quantitation of Δ 8-THC, Δ 9-THC, cannabidiol and 10 other cannabinoids and metabolites in oral fluid by HPLC–MS–MS. <i>Journal of Analytical Toxicology</i> , 46(1), 76–88	Chromatography and mass spectrometry	200 human oral fluid samples
Lu, S. J., Li, L., Duffy, B. C., Dittmar, M. A., Durocher, L. A., Panawennage, D., ... & Spink, D. C. (2021). Investigation of vaping fluids recovered from New York State e-cigarette or vaping product use-associated lung injury patients. <i>Frontiers in Chemistry</i> , 9	Chromatography and mass spectrometry	284 e-cigarettes
Meehan-Atrash, J., & Rahman, I. (2021). Novel Δ 8-Tetrahydrocannabinol vaporizers contain unlabeled adulterants, unintended byproducts of chemical synthesis, and heavy metals. <i>Chemical Research in Toxicology</i> , 35(1), 73–76	Proton nuclear magnetic resonance	27 delta-8 THC products
Miettinen, K., Leelahakorn, N., Almeida, A., Zhao, Y., Hansen, L. R., Nikolajsen, I. E., ... & Kampranis, S. C. (2022). A GPCR-based yeast biosensor for biomedical, biotechnological, and point-of-use cannabinoid determination. <i>Nature Communications</i> , 13(1), 1–16	G-protein-coupled receptor-based yeast whole-cell biosensor	–

(Continues)

TABLE 2 (Continued)

Title	Study design	n
Munger, K. R., Jensen, R. P., & Strongin, R. M. (2022). Vaping cannabinoid acetates leads to ketene formation. <i>Chemical Research in Toxicology</i> , 35(7), 1202–1205	Nuclear magnetic resonance	–
Qamar, S., Torres, Y. J., Parekh, H. S., & Falconer, J. R. (2022). Fractional factorial design study for the extraction of cannabinoids from CBD-dominant cannabis flowers by supercritical carbon dioxide. <i>Processes</i> , 10(1), 93	Supercritical fluid extraction	–
Reber, J. D., Karschner, E. L., Seither, J. Z., Knittel, J. L., Dozier, K. V., & Walterscheid, J. P. (2022). An enhanced LC–MS–MS technique for distinguishing $\Delta 8$ - and $\Delta 9$ -tetrahydrocannabinol isomers in blood and urine specimens. <i>Journal of Analytical Toxicology</i> , 46(4), 343–349	Liquid chromatography–electrospray ionization tandem mass spectrometry	–
Rzeppa, S., Große, J., Rautenberg, C., Thieme, D., Lepp, T., Vallimäe, H., & Keiler, A. M. (2021). Emergence of the less common cannabinoid $\Delta 8$ -tetrahydrocannabinol in a doping sample. <i>Drug Testing and Analysis</i> , 13(11–12), 1936–1943	Chromatography and mass spectrometry	–
Song, L., Carlson, S., Valenzuela, G., Chao, M., & Pathipaka, S. B. (2022). Development of a validated method for rapid quantification of up to sixteen cannabinoids using ultra-high-performance liquid chromatography diode-array detector with optional electrospray ionization time-of-flight mass spectrometry detection. <i>Journal of Chromatography A</i> , 1670, 462–467	Liquid chromatography diode-array detector	–
Tsujikawa, K., Okada, Y., Segawa, H., Yamamuro, T., Kuwayama, K., Kanamori, T., & Iwata, Y. T. (2022). Thin-layer chromatography on silver nitrate-impregnated silica gel for analysis of homemade tetrahydrocannabinol mixtures. <i>Forensic Toxicology</i> , 40(1), 125–131	Silica gel thin layer chromatography	–
Zumaeta, E., Morales-Colon, K., Alford, I., & Tiscione, N. (2022). Exo-THC: the impact of isobars on cannabinoid testing for seized drug and toxicology cases. <i>Paper presented at the American Academy of Forensic Sciences</i>	Chromatography and mass spectrometry	–
Other		
Reece, A. S., & Hulse, G. K. (2022). Epidemiology of $\Delta 8$ THC-related carcinogenesis in USA: a panel regression and causal inferential study. <i>International Journal of Environmental Research and Public Health</i> , 19(13), 7726	Secondary data analyses	14 598 age-adjusted cancer incidence rates
Unpublished works (under review or in progress)		
Henry, D., Christensen, E., Piesecki, A., Gilliam, L., Pool, C., Gutierrez, M., Riell, M., Holmes, L., Riggs, J., Lorber, R., Prater, Z., & Rutledge, P. (2022). Unpublished technical report: delta-8 and the 'new' cannabinoids in Denton: insights from discussions with consumers and industry. <i>Presented to Denton County Public Health Department</i>	Qualitative reports among delta-8 THC industry and consumers	–
LoParco, C. R., Olsson, S. E., Greene, K. M., Livingston, M. D., Henry, D., Trangenstein, P. J., Walker, A., & Rossheim, M. E. How are retailers describing delta-8 THC? A mixed-methods study in Fort Worth, Texas. <i>Under Review</i>	Mixed methods (humans)	133 delta-8 THC retailers
Rossheim, M. E., LoParco, C. R., Walker, A., Livingston, M. D., Trangenstein, P., Olsson, S., McDonald, K., Yockey, R. A., Lunningham, J., Kong, A., Henry, D., Walters, S., & Thombs, D. (in press). Delta-8 THC retail availability, price, and minimum purchase age. <i>Cannabis and Cannabinoid Research</i>	Telephone survey	1223 potential delta-8 THC retailers
Walker, D., LoParco, C. R., Rossheim, M. E., & Livingston, M. D. Trends in Delta-8 THC discussions on Twitter: 2020–2021. <i>Under Review</i>	Twitter trends	41 828 tweets

(Continues)

TABLE 2 (Continued)

Title	Study design	n
Articles from Google (not peer-reviewed)		
3Chi. (n.d.). About Us. https://www.3chi.com/about-3chi/	Informational page from a delta-8 THC retailer	-
Centers for Disease Control and Prevention (CDC). (2021). CDC health advisory: Increases in availability of cannabis products containing Delta-8 THC and reported cases of adverse events. https://emergency.cdc.gov/han/2021/pdf/CDC_HAN__451.pdf	CDC health advisory	-
Clayton, J. (2021). Texans enjoy the high from Delta-8 as legislators debate its legality and health experts debate its safety. https://www.tpr.org/news/2021-09-22/texans-enjoy-the-high-from-delta-8-as-legislators-debate-its-legality-and-health-experts-debate-its-safety	Texas news source	-
Colorado Department of Public Health & Environment. (2021). Re: Production and/or use of chemically modified or converted industrial hemp cannabinoids. https://hempindustrydaily.com/wp-content/uploads/2021/05/CDPHE.pdf	Colorado government bulletin	-
Cornwell, A. M. (2021). Why is delta-8 THC illegal in Colorado? Colorado state lawmakers recently banned delta-8 amid growing concerns over its safety. https://cbdoracle.com/news/policy/delta-8-thc-illegal-colorado/	CBD news source	-
Drug Enforcement Administration (DEA). (2021). Final interim rule: 21 CFR parts 1308 and 1312. https://www.deadiversion.usdoj.gov/fed_regs/rules/2020/fr0821.htm	DEA ruling	-
Drug Enforcement Administration (DEA). (2022). List of controlled substances. https://www.deadiversion.usdoj.gov/schedules/orangebook/c_cs_alpha.pdf	DEA ruling	-
Erickson, B. (2021). Delta-8-THC craze concerns chemists. https://cen.acs.org/biological-chemistry/natural-products/Delta-8-THC-craze-concerns/99/i31	News magazine article	-
Etter, K. (2021). California lab offers cautionary notes regarding delta-8 THC. https://www.marijuanatimes.org/california-lab-offers-cautionary-notes-regarding-delta-8-thc/	Article from a marijuana news source	-
Etter, K. (2021). I stand corrected: The truth about delta 8 THC. https://medium.com/seed-stem/i-stand-corrected-the-truth-about-delta-8-thc-e8085725ed9e	News magazine article	-
Feldman, E. M. (2021). Is delta-8 legal in Texas? For now – but confusion, frustration over state's 'clarification' abounds. https://www.statesman.com/story/news/2021/11/10/delta-8-thc-temporarily-legal-texas-judge-injunction-hemp-cbd-delta-9/6185212001/	Texas news source	-
Food and Drug Administration (FDA). (2022). 5 things to know about delta-8 tetrahydrocannabinol. https://www.fda.gov/consumers/consumer-updates/5-things-know-about-delta-8-tetrahydrocannabinol-delta-8-thc	FDA fact sheet	-
Foundation of Cannabis Unified Standards (FOCUS). (2021). Smoke and mirrors: delta-8 is not legal. https://www.focusstandards.org/smoke-and-mirrors-delta-8-is-not-legal/	Article from a marijuana news source	-
Grinspoon, P. (2021). Beyond CBD: Here come the other cannabinoids, but where's the evidence? https://www.health.harvard.edu/blog/beyond-cbd-here-come-the-other-cannabinoids-but-wheres-the-evidence-2021032322190	Harvard health blog	-
Johnson, L. (2021). CBD oracle lab study shows some delta-8 products are 7700% over the legal delta-9 THC limit. https://cbdoracle.com/news/delta-8-thc-products-market-study-consumer-safety-and-legality/#Executive-summary	CBD news source; experimental	51 hemp delta-8 products

(Continues)

TABLE 2 (Continued)

Title	Study design	n
Johnson, L. (2022). Lab study: over 50% of hemp delta-9 products are mislabeled, and get you higher than cannabis. https://cbdoracle.com/news/hemp-delta-9-thc-products-lab-study-consumer-safety-and-legality/	CBD news source; experimental	53 hemp delta-9 THC products
Juneau Empire. (n.d.). Where to buy Delta 8 THC online, top 10 delta 8 retailers reviewed. https://www.juneauempire.com/national-marketplace/best-place-to-buy-delta-8-online-top-delta-8-brands-to-order-delta-8-thc-buy-weed-online-in-2021-legally/	Alaska news source	–
Kight, R. (2020). Delta 8 THC: legal or not? https://cannabusiness.law/delta-8-thc-legal-or-not/	Legal overview from cannabis news source	–
Kight, R. (2021). Is delta-8 THC 'synthetic'? Does it matter? https://journal.cannabislaw.report/rod-kight-is-delta-8-thc-synthetic-does-it-matter/	Legal overview from cannabis news source	–
King, S. (2021). How some THC is legal—for now: delta-8-THC—a less-potent cousin of famed delta-9-THC—is legal enough to sell in most states. But how does it work? And will the DEA shut it down? https://www.rollingstone.com/culture/culture-features/delta-8-thc-legal-weed-explained-1113859/	News magazine article	–
Leafly (2021). Comparing THC compounds: what we know about THC-O versus delta-9 & delta-8. https://www.leafly.com/news/strains-products/comparing-thc-compounds-what-we-know-about-thc-o-versus-delta-9-delta-8	News magazine article	–
Leafly (2021). What is delta-8? https://www.leafly.com/news/science-tech/what-is-delta8-thc	News magazine article	–
Longman, M. (2021). I took a delta 8 gummy before going on a run. Things got weird—really weird. https://www.yahoo.com/now/took-delta-8-gummy-going-120035757.html	News magazine article; case report (human)	1
Michigan Poison Center. (2021). Fact sheet: emerging public health concern: delta-8 THC	Michigan fact sheet	–
Moonwlkr. (n.d.). https://moonwlkr.com/	Informational page from a delta-8 THC retailer	–
National Cancer Institute (NCI). (2021). Delta-8-tetrahydrocannabinol. https://www.cancer.gov/publications/dictionaries/cancer-drug/def/delta-8-tetrahydrocannabinol	NCI definition	–
National Industrial Hemp Council (NIHC). (n.d.). NIHC makes policy statement on delta 8 THC: The safety profile of delta 8 THC products is questionable. https://www.nihcoa.com/media-centre/nihc-makes-policy-statement-on-delta-8-thc/	Hemp news source	–
Reece, J. (2021). Mother works to draw awareness about 'pot poisoning' in children. https://www.nbc12.com/2021/06/30/mother-works-draw-awareness-about-pot-poisoning-children/	News source; case report (human)	1
Reynolds, K. (2021). Texas said delta-8 is illegal. But state troopers haven't made a single arrest. https://www.texastribune.org/2021/11/11/texas-delta-8-dps-arrests/	Texas news source	–
Roush, J., Hudalla C. (2021). The unregulated distribution and sale of consumer products marketed as delta-8 THC. U.S. https://irp.cdn-website.com/6531d7ca/files/uploaded/USCC%20Delta-8%20Kit.pdf	US Cannabis Council executive summary	–
Sreenivas, S. (2021). What is delta 8? https://www.webmd.com/mental-health/addiction/what-is-delta-8	Web MD definition	–
Swider, J. (2021). Waving the caution flag on the race for delta-8 THC. https://www.youtube.com/watch?v=zfZG1u_t4r4	Podcast/interview	–
United States (U.S.) Congress. (2019). H.R.2—agriculture improvement act of 2018: the farm bill. https://www.congress.gov/bill/115th-congress/house-bill/2	US Congress Law	–

(Continues)

TABLE 2 (Continued)

Title	Study design	n
Vaughn, J. (2021). Move aside, delta-8, Texas smoke shops are filling up with legal Delta-9 THC products. https://www.dallasobserver.com/news/move-aside-delta-8-legal-delta-9-thc-products-are-hitting-shelves-in-texas-smokeshops-12731186	Texas news source	-

Abbreviations: CBD, cannabidiol; FDA, Food and Drug Administration; NCI, National Cancer Institute; THC, tetrahydrocannabinol.

Delta-8 THC use

Popularity

To understand the potential impact that delta-8 THC may have upon public health, it is important to understand factors related to its use. There have been no nationally representative prevalence studies on delta-8 THC use. Preliminary studies have relied upon convenience sampling or trends in internet searches and thus are limited in scope [3, 22, 36]. One peer-reviewed study among a convenience sample of past-month cannabis users indicated that 17% had used delta-8 THC in the past month [37]. A study using Google trends data indicated that, in the United States, the rate of delta-8 THC searches increased by 467% from 2019 to 2020 and 850% from January to August 2021 [3]. During this time, there were 22.3 million searches for delta-8 THC [3]. Another peer-reviewed study showed that delta-8 THC Google queries increased nearly sevenfold from August 2020 to May 2021 [36]. Further, the internet search volume for delta-8 THC was higher in states without adult non-medical use of delta-9 THC legalized [3, 36]. Thus, people in those states may be looking to delta-8 as a legal THC product. Two peer-reviewed manuscripts using Twitter and Reddit data also revealed an increase in delta-8 THC-related posts in 2020 and 2021 [38; Walker et al., under review]. Although limited research indicates that delta-8 THC popularity is rising, future studies utilizing nationally representative data sets are needed to estimate population-level prevalence of use.

Reasons for use

To more clearly understand why delta-8 THC popularity seems to be rising, a few peer-reviewed studies have collected data from convenience samples to examine motives for using delta-8 THC [22, 23, 37, 39]. Reasons for using delta-8 THC were similar to those for using delta-9 THC and included to reduce anxiety/stress, to self-treat medical conditions, as a substitute for other drugs and because it was presumed to be legal [22, 23, 37, 39, 40]. Some individuals reported using delta-8 THC in place of other drugs for reasons that included fewer and less severe adverse side effects, less perceived addictiveness and withdrawal potential, greater perceived effectiveness and safety, greater retail availability and lower prices [22, 23]. Some drugs for which individuals purportedly substituted delta-8 THC included opioids, sleep aids, delta-9 THC, synthetic cannabinoids (e.g. Spice, K2), muscle relaxers and alcohol [22, 23, 39]. Although

prevalence data do not exist, research has found that most delta-8 THC users previously used delta-9 THC [23]. However, findings from these studies are limited by the use of convenience samples; specifically, these samples mainly included individuals in states without adult non-medical delta-9 THC use legalized [22, 23] or were composed of only cannabis users [37, 39]. Future research should examine factors related to delta-8 THC use using nationally representative samples.

Psychoactivity and potency

The literature demonstrates that use of delta-8 THC can have psychoactive effects, although these effects may be markedly different depending upon the manufacturer or batch [21, 42]. Delta-8 THC has been anecdotally described as being less psychoactive (i.e. having a 'milder high') than delta-9 THC with fewer negative acute side effects, including anxiety and drowsiness [2, 7, 12, 18, 21–23, 26, 27, 33, 35, 37, 39, 42–45]. As a result, delta-8 THC is colloquially referred to as 'THC lite', 'diet weed' or 'work weed' [2, 3, 12]. Although these 'less potent psychoactive effects' are a widely 'known' characteristic of delta-8 THC and often one of the main purported advantages, this has yet to be rigorously assessed. Moreover, dosage is a key factor related to the strength of psychoactive effects, and research has yet to examine the dose of delta-8 THC products people consume during a single-use event.

Research indicates both delta-9 and delta-8 THC bind to the cannabinoid G-protein-coupled receptor CB1; however, delta-8 THC has a lower binding affinity [6, 46]. As such, delta-8 THC may be a less potent psychoactive substance [6, 7, 46–48]. Limited findings from experimental studies conducted several decades ago among small samples of humans suggest that delta-8 THC has a lower psychoactive potency than delta-9 as measured by subjective responses [48–50]. However, the delta-8 THC used in this study probably differs from many of the retail products available in the market today, given that it was laboratory-grade pure delta-8 THC.

Importantly, the potency of delta-8 THC varies drastically; people may underestimate the effects and have widely varying expectations and experiences [21, 41]. One study in 2020 tested 1500 delta-8 THC concentrates from across the United States; only six had delta-9 THC levels compliant with the Farm Bill [51]. Similarly, another study [21] tested 51 delta-8 THC products; 76% had delta-9 THC levels above the legal limit of 0.3%, with some products having up to 23% delta-9 THC. Many products also had inaccurately labeled delta-8 THC levels (up to 40% different than the labeled value) [21]. Furthermore, there

may be marked differences between batches, given that there are no regulations in how often batches should be tested for potency and the possibility that batches between businesses become integrated during packaging and distribution. Thus, although often marketed as a less potent form of THC, use of delta-8 THC products may yield unpredictable psychoactive effects.

Potential benefits

There may be potential benefits to using delta-8 THC; however, there is limited related information. Peer-reviewed studies examining the potential benefits of delta-8 THC use have been almost exclusively studied in laboratory settings using animal or cell models [52–63]. Results suggest that delta-8 THC use may be associated with decreased chemotherapy side effects, analgesic effects, decreased seizure activity, lower intra-ocular eye pressure, decreased cancer cell proliferation, decreased depressive symptoms and decreased nicotine use and withdrawal [53, 54, 56–64]. However, only one study used human subjects to assess potential benefits (i.e. reduced vomiting among children undergoing cancer treatment); this study only had a sample size of $n = 8$ and did not have a control group [64].

Potential consequences

Given the rapid rise in popularity, it is important to understand potential consequences that may arise related to use of delta-8 THC. However, there is limited peer-reviewed research on the potential harms of using delta-8 THC in humans. Previous research using animal or cell experimental models with limited samples indicated that delta-8 THC use was associated with vasoconstriction, adverse effects on sperm, hepatic injury and inflammation and stunted growth [52, 65–67]. Additionally, one study conducting secondary analyses of data sets gathered by the Centers for Disease Control and Prevention (CDC) and the Substance Abuse and Mental Health Services Administration (SAMHSA) suggested that delta-8 THC use may be associated with an increased risk of cancer [78].

Mentions of delta-8 THC are prevalent on Reddit, with research indicating many posts related to brands perceived as unsafe or 'fake', types of products, legal status, safety and experiences [38]. Most information regarding negative consequences of delta-8 THC use in humans comes from case reports and news articles [69–72]; however, the FDA and CDC have formally advised consumers to be cautious [4, 33, 73]. From 1 January 2021 to 28 February 2022 there were 2362 calls to poison control relating to delta-8 THC, with 41% of these cases occurring among minors [4, 33]. Importantly, 40% of all cases were due to unintentional exposures to delta-8 THC, and 82% of these unintentional exposures occurred among minors [4]. Moreover, 70% of calls required a health-care evaluation, with 45% of those being minors [4]. Overall, 8% required critical care, and one pediatric case resulted in a fatality [4]. Most hospitalizations due to

delta-8 THC use occur from using edibles, most often in gummy form [4, 18, 69, 71–76]. Cases that resulted in hospitalization often involved one or more of the following symptoms: abdominal pain, extreme paranoia, depression, suicidal ideation, nausea, deep sedation, slowed breathing, decreased blood pressure, chest pain and rapid changes in heart rate [74, 75, 77]. Moreover, these negative consequences were observed disproportionately more in states where adult non-medical cannabis retail and use is not legal [33].

Research indicates that the intoxicating effects from using delta-8 THC are similar to those from delta-9 THC use and include lethargy, impaired coordination, slurred speech, low blood pressure and rapid changes in heart rate, and in rare instances may lead to difficulty breathing, sedation and coma [17, 33]. This is concerning when considering findings presented by one study [1] which demonstrated that, in cases of driving while under the influence of drugs, the proportion of delta-8 THC in e-cigarette and blood samples has been rising.

Consequences from delta-8 THC use may disproportionately impact certain populations. One study showed that delta-8 THC retailers in Fort Worth, Texas, tended to be disproportionately located in areas with more socio-economic deprivation compared to locations that did not sell delta-8 THC [34]. Moreover, employees of these retail stores tended to share less information about delta-8 THC when they were located in areas with more socio-economic deprivation [16]. Thus, disadvantaged subgroups of the population may be disproportionately burdened by the potential consequences arising from delta-8 THC use.

E-cigarette or vaping use-associated lung injury (EVALI)

One type of consequence is related to the way in which delta-8 THC is typically used; namely, through vaping devices [22, 78]. Given the lack of regulations, research indicates byproducts and contaminants in delta-8 THC products may result in similar consequences to those observed from the EVALI outbreak [79, 80]. There were more than 2000 cases of EVALI from 2019 to 2020 in the United States, with health outcomes including respiratory distress, acute lung injury and death [81–83]. Interestingly, several research studies examining EVALI cases from 2019 to 2020 revealed that delta-8 THC was present in some of these vaping devices, often at levels above what would be naturally expected [84–87]. Preliminary research indicates that vaping cannabis products with acetates (which can be residual from synthesizing delta-8 THC) may result in harmful ketone formation (a highly reactive poisonous gas), similar to how vaping products with vitamin E formed ketones that caused EVALI [88].

Synthesis

Many of the potential consequences related to delta-8 THC use are related to the manufacturing process. Because the amount of delta-8 THC naturally occurring in the *Cannabis* plant is so small it would hold

almost no economic value to extract, due to the high associated costs [1, 5–7]. As such, all the delta-8 THC currently available in the market-place is synthetically created, most often from CBD [4, 10, 17, 84]. CBD can be easily converted into delta-8 THC using household chemicals, and this process has been colloquially referred to as ‘kitchen chemistry’ [17, 21, 27, 89, 90]. Many of those who create delta-8 THC have neither a background in chemistry nor any formal training, and have limited knowledge about the process [5, 18, 21]. Delta-8 THC synthesis is not regulated including the ingredients used, contents, purity, sanitation, quality or safety [2, 22, 93].

Chemical byproducts

Although the conversion process of delta-8 THC from CBD is relatively easy, the process often creates various unpredictable and harmful chemical byproducts [10, 27, 33, 47, 73, 79, 87, 92]. Several laboratory studies examining the chemical composition of delta-8 THC products have indicated the presence of harmful residual solvents and other contaminants such as olivetol, sulfuric acid, hydrochloric acid, other toxic solvents, pesticide and heavy metals [18, 21, 73, 92–94].

Chemically determining if THC is delta-8 or delta-9 is difficult, costly and time-consuming [2, 5, 17, 27, 45, 47, 95–103]. Although in the preliminary stages of research, chromatography methods have been developed to distinguish between different manufacturing methods [89]. These methods may be important to determine common production manufacturers and batches in the case of potential outbreaks with particularly hazardous products [89], given the presence of delta-8 THC among law enforcement drug seizures and urine drug testing [101–103].

Purification and laboratory testing

Despite the numerous contaminants identified, delta-8 THC manufacturers are not federally required to have a purification process in place or conduct quality control [21, 35, 93]. Moreover, there are no standards for product testing such as when or how many times a product should be tested. One study [21] found that, of 51 delta-8 THC manufacturers examined, 84% had some form of laboratory results available; however, two-thirds of these (67%) only tested for THC potency and not for impurities. Furthermore, some testing facilities are not certified by the International Organization for Standardization (ISO), meaning that they can use any technique [5, 104]. Some blogs and industry reports suggest that ‘lab shopping’ (i.e. testing products at multiple locations and selecting the ‘cleanest/safest’ reports) and falsifying laboratory reports are common [5, 21, 41, 76, 104]. One study examined the laboratory reports of 20 delta-8 THC retailers and found that two reports (10%) were falsified, one of which originally reported the presence of heavy metals [21].

Retail availability

Delta-8 THC is widely available and easily accessible, as retail is not limited to regulated dispensaries [33]. Because of the lack of regulation, delta-8 THC products can be sold in smoke shops, on-line or in gas stations [21, 27, 106]. The type of retail location may be associated with the strength, quality or consistency of products [21]. A qualitative study of delta-8 THC users suggests that they often purchase it from smoke shops where they are familiar with the staff and they find the products to be trustworthy; products sold in gas stations are perceived by some as untrustworthy and unsafe [Henry et al., 2022, personal communication]. These perceptions may reflect first-hand experiences with products that have resulted in undesirable effects. A study that examined the on-line retail environment of delta-8 THC [21] documented more than 160 on-line delta-8 THC retailers, with more than 4200 unique products for sale. Because there is no governing body holding delta-8 THC retailers accountable for adhering to state laws, most on-line retailers ignore state bans and continue to ship products throughout the United States, including states where it is considered illegal [3, 105].

Price

Delta-8 THC products tend to be less expensive compared to delta-9 THC products, even in states where non-medical delta-9 THC is legally sold to adults [20, 21, 26]. Importantly, low cannabis prices tend to be associated with an earlier age of initiation, as well as higher quantity and greater frequency [106–108]. Although it is difficult to directly compare the prices because of the large variability in potency, simply comparing the mg/dollar ratios shows that delta-8 THC products tend to be less expensive than delta-9 THC [105, 109–112].

On-line sale of delta-8 THC frequently has low shipping costs [105] or free shipping [111], bundles and subscription services [105], money-back guarantees, pop-ups offering free products and giveaways [105, 113, 114]. Low pricing is often used as a marketing tool and increases demand, particularly among those with a limited income including young people, which may be cause for concern [115–117].

Marketing, packaging and labeling

Product packaging is an important element of marketing because it may affect the perceived safety of a product, as well as who is most attracted to using a product (e.g. youth) [79, 118]. However, there are no federal regulations on the marketing of delta-8 THC products, and the packaging of delta-8 THC products may have misleading or false claims [2, 18]. For example, claims such as being ‘100% natural’, ‘pure Delta-8’ or ‘THC-free’ are false, given that all the delta-8 THC in the market-place is derived from CBD and therefore cannot feasibly be naturally grown or pure delta-8 THC, due to the compounds required to synthesize it [4, 5, 16, 17, 33, 90, 91, 104, 113]. Potentially misleading labels that include those stating ‘CBD’ or ‘hemp-derived’ may

lead individuals to believe the product is non-psychoactive [16, 17, 33, 90, 91, 104, 113, 119]. Moreover, stating that delta-8 THC products are 'FDA-approved' or made with 'organic ingredients' may make the products sound safer and healthier, despite there being no FDA approval on any delta-8 THC products and the inability for it to be organic due to synthesis [4, 16, 18, 33, 91, 104, 113, 119].

Although clearly marked packaging mentioning psychoactive effects is required for delta-9 THC products sold in licensed locations, it is not required for delta-8 THC [4, 5, 33, 91, 104]. This could be a major reason for the large number of accidental exposure cases, resulting in calls to US poison control centers [4]. Further, many delta-8 THC products do not have warning labels [21]. As a result, some individuals may perceive use of delta-8 THC products to be safe [21].

On-line delta-8 THC retailers employ marketing strategies, including the use of keywords (e.g. popular, limited supply, selling fast) and product reviews to target individuals' normative perceptions and increase web traffic [105, 120]. One important keyword that may be used is mentioning that their delta-8 THC products are 'shipped discreetly', which we believe may target young people and those living in states where sale of cannabis products is illegal [105, 115].

Age restrictions and youth-oriented marketing

Despite numerous consequences among minors [4], there are no federal restrictions on the minimum purchase age for delta-8 THC products as of August 2022 [4, 10, 21, 27]. Delta-8 THC products are readily available to young people on-line because many on-line retailers do not implement age verification techniques [21]. One study [21] demonstrated that among 51 on-line retailers examined, only six required some form of age verification for on-line purchases. Also of concern, child-resistant packaging is not required for delta-8 THC products, despite the increasingly common use of this packaging for delta-9 THC products [2, 18]. Having more secure packaging may be associated with fewer accidental exposures among children, given that many of the packages look like food and beverage products that children are used to consuming [18, 33, 69, 73, 75, 121–123]. Youth-oriented delta-8 THC product marketing includes the use of brightly colored packages, copyright-infringing cartoon characters (e.g. Cheetos, Scooby Doo) and sweet/fruity flavors including well-known candy brands (e.g. Nerds, Oreos, Sour Patch Kids, Skittles) [3, 21, 32, 105].

DISCUSSION

This scoping review summarizes the literature relating to delta-8 THC. Most research on delta-8 THC is largely anecdotal, not peer-reviewed, and does not involve human subjects [3, 11, 17, 36]. Although delta-8 THC is federally legal [14], the DEA's recent ruling seems to be contradictory to the Farm Bill [8, 9], leading to legal ambiguity of delta-8 THC legality. Regardless, delta-8 THC products are widely available on-line and, in most states, in retail stores for

inexpensive prices [21, 105, 115]. However, the synthesis, marketing and sale (e.g. minimum purchase age) of delta-8 THC products are not federally regulated and minimal state regulations exist [17]. Use of delta-8 THC and related negative consequences appear to be increasing, particularly among adolescents and young adults [1–3]. Future human subjects research is needed to more clearly understand potential benefits and consequences of delta-8 THC use. There is no systematic surveillance of delta-8 THC use, so prevalence of use is largely unknown. Moreover, prevalence of use may change rapidly as new brands and products emerge and as related state and federal laws change.

Laws need to be enhanced to reduce access and use by children. Previous research indicates that laws regulating the synthesis, retail and use of delta-9 THC help to reduce access to those aged under 21, as products are sold only in licensed and regulated dispensaries that use consistent age verification procedures [124–126]. The CDC and FDA recommend implementing age restrictions, requiring child-safe packaging, reducing youth-oriented marketing, consistent contaminant and safety testing, product labeling requirements, reporting the total THC content on cannabis products and mentioning the potential for psychoactivity [4, 33]. Future research should be conducted to examine the comparative psychoactive effects and potency between delta-8 and delta-9 THC.

Because of the similarities between delta-8 THC and delta-9 THC use [73, 103], existing delta-9 THC laws could be applied to delta-8 THC. However, additional safety standards may be needed to mitigate harms related to the synthetic derivation of THC products. It is important to note that banning only one type of THC (e.g. delta-8) may result in other psychoactive products becoming more popular [e.g. delta-10 THC, hexahydrocannabinol (HHC), THC-O-acetate], which are generally less studied than delta-8 THC [21, 92, 105]. Thus, it is important to consider all the different types of psychoactive substances in the *Cannabis* plant when developing future laws. One limitation of the present review is the exclusive focus upon delta-8-THC and no other hemp-derived cannabinoids. Although most of the published literature focuses upon delta-8 THC, future work should synthesize information related to the other THC variants. Furthermore, future research should focus upon increased surveillance of delta-8 THC and other synthetic cannabis products as well as related factors, using nationally representative samples. Global research on delta-8 THC is also important, as these US laws may influence the marketplace globally.

AUTHOR CONTRIBUTIONS

Cassidy R. LoParco: Conceptualization; methodology; investigation; writing—original draft. **Matthew E. Rossheim:** Conceptualization; supervision; writing—review and editing. **Scott T. Walters:** Supervision; writing—review and editing. **Zhengyang Zhou:** Supervision; writing—review and editing. **Sofia Olsson:** Methodology. **Steven Y. Sussman:** Writing—review and editing.

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DECLARATION OF INTERESTS

None.

DATA AVAILABILITY STATEMENT

Articles included in this review were compiled from publicly accessible databases and websites. Data sharing is not applicable to this article, as no new data were created or analysed in this study.

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